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Longitudinal associations between mother-child attachment security in toddlerhood and white matter microstructure in late childhood: A preliminary investigation.

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Abstract

Early childhood experiences are considered to influence the strength and effectiveness of neural connections and thus the development of brain connectivity. As one of the most pervasive and potent early relational experiences, parent-child attachment is a prime candidate to account for experience-driven differences in brain development. Yet, knowledge of the effects of parent-child attachment on brain structure in typically developing children is scarce and largely limited to grey matter, whereas caregiving influences on white matter (i.e., neural connections) have seldom been explored. This study examined whether normative variation in mother-child attachment security predicts white matter microstructure in late childhood and explored associations with cognitive inhibition. Mother-child attachment security was assessed using home observations when children (N=32, 20 girls) were 15 and 26 months old. White matter microstructure was assessed using diffusion magnetic resonance imaging when children were 10 years old. Child cognitive inhibition was tested when children were 11 years old. Results revealed a negative association between mother-toddler attachment security and child white matter microstructure organization, which in turn related to better child cognitive inhibition. While preliminary given the sample size, these findings add to the growing literature that suggests that rich and positive experiences are likely to decelerate brain development.

Keywords

Diffusion tensor imaging, structural connectivity, white matter, parent-child relationships, early childhood environment, brain development.

Longitudinal associations between mother-child attachment security in toddlerhood and white matter microstructure in late childhood: A preliminary investigation.

Brain development results from a complex orchestration of genetic endowment and environmental factors. Among the latter, early childhood relational experiences are thought to have a critical impact on brain development well beyond the first years of life (Belsky & de Haan, 2011; Cicchetti, 2016). As one of the most pervasive and potent relational experiences of early childhood, parent-child relationships are prime candidates to account for experience-driven differences in children's brain development. In line with this, empirical studies suggest that positive early caregiving experiences (e.g., exposure to warm and responsive parenting behavior, secure parent-child attachment) may influence child brain development. Specifically, normative variation in different indicators of the quality of early caregiving relationships predicts differences in child grey matter volume (Bernier et al., 2019; Kok et al., 2015; Leblanc et al., 2017; Lee et al., 2019; Luby et al., 2012, 2016; Rifkin-Graboi et al., 2015; Sethna et al., 2017, 2019), thickness (Kok et al., 2015; Leblanc et al., 2022), activity (Bernier et al., 2016; Biro et al., 2021; Hane et al., 2010), and functional connectivity (Dégeilh et al., 2018a; Hanford et al., 2018; Perone & Gartstein, 2019; Rifkin-Graboi et al., 2015; Thijssen et al., 2017; Q. Wang et al., 2019), as well as grey matter development in childhood and adolescence (Luby et al., 2016; Whittle et al., 2014). In spite of these increasingly documented links between normative variation in caregiving indices and child grey matter structure and functioning, including with the same cohort as in the current study (Bernier et al., 2019; Dégeilh et al., 2018b; Leblanc et al., 2017, 2022), the associations between caregiving and child white matter have seldom been investigated, particularly in the general population.

White matter corresponds to neuronal fibers, which in many cases are organized in tracts that serve as ‘superhighways’ connecting different brain regions for the rapid transfer and processing of information. Four studies reported associations between caregiving and total brain white matter volume (Kok et al., 2015, 2017) and limbic white matter microstructure (Cortes Hidalgo et al., 2019; Lee et al., 2019). In addition, normative variation in early caregiving experience may influence the pace of white matter microstructure development (Lee et al., 2019).

White matter microstructure, which reflects more subtle changes in the developing brain than gross white matter volumes (Tamnes et al., 2018), is typically assessed using diffusion magnetic resonance imaging (MRI). Diffusion tensor imaging (DTI) allows for extracting quantitative diffusion parameters from diffusion MRI that reflect the microstructural organization of white matter fibers: fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD). Age-related increases in FA and decreases in MD and RD generally reflect white matter microstructure development through late childhood and adolescence (Krogsrud et al., 2016; Lebel & Deoni, 2018; Tamnes et al., 2018). Findings for AD are mixed, with some studies reporting no age-related change, others reporting age-related decreases and still others reporting increases (Lebel et al., 2017).

Parent-child attachment security is a widely documented and well recognized indicator of the quality of early parent-child caregiving relationships (Cassidy & Shaver, 2016). Decades of empirical research and several meta-analyses have shown that greater parent-child attachment security in infancy and early childhood is a reliable predictor of a range of child outcomes, including better social competence, emotion understanding, emotion regulation, and quality of peer relationships, as well as fewer behavior and attention problems in children (Cooke et al.,

2019; Deneault et al., 2021; Fearon et al., 2010; Groh et al., 2014; Madigan et al., 2016; Pallini et al., 2014, 2018, 2019). Such convincing links between parent-child attachment and multiple child outcomes are often believed to be attributable to the intermediate effects of early attachment on the neural structures that support child functioning (Belsky & de Haan, 2011; Tottenham, 2014).

