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Prenatal prolactin predicts postnatal parenting attitudes and brain structure remodeling in first-time fathers

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Abstract

Despite the important contributions that fathers make to parenting, the neurobiological underpinnings of men's adaptation to parenthood are still not well understood. The current study focuses on prolactin, a hormone that has been extensively linked with reproduction, lactation, and parental behavior in mothers. There is preliminary evidence that it may also reflect the transition to sensitive fatherhood. We sampled prolactin in 91 first-time expectant fathers who participated in a laboratory visit along with their pregnant partners. Fathers' prolactin levels were correlated with their partners' prolactin levels. Men's prolactin levels during their partner's pregnancy were associated with their self-reported antenatal bonding to the unborn infant. Prenatal prolactin levels in fathers also predicted more positive attitudes toward fatherhood at three months postpartum, including lower parenting stress, greater enjoyment of the infant, and a more attunement-oriented parenting style. Within a smaller sample of 32 men who participated in MRI scanning before and after their child's birth, prenatal prolactin also predicted greater reductions in grey matter volume in the left posterior cingulate, left insula, and left nucleus accumbens. In conclusion, men's prenatal prolactin may reflect their perceptions of fatherhood and changes to their perinatal brain structure.

Graphical Abstract:

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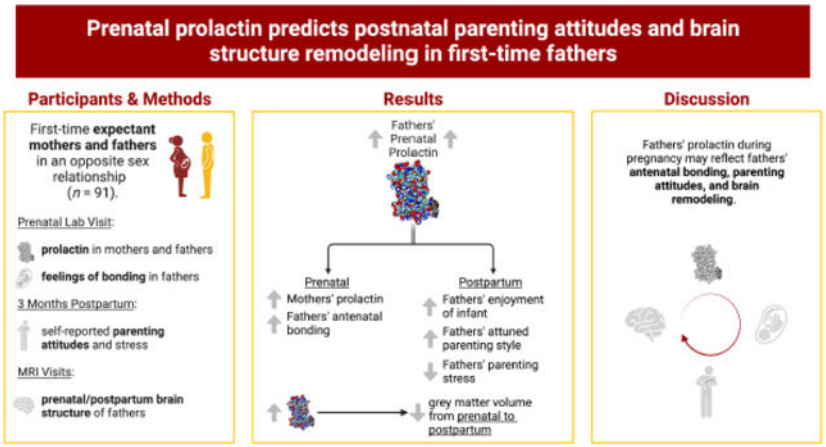

Keywords

Prolactin; transition to parenthood; fatherhood; parent-infant bonding; grey matter

1. Introduction

Fathers make important contributions to parenting, and children with involved fathers show better outcomes across multiple domains (Cabrera et al., 2007; Wilson & Prior, 2011). However, the neurobiological underpinnings of fatherhood have been understudied compared to mothers. Although mothers experience more obligate physical transformations during pregnancy and postpartum, men's neurobiology might also reflect their adaptation to parenthood (Horrell et al., 2021). Prolactin is one hormone that appears to play a role in reproductive transitions in both human fathers and rodents, birds, and non-human primates. Named for its role in promoting lactation in mothers, it has also been called the "hormone of paternity" and has been linked to fathering behavior among biparental mammals (Schradin & Anzenberger, 1999).

Prolactin is a polypeptide hormone secreted and stored primarily in the anterior pituitary gland (Al-Chalabi et al., 2020). Though best known for its role in lactation and maternal behavior, prolactin supports hundreds of physiological functions across species (Hashemian et al., 2016). Males and non-lactating, non-pregnant females have characteristically low levels of prolactin relative to pregnant and lactating mothers (Al-Chalabi et al., 2020), but preliminary evidence suggests that prolactin rises in human men in late pregnancy (Storey & Ziegler, 2016) and after contact with their infants (Gettler et al., 2011).