Neural circuits are particularly sensitive to environmental influences during peak periods of development characterized by significant changes in their organization (Tottenham, 2014). Very rapid changes in diffusion parameters occur during early childhood, making it a particularly sensitive period for environmental influences on white matter microstructure development (Lebel & Deoni, 2018). Thus, white matter microstructure organization is likely to be influenced by the quality of young children's attachment relationships with their primary caregivers; however, this has not yet been fully investigated.

Among the studies examining the associations between caregiving and brain development, only a handful of studies have directly addressed prediction from early parent-child attachment, and they have almost exclusively focused on grey matter. Two studies suggested that more insecure mother-child attachment in early childhood predicted larger grey matter volume in the amygdalae in adulthood (Lyons-Ruth et al., 2016; Moutsiana et al., 2015). Three other studies conducted with children revealed that more secure or organized mother-toddler attachment was predictive of larger grey matter volume in frontal and temporal regions (Leblanc et al., 2017), but thinner cortices in bilateral middle and superior frontal gyri (Leblanc et al., 2022) as well as lower limbic grey matter volumes (Cortes Hidalgo et al., 2019) in late childhood. Cortes Hidalgo et al. (2019) also reported the only association to date between attachment and white matter: they found that organized attachment was predictive of lower white matter microstructure

organization in the uncinate fasciculus. However, they restricted their analyses to a global white matter microstructure metric (averaging the white matter of all brain regions in a single score) and to three white matter tracts related to the limbic system. Yet, associations between parent-child attachment and child white matter microstructure in the rest of the brain appear equally plausible.

Current Study

The current longitudinal study aimed to investigate whether normative variation in mother-child attachment security in toddlerhood predicts white matter microstructure in late childhood. Taking into account Cortes Hidalgo et al.'s (2019) large-scale study, we aimed to offer complementary insight into the influence of attachment on the developing brain in several ways. First, owing to the extremely young state of the literature on attachment and white matter, we adopted a whole-brain voxel-wise approach, rather than an a priori regions-of-interest approach that may exclude potentially valuable information from brain regions that are not selected. The use of a whole-brain approach is also conservative, as it involves the implementation of strict statistical corrections to guard against Type-I error. Second, in addition to the commonly used DTI metrics of FA and MD, we also investigated AD and RD, which provide more direct measures of the microstructural dimensions (Alexander et al., 2011). The pattern of change across these four DTI metrics allows interpretation of potential underlying biological processes (Tromp, 2016). Third, we used a small sample that was very well characterized in terms of early mother-child attachment security, with two time points of observation performed in the naturalistic home context to maximize ecological validity. These observations were rated with the Attachment Behavior Q-Sort (AQS; Waters & Deane, 1985), which yields a continuous score for attachment security rather than assignment to a particular attachment category as with the

Strange Situation Procedure (SSP; Ainsworth et al., 1978). A continuous approach is coherent with the underlying structure of individual differences in attachment (Fraleay & Spieker, 2003) and maximizes statistical power by affording excellent detection of fine individual differences, which may be especially advantageous in the context of small sample sizes (Groh et al., 2019). Finally, given the small sample size and the dearth of previous studies addressing associations between attachment and white matter microstructure, it was deemed critical to avoid chance findings. Thus, in addition to the whole-brain approach that is inherently conservative due to the associated statistical corrections, we probed the functional significance of any relations observed between mother-child attachment and white matter microstructure *a posteriori*. Given that previous studies report an association between white matter microstructure organization and cognitive inhibition in children and adolescents (Noble et al., 2013; Treit et al., 2014), and that early attachment security is a demonstrated antecedent of effortful control (Pallini et al., 2018) and executive functioning (Bernier et al., 2015) – both of which have strong inhibition components –, we focused on child cognitive inhibition in the present sample to conduct empirically-driven correlational analyses between white matter and child behavior.

Based on previous studies of the associations between caregiving experiences (attachment: Cortes Hidalgo et al., 2019; sensitivity: Lee et al., 2019) and child white matter microstructure in typically developing children, we hypothesized that greater attachment security would be associated with lower (i.e., less adult-like) organization of white matter microstructure, as reflected by lower FA. Given the inconsistency of findings concerning MD and the lack of relevant investigation of RD and AD, no a priori hypothesis was formulated for these diffusion metrics. Given the scarcity of literature on attachment security and white matter microstructure

in typically developing children, no a priori hypotheses were formulated with regards to location of putative associations.

Method

Participants

Participants in this study ($N=32$) were followed annually as part of a larger longitudinal project investigating early relational predictors of several facets of child development (Bernier et al., 2020). Here, we report on attachment security assessed when children were 15 ($M=15.68$, $SD=0.96$, range=14.50–18.0 months) and 26 months of age ($M=26.40$, $SD=0.76$, range=25.0–27.57 months), child brain white matter microstructure measured at 10 years ($M=10.61$, $SD=0.46$, range=10.0–11.67 years), and child cognitive inhibition tested at 11 years ($M=10.98$, $SD=0.35$, range=10.33–11.69 years), namely at the timepoint in the larger study's protocol that was closest to the MRI exam (which constituted an additional timepoint inserted in between two regular follow-up visits). The study was approved by the local human research ethics committee and all families provided written informed consent for participation.

Families were initially recruited from birth lists randomly generated by the Ministry of Health and Social Services. Inclusion criteria were full-term pregnancy (i.e., at least 37 weeks of gestation) and the absence of any known disability or severe delay in the infant. When children were 10 years of age, they were invited to undergo an MRI exam including a diffusion MRI sequence. Inclusion criteria for the MRI study were the absence of neurological or psychiatric disorders, traumatic brain injury, psychoactive medication, and standard MRI contraindications. Of the 64 families approached for the current study, 39 (60.94%) agreed to participate. However, four (6.25%) children were not eligible due to standard MRI contraindications (e.g., braces); thus, 35 children underwent MRI acquisition (54.69%). These 35 families did not differ from

those who declined (N=25) or were not eligible (N=4) in terms of family income, parental age, education, ethnicity, language spoken at home, child sex, or mother-child attachment at either assessment time point (sociodemographic information is shown in Table 1, all $ps \geq .23$).

INSERT TABLE 1 ABOUT HERE

Of the 35 children who took part in the MRI exam, one was excluded from analyses due to significant motion and one because of suspected neuropathology. In addition, due to technical issues, diffusion MRI data of one participant were missing. Therefore, data from 32 children (20 girls and 12 boys) and their mothers were used in the current analyses. There were no sociodemographic differences between families included in the analyses (N=32) and those who declined or were not eligible (N=29), all $ps \geq .17$.

Data Collection

Mother-Child Attachment Security

Attachment security was assessed at 15 and 26 months during home visits using the AQS (Waters & Deane, 1985), considered to be of the few “gold-standard assessments” in attachment research (Van IJzendoorn et al., 2004). The 70- to 90-minute home visits (described in more detail in (Bernier et al., 2015)) were modeled after the work of Pederson and Moran (1995). The procedure aimed at reproducing the multitasking challenge that is characteristic of parenting a toddler and was thus purposely designed to create a situation during which maternal attention was solicited by both child demands and research-related tasks (e.g., mothers had to fill in questionnaires while their toddler was not supervised by the research assistant). Restricting maternal availability to child demands is a classic trigger of the attachment system in early childhood and is thus often used in conjunction with the AQS to maximize the ecological validity of observations (e.g., Tarabulsky et al., 2005). Extensively trained research assistants (see

(Bernier et al., 2015)) observed mother–child interactions throughout these two visits and subsequently rated the AQS.

The AQS consists of 90 items measuring the quality of the child’s attachment behaviors toward a specific figure (the mother in this case). Each item of the AQS describes a potential child behavior. Based on observations performed throughout the home visits, research assistants sorted those behaviors into nine clusters of 10 cards each, ranging from “very similar to” to “very unlike” the observed child’s behaviors. The global score for attachment security consists of the correlation between the observer’s sort of the 90 items and a criterion sort for the prototypically secure child (Waters & Deane, 1985). Attachment security scores can thus range from -1.0 (highly insecure) to 1.0 (highly secure). Prototypical security represents a fluid balance between exploration of the environment and appropriate reliance on the caregiver for support when needed. 25% of the home visits were conducted by two research assistants, who then completed the AQS independently; intraclass correlation (ICC) between the two raters’ sorts was=.71 at 15 months and .72 at 26 months, indicating adequate inter-rater reliability. The reliability and construct validity of the AQS are well demonstrated by meta-analytic data (Cadman et al., 2018; Van Ijzendoorn et al., 2004).

The AQS score was missing for one child at 15 months and two children at 26 months. In line with recommendations for best practices for handling missing data, multiple imputation was employed to estimate these three missing values (Enders, 2010) using the Markov Chain Monte Carlo procedure (Geyer, 1992) in SPSS software version 24.0 (IBM Corp., Armonk, NY). Because standard neuroimaging analysis software programs cannot handle imputed datasets, the resulting imputed attachment scores were averaged across the 10 imputed datasets and then used in the main analyses described below. The imputations were performed based on the original 64

families using child sex and age at each visit, parental age and education at the time of recruitment, as well as the other attachment score (15- or 26-month) as predictors.

In line with meta-analytic data showing that the AQS has moderate temporal stability (meta-analytic $r=.28$; Van Ijzendoorn et al., 2004), the correlation between mother-child attachment at 15 and 26 months was $r=.33$. Thus, in order to reduce situational and measurement error, scores at 15 and 26 months were averaged ($M=0.51$; $SD=0.18$; range= $0.07-0.77$), and this aggregate score was used in all subsequent analyses as a predictor of white matter microstructure.

Diffusion MRI Acquisition

When children were aged 10 years, neuroimaging data were collected using a 32-channel head coil on a Siemens 3Tesla scanner (MAGNETOM Trio, Siemens, Erlangen, Germany) during a 35-minute MRI exam that included structural, resting-state, and diffusion sequences. The diffusion MRI data were acquired using an echo-planar imaging sequence with a resolution of 2 mm isotropic (repetition time (TR)=9,100ms; echo time (TE)=94ms; flip angle=90°; 66 slices; slice thickness=2mm; gap=2mm; matrix=120x120; field of view (FoV)=240mm; in-plane resolution: 2x2mm; duration: 311seconds). In total, 2 volumes without diffusion weighting (b-value=0s/mm²) and 30 volumes with diffusion weighting (b-value=1000s/mm²) were acquired.