Prolactin and paternal care

Prolactin has been linked with paternal caregiving in species where males participate in parenting (Schradin & Anzenberger, 1999). Prolactin levels correlated with paternal care in 25 species of monogamous birds (Buntin, 1996). In fish species with paternal care, experimentally manipulated prolactin levels increased parenting behaviors in non-fathers (de Ruiter et al., 1986), whereas prolactin inhibition reduced paternal behaviors (Kindler et al., 1991). Similarly, higher prolactin levels have been observed in marmoset and tamarin

fathers compared to non-fathers of the same species (Ziegler et al., 2009). Of note, tamarin fathers' prolactin levels begin increasing starting at mid-gestation and reach their highest concentration in the last month before birth (Ziegler et al., 2000, 2004). Because tamarin fathers begin carrying their offspring within hours of birth, researchers have inferred that the prenatal increase in prolactin levels prepares fathers for caregiving (Ziegler et al., 2009). Male Goeldi monkeys, which do not start carrying infants until a few weeks after birth, show stable prolactin levels during pregnancy that increase in the weeks after birth leading up to the onset of their parental behaviors.

Consistent with bird, fish, and primate models, human paternal prolactin appears to be associated with preparation for fathering. Men's prolactin levels increase just before birth, continue to increase in the first few weeks postpartum (Storey, 2000), and remain stable throughout the first six months postpartum (Gordon et al., 2010). Most research on prolactin in human fathers has looked at short-term reactivity to parenting-relevant situations rather than at basal levels, and has suggested that prolactin is linked with fathers' responses to infant cues. For example, Fleming et al. (2002) exposed experienced fathers, new fathers, and non-fathers to infant cries and collected prolactin before and after exposure to stimuli. Fathers with higher baseline prolactin levels were more alert and positive in response to infant cries. Additionally, Delahunty and colleagues (2007) found that first-time expectant fathers who reported greater "concern" upon listening to a baby cry subsequently showed larger postpartum prolactin increases when holding their infant. In another study by Gordon and colleagues (2010), fathers' prolactin levels were positively associated with their facilitation of toy exploration during free play with their infants. The current study extends these limited findings to test associations between prenatal paternal prolactin and fathers' postpartum adjustment to fatherhood, including their perceptions of father-child bonding, parenting stress, and parenting beliefs.

Hormonal linkage across the transition to parenthood

Expectant fathers may entrain with pregnant partners as part of their hormonal adaptation to new parenthood. In one study, stronger prenatal correlations in testosterone within cohabiting couples predicted men's greater postpartum investment in the co-parenting relationship (Saxbe et al., 2017). Cortisol levels have also been found to be linked in couples transitioning to parenthood (Saxbe et al., 2015). Two studies examining hormonal linkage in pregnant couples draw on the same sample of couples that are included in the current study. In one, partners showed positively correlated levels of cortisol during a prenatal lab visit, and stronger correlations predicted fewer postpartum depressive symptoms in fathers (Khaled et al., 2021). In another study, couples showed positive correlations in testosterone levels, and greater within-couple linkage predicted higher paternal postpartum relationship satisfaction (Cardenas, et al., under review). Only one study, to our knowledge, tested prenatal prolactin levels in both mothers and fathers (Storey, 2000), and found that both men and women tended to show higher prolactin levels in late pregnancy than in early pregnancy or the early postpartum period, but prenatal prolactin levels were not correlated within couples. However, the null results may have been due to lack of statistical power, given that only 20 couples participated during pregnancy. The current study tests within-couple

correlations in prenatal prolactin in a larger sample of couples as a potential marker of men's entrainment with their pregnant partners as they transition to fatherhood.

Hormones and the fathering brain

Recent evidence suggests that the paternal brain shows morphological remodeling across the transition to parenthood. Martínez-García et al. (2022) found cortical volume reductions from prenatal to postpartum in two samples of first-time fathers (including 20 fathers from the current study) but not in a comparison sample of non-fathers. Compared to the consistent and prominent pregnancy-induced changes reported in human mothers(Hoekzema et al., 2017, 2022), changes in fathers were less pronounced and uniform (Martínez-García et al., 2022), and were not detected in an earlier study of the same fathers that used a different data analysis approach (Hoekzema et al., 2017). Another study found that men showed significant reductions in grey matter volume in posterior midline cortical regions (precuneus and posterior circulate) from prenatal to postpartum, and these volume reductions were associated with fathers' responses to infant stimuli (Paternina-Die et al., 2020). The transition to motherhood has also been associated with subcortical remodeling, including volume reductions in the ventral striatum, the region that contains the nucleus accumbens (Hoekzema et al., 2020). Among biparental non-human mammals, brain changes have been associated with fatherhood, particularly within subcortical structures such as the hippocampus, amygdala, and nucleus accumbens (Horrell et al., 2021). In the same sample of fathers included in the current study, we found that higher prenatal oxytocin levels predicted greater perinatal change in left hippocampus volumes (Saxbe et al., 2023). However, no studies have examined associations between paternal prolactin and brain structure in human males. There are also no studies, to our knowledge, linking maternal prolactin with brain structure in human females, with the exception of one study, which found that the grey matter volume of the insula mediated the positive association between prolactin and postpartum depression in mothers (Cheng et al., 2022).