Child Cognitive Inhibition

Child cognitive inhibition was measured when children were 11 years old using the Delis–Kaplan Executive Function System (Delis et al., 2001) Color-Word Interference Task (CWIT). Similar to the Stroop task (Golden, 1978), the CWIT includes a cognitive inhibition trial in which the participant is presented with a page containing the words “red”, “green”, and “blue” printed incongruently in green, blue, or red ink. The participant is asked to name the color in which each word is printed (inhibiting the prepotent response of reading the word) as quickly

as possible without making mistakes. The dependent variable of interest was the Total Inhibition Errors Scaled Score, a score similar to the one used by Noble et al. (2013). Higher scores reflect better cognitive inhibition performance.

Diffusion MRI Preprocessing

After all diffusion images were visually inspected for motion artefacts and image quality, data pre-processing was performed using FDT (Behrens et al., 2003, 2007) and TBSS (Smith et al., 2006), part of FSL (Smith et al., 2004). First, eddy current-induced distortions and head motions were corrected using the Eddy tool (Andersson et al., 2016; Andersson & Sotiropoulos, 2016). A second quality check was performed based on the eddy outlier report to include only the scans with no or minimal motion artifacts in subsequent analyses. Applying quality criteria by Krogsrud et al. (2016), scans of all participants included in the analyses (N=32) were deemed good (no volumes >10 slices of signal dropout detected). Brain extraction was performed using BET (Smith, 2002) to remove non-tissue components, and a diffusion tensor model was fitted at each voxel to the raw diffusion data using DTIFIT. All subjects' FA data were then aligned into a common space using the nonlinear registration tool FNIRT (Andersson et al., 2007), which uses a b-spline representation of the registration warp field (Rueckert et al., 1999). To this end, and as recommended for pediatric samples (<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/TBSS/UserGuide>), every FA image was aligned to every other one to identify the “most representative” image of the current pediatric sample. This “most representative” image was then used as the target image to align the other images. Next, the mean FA image was created and thinned to create a mean FA skeleton which represents the centers of all tracts common to the group. The mean FA skeleton was thresholded at 0.25. Each participant's aligned FA data were then projected onto this skeleton and the resulting data fed into voxel-wise cross-subject statistics. Finally, FA-derived

nonlinear warps and skeleton projection were applied to other diffusion tensors (AD, RD and MD).

Statistical Analyses

Diffusion MRI Statistical Analyses

Voxel-wise statistical analyses of the DTI metrics (FA, AD, RD and MD) were carried out using Randomise (Winkler et al., 2014) with 5,000 permutations. General linear model (GLM) analyses were run with child age, sex and maternal education as covariates to investigate each DTI metric in relation to mother-child attachment security (positive and negative relations were tested using t-contrasts). The threshold-free cluster enhancement (Smith & Nichols, 2009) method was used to identify statistically significant clusters with a threshold level at $p < .05$ (one-tailed) corrected for family-wise error (FWE) and a minimum size of 50 voxels (50 mm³).

Correlations between White Matter Microstructure and Child Cognitive Inhibition

To examine the associations between white matter microstructure and child cognitive inhibition, we performed partial correlations between relevant DTI metrics and the CWIT Total Inhibition Errors Scaled Score. Cognitive inhibition has been associated in prior research with microstructure measures in most of the white matter tracts found here to be associated with mother-child attachment (as described below), namely the corpus callosum, the cingulum, the cerebral peduncle, and the superior longitudinal fasciculus (Noble et al., 2013; Treit et al., 2014). Thus, DTI metrics values were extracted in all significant clusters (previous analysis) localized in these tracts for each participant. When a tract was covered by more than one cluster, DTI metrics values were extracted in the largest cluster only. Then, partial correlations between each tract's DTI metric and cognitive inhibition were conducted, adjusting for child age (at MRI), sex and maternal education.

Results

Predicting White Matter Microstructure from Mother-Child Attachment

Voxel-wise GLM analyses were performed to examine whether mother-child attachment security in toddlerhood predicted each DTI metric (FA, AD, RD, and MD) at 10 years. The results are shown in Table 2 and Figure 1.

INSERT TABLE 2 AND FIGURE 1 ABOUT HERE

After accounting for child age, sex, and maternal education, more secure mother-child attachment was associated with significantly lower FA and higher RD in the bilateral corpus callosum (genu and body), cingulum, corticospinal tract and the left superior longitudinal fasciculus. In addition, more secure mother-child attachment was associated with significantly lower FA in the right superior longitudinal fasciculus, bilateral inferior fronto-occipital fasciculus and right cerebral peduncle. No significant relation was observed between mother-child attachment security and either AD or MD.