The current study

In this study, we examined whether prolactin levels in first-time fathers cohabiting with a pregnant partner was associated with their preparation for, and adjustment to, parenthood. We also examined whether fathers' prenatal prolactin levels predicted changes in brain structure over the transition to parenthood. We sought to extend the limited research on prolactin in human fatherhood by testing four hypotheses:

1. Consistent with research finding hormonal linkage within couples, we expected fathers' prolactin levels to be correlated with their partners' prolactin levels during pregnancy.
2. We expected fathers' prenatal prolactin levels to correlate with antenatal bonding with the unborn infant.
3. We expected prenatal prolactin to predict fathers' self-reported parenting attitudes at three months postpartum: increased postnatal bonding, increased attunement-oriented parenting beliefs, and decreased parenting stress.

4. We expected that fathers' prenatal prolactin would predict fathers' grey matter volume changes in the cortex and subcortex from prenatal to postpartum. Given that no studies to our knowledge have examined prolactin in conjunction with grey matter volume in human parents, we based our neural hypotheses on the research summarized above, and planned to focus on the precuneus, posterior cingulate, nucleus accumbens, hippocampus, amygdala, and insula.

2. Material and Methods

2.1 Participants

Heterosexual fathers who were expecting their first child and cohabiting with their partners were recruited during their partner's pregnancy from the greater Los Angeles area through fliers posted in obstetricians' offices, at community health clinics, and on social media. Fathers and their partners were recruited as part of the Hormones and Attachment across the Transition to Childrearing (HATCH) study, a large longitudinal study that included multiple waves of data reflecting hormones, brain, behavior, and self-report measures. Demographics for all fathers are shown in Table 1.

Of the 100 couples initially recruited into this study, 93 fathers and 92 mothers had prenatal prolactin data available; missing data were due to issues with plasma collection, storage, or laboratory processing. Two fathers and three mothers were dropped from analyses due to outlier values (>3 SD from the mean), leaving 91 fathers and 89 mothers for the current study's analyses. The antenatal bonding measure was added to the study after data collection had already begun, so 61 fathers who provided prolactin data also completed this measure. At three months postpartum, data were missing for 19 fathers due to attrition from this study wave, yielding a sample size of 72 fathers who provided both prolactin and three-month questionnaire data. The postpartum bonding measure was also added to the study after data collection had already begun, so 66 fathers who provided prolactin data also completed this measure (see Figure 1 for sample size details).

The MRI subsample comprised 38 fathers who participated in MRI scanning and provided both prenatal and postpartum scan data. The MRI study was launched several years after beginning the larger longitudinal study. Exclusion criteria for providing MRI data included contraindications for magnetic resonance imaging (MRI), such as neurological conditions, movement disorders, left-handedness, psychotropic medication use, history of brain injury, or severe learning disability. Of the fathers that provided usable MRI data, 32 also had prenatal prolactin data available.

Across all study variables, missingness was not associated with fathers' age, education, smoking status, or body mass index (BMI). Missingness was not associated with any other independent variable or covariate tested in the current analyses.

2.2 Procedure

The present study reported on data collected as part of the HATCH study. The larger study consisted of four in-person visits during the perinatal period, as well as two virtual data collection timepoints at three and twelve months postpartum. The four in-person visits

included couple laboratory visits during pregnancy and at six months postpartum, as well as father-only MRI visits at approximately the same time.

During the prenatal laboratory visit, which occurred during mid-to-late pregnancy (20–35 weeks) and lasted 3–4 hours, expectant couples were asked to engage in three 10–15 minute video-recorded discussions focused on their relationship and preparation for parenthood. Following the three discussions, partners were separated into different rooms, where they completed a computerized battery of demographic and psychosocial questionnaires, including the Paternal Antenatal Attachment Scale (PAAS). At the end of their prenatal laboratory visit, a licensed phlebotomist performed blood draws on each partner for plasma prolactin sampling. Similar procedures were followed during the six month postpartum visit, which is not reported on in the current study. At the prenatal MRI visit, which typically occurred within one to two weeks following their prenatal in-laboratory visit, eligible, expectant fathers completed a high-resolution structural scan. Additional information can be found in other published studies using the HATCH data, including Cardenas et al., 2021, under review; Khaled et al., 2020, 2021; Martínez-García et al., 2022; Saxbe et al., 2023.

Approximately three months following their infant's birth, each partner individually completed follow-up questionnaires remotely via the online Qualtrics platform, including the Parenting Stress Index – Short Form (PSI-SF), Baby Care Questionnaire (BCQ), and Paternal Postpartum Attachment Scale (PPAS). Between 6–18 months (median = 7 months) following their infant's birth, fathers participating in the MRI sub-study returned for a postpartum MRI visit, where they again completed a high-resolution structural scan. This timing varied due to COVID pandemic lockdowns in spring 2020, which delayed the scheduling of the last ten postpartum scans. The range among fathers who returned for their scan visit before pandemic lockdowns was 6–10 months postpartum, whereas among fathers who returned after pandemic lockdowns, the postpartum scan ranged from 8–18 months. For this reason, we controlled for postpartum scan timing in all analyses that included the brain structure data. We conducted a series of independent samples *t*-tests to compare fathers who returned for their postpartum scans before or after the onset of the pandemic. We found no significant differences in fathers' prenatal prolactin, antenatal bonding, parenting behaviors, or brain volume changes.

2.3 Measures

Mean scores for key study measures can be found in Table 1. Table 2 shows zero-order correlations between key study variables with the exception of the brain structure variables, which are shown in a partial correlation table in Table 4.

2.3.1 Antenatal bonding—Prenatal paternal bonding was measured using the Paternal Antenatal Attachment Scale (PAAS; Condon, 1993), a 14-item self-report questionnaire that assesses expectant fathers' thoughts, feelings, and expectations for their developing baby. All responses are rated on a five-point scale, with higher summed scores reflecting stronger prenatal bonding, including how often the expectant parent has thought about the baby and how the parent expects to feel when they first see their baby after birth. The PAAS has been well-validated across multiple samples and has demonstrated high reliability and validity

with mothers and fathers (Condon & Corkindale, 1998; Della Vedova & Burro, 2017). Within our sample, reliability for the paternal version of the scale was acceptable (α = .85).

2.3.2 Attunement-oriented beliefs about parenting—Fathers' beliefs about attunement-oriented parenting styles were measured using the attunement subscale of the Baby Care Questionnaire (BCQ; (Winstanley & Gattis, 2013). The BCQ is a 30-item self-report questionnaire that asks participants to rate how strongly they agree or disagree with statements relating to sleeping, feeding, and soothing their baby using a four-point Likert scale (1 = "strongly disagree"; 4 = "strongly agree"). The BCQ generated two subscales: "structure," which reflects parents' endorsement of a more structured parenting style that relies on routines and schedules, and "attunement," which reflects parents' endorsement of a parenting style that is responsive to in-the-moment infant cues. The BCQ attunement subscale score is generated by averaging scores on attunement items (e.g., "babies benefit from physical contact with parents when they wake during the night."). Prior research has demonstrated the BCQ's acceptable reliability and validity (Winstanley & Gattis, 2013), and the scale had acceptable reliability (α = .83) in our sample.

2.3.3 Parenting stress—Parenting stress was measured using the Parenting Stress Index - Short Form (PSI-SF; Abidin, 1990), a 36-item self-report measure used to evaluate parenting stress across three distinct subscales: parental distress, parent-child difficult interaction, and difficult child. These subscales reflect the level of distress surrounding parenting, parental dissatisfaction about interactions with their child, and stress as a result of their child's difficult behaviors, respectively. Items are rated on a five-point Likert scale (1 = "strongly agree", 2 = "agree", 3 = "not sure", 4 = "disagree", and 5 = "strongly disagree") and scores are obtained by reverse scoring each item and summing their values. The current study assessed overall parenting stress, which combines each subscale score to generate a total stress score. Higher total scores are indicative of experiencing higher parenting stress. Prior research has demonstrated the PSI-SF's acceptable reliability and validity (Aracena et al., 2016), and reliability in the current sample was acceptable (α =.92).