Exploratory partial correlations between FA/MD in significant clusters (main analysis) and attachment scores at 15 and 26 months separately suggested that results were comparable when analyzing 15-month and 26-month attachment separately (see Table S1, supplemental material).

Associations between White Matter Microstructure and Child Cognitive Inhibition

Partial correlations (adjusted for child age (at MRI) and sex as well as maternal education) are shown in Table 2. They revealed significant negative associations between FA and child cognitive inhibition in the body of the corpus callosum ($r=-.39, p=.04$), the right cingulum ($r=-.45, p=.02$), and cerebral peduncle ($r=-.46, p=.01$). In addition, significant positive associations between RD and child cognitive inhibition were observed in a large cluster covering

the body of the corpus callosum, the cingulum and the corticospinal tracts ($r=.44, p=.02$), and in the left superior longitudinal fasciculus ($r=.45, p=.02$). Thus, children with lower FA and higher RD in these tracts displayed better cognitive inhibition. Note that these associations remained significant when color denomination speed and reading speed in the CWIT were covaried. Given the number of analyses run, we applied a false discovery rate (FDR) correction using the Benjamini-Hochberg method (Benjamini & Hochberg, 1995). All significant associations survived this correction, except for that between cognitive inhibition and FA in the body of the corpus callosum, which became marginally significant ($p\text{-FDR}=.07$). Of note, there was also a significant and positive correlation between mother-child attachment and child cognitive inhibition ($r=.49, p=.01$).

Discussion

The present 10-year longitudinal study examined whether normative variation in mother-child attachment security in toddlerhood predicts a key feature of the developing brain, namely white matter microstructure, and explored associations with cognitive inhibition. As hypothesized, the results revealed a negative association between mother-child attachment security and child white matter microstructure organization. Specifically, higher security of attachment in toddlerhood predicted lower FA and higher RD in several white matter tracts including the corpus callosum, the cingulum, the corticospinal tract, the superior longitudinal fasciculus, the inferior fronto-occipital fasciculus, and the right cerebral peduncle. Lower FA and higher RD in these tracts were, in turn, associated with better child cognitive inhibition, which itself was related to attachment in a theoretically-expected direction. These findings are consistent with, and extend, those from previous studies of the association between caregiving experiences and white matter microstructure in typically developing children that focused on

limbic regions (Cortes Hidalgo et al., 2019; Lee et al., 2019). Together, these studies converge to suggest that early childhood exposure to positive caregiving experiences (i.e., secure or organized attachment and maternal sensitivity) may lead to decelerated development of children's white matter microstructure.

It is generally assumed that greater organization of white matter microstructure reflects optimal white matter development, given that age-related increases in white matter microstructure organization are often observed (reflected by higher FA and lower MD and/or RD). However, brain development trajectories vary from one child to another as the result of the complex interaction between genes, environment, and experiences. In this respect, recent theory suggests that early life experiences influence the pace of brain development, with positive and rich experiences likely to decelerate brain development and enhance plasticity, thereby maximizing the window of time during which the brain is sensitive to experience and learning (Tooley et al., 2021). The current findings, as well as those of the two previous studies on attachment or maternal sensitivity and white matter microstructure (Cortes Hidalgo et al., 2019; Lee et al., 2019), are consistent with this theory.

In children, an increase in FA along with a decrease in RD likely reflect higher myelination (Krogsrud et al., 2016; Song et al., 2005; Uda et al., 2015). Thus, the lower FA and higher RD observed in children with a history of more secure attachment to their mother may reflect reduced myelination. Developmental processes, including myelination, decrease the brain's ability to change, namely its plasticity, as children get older (Tooley et al., 2021). Thus, slower (more protracted) white matter development in children more securely attached to their parent may offer more time for brain plasticity and thus improved cognitive abilities. Congruent with this hypothesis, recent findings suggest that adolescents showing rapid (accelerated) maturation

of functional connectivity have poorer cognitive outcomes compared to those showing slower (protracted) maturation of functional connectivity (Calabro, 2019). Moreover, a study of structural brain development reported that children with superior intelligence have a particularly plastic cortex, with a prolonged phase of cortical increase and delayed onset of synaptic pruning in adolescence compared with children of average intelligence (Shaw et al., 2006).

In the current study, children with lower white matter organization (i.e., lower FA and higher RD) also displayed better cognitive inhibition. Such negative associations between white matter microstructure organization and better functioning in children and adolescents have been reported in the literature. Indeed, higher educational attainment and better cognitive inhibition performance have been found to be negatively associated with FA in the same white matter tracts as those identified in the current study, namely the superior longitudinal fasciculus, the cingulum bundle and the anterior corona radiata (Noble et al., 2013; Treit et al., 2014). Likewise concerning MD, a recent study reported that empathy and cooperativeness were positively correlated with MD in the dorsal part of the anterior cingulate cortex, the lateral prefrontal cortex, and the insula among young adults (18–27 years old; Takeuchi et al., 2019). Thus, the current findings may suggest that secure attachment provides children with a prolonged period of white matter development during which optimal socio-cognitive development can unfold. However, longitudinal neuroimaging studies of trajectories of white matter development are needed to test this hypothesis. We cannot exclude that at other developmental periods or in different white matter tracts from those observed in this study, higher security of attachment might predict higher white matter microstructure organization, which in turn might be associated with better child functioning.

This study was strengthened by its prospective longitudinal design, the two assessments of mother-child attachment security with a gold-standard observational measure in the naturalistic context of the family home, and the analysis of multiple DTI metrics that provide a more comprehensive understanding of underlying mechanisms (Hasan, 2006). These analyses were based on a very well-characterized sample. Consistent with the large literature on mother-child attachment (Cadman et al., 2018; De Wolff & Van Ijzendoorn, 1997; Groh et al., 2017), previous reports on the same cohort showed that the attachment security scores used in the current report are positively associated with several indicators of child cognitive functioning and socio-emotional adjustment as well as with putative maternal predictors of mother-child attachment security (e.g., Bernier et al., 2020; Laranjo et al., 2014a; Matte-Gagné et al., 2018; Sirois & Bernier, 2018), providing confidence in the validity of these scores. Furthermore, special attention was paid to diffusion MRI quality control and artifacts correction, particularly head motion – one of the main confounds in pediatric samples (Tamnes et al., 2018) –, including manual inspection of data, eddy and head motion correction, and outlier detection. Finally, severe statistical precautions were used to control for false positives, including 5,000 permutations, and statistically significant clusters identified using the threshold-free cluster enhancement method (Smith & Nichols, 2009) with FWE-corrected p -values and minimum cluster size.

Limitations

The current results must be interpreted in the context of some study limitations. Most notably, the links between mother-child attachment and child white matter microstructure may be underestimated because of the limited statistical power related to the modest sample size and the strict statistical controls implemented. Because small samples also yield more unstable

estimates, it is important that future studies use larger samples to test the robustness of the associations observed here. However, the fact that child cognitive inhibition, a documented correlate of white matter microstructure, was associated with DTI metrics in several of the same white matter tracts as attachment lessens the odds that the observed DTI-attachment links are spurious. Given the delay between the MRI exam and the cognitive inhibition assessment ($M=-4.79$, $SD=6.71$, range=-14.07–11.87 months), which were assessed at two different timepoints, we cannot exclude that the association between white matter microstructure and inhibition may have been influenced by intervening factors. We also used a relatively homogeneous middle-class community sample, which limits the generalizability of the results.

Although longitudinal, the non-experimental design of this study precludes causal inference and determination of directionality. The possibility of reverse causation, namely that lower white matter organization was already present in these children in toddlerhood and may have predisposed them to form a more secure attachment relationship with their mother, 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 result of bidirectional influences (see Rifkin-Graboi et al., 2019). Lastly, given the relations between attachment and cognitive inhibition (Pallini et al., 2018, 2019), one possibility raised by the current findings is that white matter development is one of the neural substrates through which early attachment transits to promote children’s capacity to inhibit their impulsive thoughts and behaviors. Although a mediation analysis would be the optimal statistical approach to examine this presumed three-way relation between mother-child attachment, white matter microstructure, and child cognitive inhibition, the current study was under-powered to properly test for mediation. Accordingly, the preliminary correlational analyses are presented in the spirit of

encouraging larger-scale hypothesis-driven investigations. Overall, it appears important that the innovative findings of this small-scale study be replicated in independent, larger, and more diverse samples.

Future directions

Child sex and pubertal status may influence brain maturation during adolescence, including white matter microstructure development, resulting in different growth patterns between individuals (Herting et al., 2012; Schmithorst et al., 2008; Simmonds et al., 2014; Tamnes et al., 2018; Y. Wang et al., 2012). The limited size of the current sample prevented us from investigating and disaggregating the effects of attachment, sex, and pubertal status on brain white matter development. This is an important question that should be investigated in larger samples.

Furthermore, although the AQS is one of the gold-standard measures of the attachment field, one of its limitations is that it does not allow for the assessment of attachment disorganization. Given that disorganized attachment is associated with lower inhibitory control (Pallini et al., 2018), future studies could use the Strange Situation Procedure to investigate potential neural substrates of the associations between disorganized attachment and inhibition.

Future studies with larger samples could also investigate the hypothesis that differential susceptibility to caregiving experiences, depending on children's own behavioral and neural phenotype, allows some children to benefit from caregiving experiences more than others (Ilyka et al., 2021). For example, infants' communication has been found to moderate the relation between paternal sensitivity and cerebellar volumes (Sethna et al., 2019). Thus, research could investigate whether children's characteristics likewise moderate the association between caregiving experiences and white matter microstructure.

Finally, a long-lasting question in developmental science pertains to directionality. Further longitudinal research involving repeated assessments of attachment, white matter microstructure, and cognitive inhibition (as well as other child outcomes) is necessary to unravel the complex transactional influences that are likely to underlie the associations between parent-child relations, neural development, and child functioning.