2.3.4 Postnatal bonding—Father-infant postpartum bonding was measured using the Paternal Postnatal Attachment Scale (PPAS; Condon et al., 2008), a 19-item self-report measure. Items are rated on a five-point Likert scale, with higher scores indicating greater levels of father-infant bonding. The PPAS generates three subscales: patience and tolerance (8 items), affection and pride (4 items), and pleasure in interaction (7 items). Within our sample, reliability for the patience and tolerance subscale was acceptable (α = .73) and reliability for the affection and pride pleasure in interaction subscales were minimally acceptable (α = .61; α = .68).

2.3.5 Prolactin—Blood for plasma prolactin assay was collected into sterile Ethylenediamin tetra-acetic acid (EDTA) vacutainer tubes at the prenatal and postpartum visits. The aliquots were stored at −80 C and then shipped on dry ice to the University of Miami School of Medicine Diabetes Research Institute (Armando Mendez, PI) for processing. We truncated the data to +3 standard deviations and dropped two values for fathers and three values for mothers.

2.3.6 Neuroimaging

MRI data acquisition.: Whole-brain images were collected on a Siemens 3 Tesla MAGNETON Prisma System scanner. High-resolution, T1- weighted images were obtained via a 3D Magnetization Prepared Rapid Acquisition Gradient Echo (repetition time, 2530 ms; echo time, 3.13 ms; flip angle, 10°), with an isotropic voxel resolution of 1 mm (Pawluski et al., 2022).

Image processing.: MR T1-weighted structural images were processed with the FreeSurfer longitudinal stream (version 7.1.1; Iglesias et al., 2015) to estimate brain volumes. Images were processed independently at each timepoint, and the pipeline created an unbiased within-subject template as an initialization point to produce longitudinal series with higher reliability and statistical power. This stream includes motion and intensity correction, skull removal, transformation into stereotaxic (MNI) space, white matter segmentation, and reconstruction of the white matter and cortical surfaces. We next applied a FreeSurfer tool that automatically segments cortical and subcortical volumes using a module that jointly segments within-subject scans (Preacher & Hayes, 2008). FreeSurfer reconstructions of specific structures were visually inspected and manually corrected where needed as per FreeSurfer's guidelines. For each subject, longitudinal volume percentage change was calculated by subtracting the prenatal volume from the postpartum volume of each structure, dividing by prenatal volume, and multiplying by 100. More details on brain volume changes within part of this sample are provided in Martínez-García et al., 2022.

2.4 Data Analysis Plan

We fit a series of multiple linear regression models to test the association between fathers' prenatal prolactin and mothers' prenatal prolactin (Model 1), fathers' antenatal bonding with their infant (Model 2), fathers' postpartum parenting stress (Model 3), fathers' postpartum attunement-based parenting beliefs (Model 4), fathers' postpartum parenting pleasure (Model 5), affection (Model 6), and patience (Model 7). We conducted a series of partial Pearson correlations to explore the association between fathers' prolactin and changes in gray matter volume from prenatal to postpartum across brain regions. Models 1 and 2 were cross-sectional (i.e., predictors and outcomes were measured at the prenatal visit), and fathers' prolactin was included as the outcome measure. Models 3–7 were longitudinal, with fathers' prenatal prolactin predicting outcomes measured at three months postpartum (Models 3–7). Due to positive skew in father's prenatal prolactin (skewness = 4.76), we applied a square-root transformation (Bartlett, 1936), which afforded a better correction for non-normality compared to a logarithmic transformation.

In the models that use self-reported parenting attitudes and stress, as well as the model testing the association between maternal and paternal prolactin, we statistically controlled for father's age, education, smoking, and BMI. Self-reported height and weight were used to calculate BMI. Additionally, we controlled for pregnancy stage (days of pregnancy, as reported by the mother) at the prenatal visit in Models 1 and 2 and infants' age at the time of the 3-month surveys in the remaining models. Sensitivity power analyses conducted in G*Power (v. 3.1.9.7; Faul et al., 2009) indicated that we were sufficiently powered to detect small to medium effect sizes in models that included prolactin and self-report measures (i.e.,

f^2 = .10 - .12) with a power of .80 and α = .05 (Cohen, 1992; see Supplementary Materials for details).