Conclusion

The findings of this longitudinal study, albeit preliminary given the sample size, suggest that normative variation in the security of mother-child attachment during toddlerhood is associated with differences in white matter microstructure organization almost 10 years later, which are in turn related to child cognitive inhibition. These findings add to the growing interest in research linking attachment to child brain markers (e.g., Cortes Hidalgo et al., 2019; Leblanc et al., 2017, 2022; Lyons-Ruth et al., 2016; Moutsiana et al., 2015; Puhmann et al., 2021; Schoett et al., 2021). Future longitudinal studies should examine whether positive early caregiving experiences decelerate white matter microstructure development and enhance child brain plasticity, thereby promoting learning.

Data Availability Statement.

Due to the nature of this research, participants of this study did not agree for their data to be shared publicly; therefore, supporting data are not available.

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Table 1

Sociodemographic information of families whose child underwent the magnetic resonance imaging (MRI) exam (N=35) and those who declined (N=25) or were not eligible (N=4) to participate.

	Accepted MRI N=35	Declined MRI or not eligible N=29	<i>t/chi</i> ²	<i>p</i>
Family income [< CAD\$20k]. N (%)	2 (5.71)	0 (0)		
Family income [CAD \$20k – 39k]. N (%)	4 (11.43)	3 (10.34)		
Family income [CAD \$40k – 59k]. N (%)	3 (8.71)	3 (10.34)		
Family income [CAD \$60k – 79k]. N (%)	5 (14.28)	10 (34.48)	11.22	.34
Family income [CAD \$80k – 99k]. N (%)	9 (25.71)	2 (6.89)		
Family income [> CAD \$100k]. N (%)	11 (31.43)	8 (27.59)		
Family income [Not answered]. N (%)	1 (2.86)	3 (10.34)		
Maternal age at recruitment (years). <i>M</i> (<i>SD</i> , [range])	31.63 (5.05, [20-45])	32.02 (3.50, [24-38])	-0.35	.72
Paternal age at recruitment (years). <i>M</i> (<i>SD</i> , [range])	33.40 (5.29, [22-44])	34.04 (4.87, [25-44])	-0.50	.62
Maternal education (years). <i>M</i> (<i>SD</i> , [range])	15.40 (2.22, [10-18])	15.26 (2.32, [10-18])	0.24	.81
Paternal education (years). <i>M</i> (<i>SD</i> , [range])	15.60 (1.94, [11-17])	15.01 (2.10, [11-18])	1.16	.25
Ethnicity mother [Caucasian]. N (%)	28 (80)	23 (79.31)		
Ethnicity mother [Caribbean]. N (%)	2 (5.71)	3 (10.34)		
Ethnicity mother [Latin American]. N (%)	2 (5.71)	0 (0)		
Ethnicity mother [African]. N (%)	1 (2.86)	0 (0)	6.65	.76
Ethnicity mother [Middle East]. N (%)	0 (0)	1 (3.45)		
Ethnicity mother [Other]. N (%)	2 (5.71)	0 (0)		
Ethnicity mother [Not answered]. N (%)	0 (0)	2 (6.89)		

Ethnicity father [Caucasian]. N (%)	26 (74.29)	19 (65.52)		
Ethnicity father [Asian]. N (%)	2 (5.71)	0 (0)		
Ethnicity father [Caribbean]. N (%)	1 (2.86)	0 (0)		
Ethnicity father [Latin American]. N (%)	2 (5.71)	2 (6.89)	14.19	.29
Ethnicity father [African]. N (%)	2 (5.71)	0 (0)		
Ethnicity father [Middle East]. N (%)	0 (0)	5 (17.24)		
Ethnicity father [Other]. N (%)	2 (5.71)	0 (0)		
Ethnicity father [Not answered]. N (%)	0 (0)	3 (6.89)		
Language at home [French]. N (%)	26 (74.28)	24 (82.76)		
Language at home [English]. N (%)	4 (11.43)	2 (6.89)		
Language at home [Italian]. N (%)	1 (2.86)	1 (3.45)		
Language at home [French + Other]. N (%)	2 (5.71)	0 (0)		
Language at home [Not answered]. N (%)	2 (5.71)	2 (6.89)		
Sex [girls]. N (%)	21 (60)	13 (44.83)	1.47	.23
Mother-child attachment at 15 months. <i>M</i> (<i>SD</i> , [range])	.48 (.26, [-.28-.75])	.48 (.21, [-.03-.82])	0.12	.90
Mother-child attachment at 26 months. <i>M</i> (<i>SD</i> , [range])	.55 (.16, [.14-.79])	.49 (.32, [-.42-.83])	1.00	.32

Note. *M* = mean; *SD* = standard deviation.

RD – Positive Associations								
Body of corpus callosum	L/R	-6	-29	21	9,777	.031	.44	.02*
Cingulum								
Corticospinal tract								
Superior longitudinal fasciculus	L	-51	-1	23	429	.046	.45	.02*
Genu of corpus callosum	R	9	25	-20	158	.048	.11	.59
	R	5	22	-1	120	.047	-	-

Note. MNI=Montreal Neurological Institute; FA=fractional anisotropy, L=left; R=right; AD=axial diffusivity; MD=mean diffusivity; RD=radial diffusivity. #Partial correlations were performed only in tracts with already documented associations to cognitive inhibition in children and adolescents, namely the corpus callosum, the cingulum, the cerebral peduncle, and the superior longitudinal fasciculus (Noble et al., 2013; Treit et al., 2014). When a tract was covered by more than one cluster, partial correlation was performed in the largest cluster only. **p*-values surviving false discovery rate correction

Figure 1

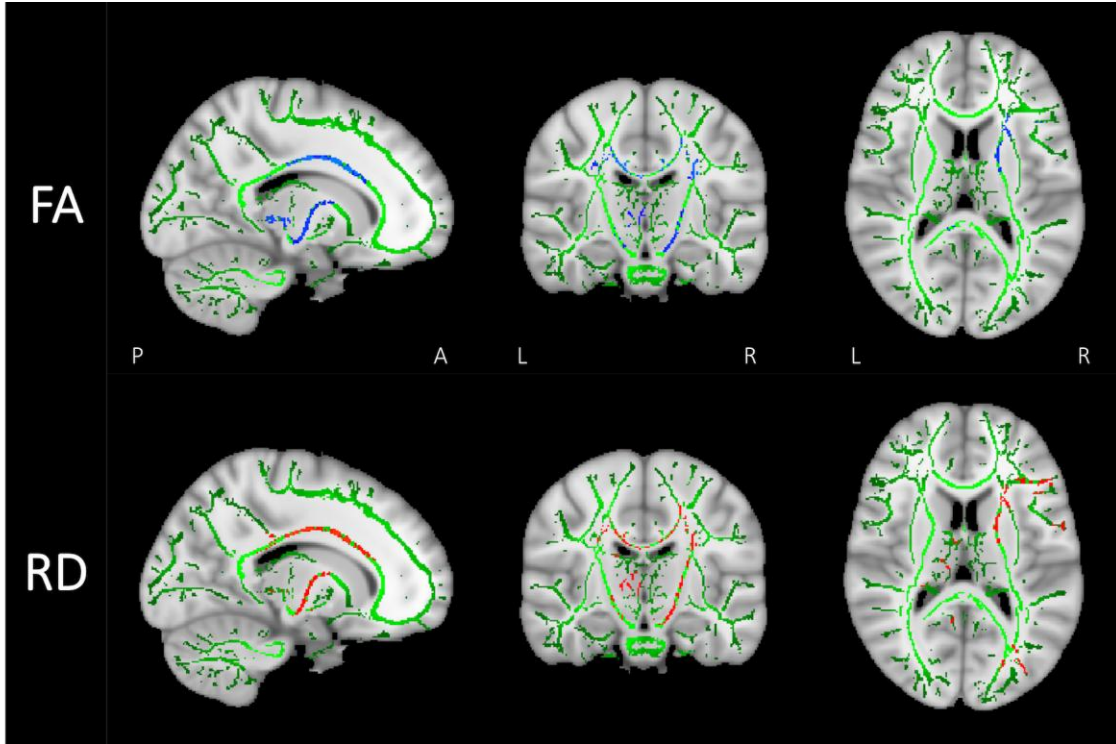


Figure 1. Higher mother-child security of attachment predicts lower fractional anisotropy (FA; Blue) and higher radial diffusivity (RD; Red) at 10 years. Green=white matter skeleton. P=posterior; A=anterior, L=left; R=right; RD=radial diffusivity.

Table S2

Exploratory partial correlations between fractional anisotropy/radial diffusivity in significant clusters (main analysis) and attachment at 15 and 26 months separately. FDR-p: False Discovery Rate (FDR) adjusted p-values.

Region	Attachment at 15 months		Attachment at 26 months	
	<i>r</i>	<i>FDR-p</i>	<i>r</i>	<i>FDR-p</i>
Fractional anisotropy				
Body of corpus callosum	-.56	.003	-.70	.002
Corticospinal tract	-.72	.002	-.68	.002
Cingulum	-.48	.01	-.69	.002
Corticospinal tract	-.69	.002	-.62	.002
Cerebral peduncle	-.65	.002	-.60	.002
Genu of corpus callosum	-.74	.002	-.49	.01
Superior longitudinal fasciculus	-.47	.01	-.45	.01
Inferior fronto-occipital fasciculus	-.71	.002	-.46	.01
Superior longitudinal fasciculus	-.24	.21	-.55	.003
Corticospinal tract	-.53	.004	-.55	.003
Corticospinal tract	-.59	.002	-.42	.02
Inferior fronto-occipital fasciculus	-.56	.002	-.57	.002
Superior longitudinal fasciculus	-.47	.01	-.47	.01
Inferior fronto-occipital fasciculus	-.46	.01	-.56	.003
Radial diffusivity				
Body of corpus callosum				
Cingulum				
Corticospinal tract	.66	.001	.78	.001
Superior longitudinal fasciculus	.59	.001	.63	.001
Genu of corpus callosum	.58	.001	.57	.001
Genu of corpus callosum	.64	.001	.56	.001