In the models that included brain structure variables, we controlled for fathers' education and the length of time between the infant's birth and the father's postpartum MRI scan. The latter covariate was included to control for delays in the scheduling of some fathers' postpartum MRI scans due to the onset of the COVID-19 pandemic in Spring 2020. Given the smaller sample size of the brain structure data, our analyses were sufficiently powered to detect only moderate to large effect sizes (f^2 = .26) with a power of .80 (Cohen, 1992). Therefore, we statistically controlled for only two covariates in these models to preserve power. We ran both linear regression models and partial correlations between prolactin and brain structure controlling for these two covariates and results were identical, so we present the partial correlations here for parsimony. Given that we tested 10 brain structures (left and right precuneus, posterior cingulate, nucleus accumbens, hippocampus, and insula) we applied the Bonferroni correction for multiple comparisons by adopting a *p*-value threshold of 0.005.

Covariates were added hierarchically to each model; control variables were entered first, followed by the focal variable of interest. For example, in Model 1, control variables were entered into the linear model prior to adding mothers' prenatal prolactin.

3. Results

3.1 Hypothesis 1: Linkage with maternal prolactin

Consistent with other studies of prolactin in mammalian males and females, pregnant women's prolactin levels were much higher (19 times higher) than their male partners. Mothers' and fathers' prolactin levels were positively correlated with each other at the prenatal visit (r(85)=0.225, p=.039; see Table 2 for zero-order correlations between key study variables). This association held in a regression model (Table 3, Figure 2) that included the covariates of paternal age, education, smoking history, pregnancy stage (days of pregnancy), and maternal and paternal body mass indices. Pregnancy stage was positively associated with maternal prolactin (r(89)=0.318, p=.002, but was not correlated with paternal prolactin (r(91)=.129, p=.223).

3.2 Hypothesis 2: Cross-sectional associations between men's prenatal prolactin and self-report measures in pregnancy.

As expected, men with higher prolactin levels at the prenatal visit also reported significantly stronger feelings of bonding to their unborn infant at that same visit (Table 3, Figure 2).

3.3 Hypothesis 3: Longitudinal associations between men's prenatal prolactin predicting early self-report parenting outcomes at three months postpartum.

As hypothesized, men with higher levels of prenatal prolactin reported more positive adaptation to parenthood at three months, including lower levels of parenting stress and greater postpartum endorsement of attuned parenting styles (Table 3, Figure 2). Contrary to expectations, prenatal prolactin predicted only one of three postnatal bonding subscales:

prolactin predicted fathers' pleasure in interaction with their infant, but not their affection and pride in, or patience and tolerance for, their infant.

3.4 Hypothesis 4: Longitudinal associations between men's prenatal prolactin and subcortical grey matter volume remodeling from prenatal to postpartum.

We found that fathers' greater prenatal prolactin predicted greater reductions in grey matter volume in the left insula, left posterior cingulate, and left nucleus accumbens from prenatal to postpartum (Table 4). However, only the results for the left nucleus accumbens and left posterior cingulate cleared the adjusted *p*-value threshold for multiple comparisons. Prenatal prolactin did not predict changes in grey matter volume in the hippocampus, precuneus, or the right insula, posterior cingulate, or nucleus accumbens.

4. Discussion

Among first-time expectant fathers who visited the lab with their partners during mid-to-late pregnancy, men's plasma prolactin levels were positively correlated with their pregnant partners' prolactin levels, and also with men's self-reported antenatal bond with the unborn infant. Higher prenatal prolactin also predicted self-reported adjustment to fatherhood at three months postpartum, including greater pleasure in interacting with the infant, lower paternal parenting stress, and more attunement-oriented beliefs about parenting. Men with higher prenatal prolactin levels also showed larger prenatal-to-postpartum reductions in grey matter volume in the left posterior cingulate and nucleus accumbens. Other studies of mothers and fathers have linked perinatal grey matter volume reductions with increases in bonding and responsiveness to infants (e.g., Paternina-Die et al. (2020) found that fathers who lost more grey matter volume in the posterior cingulate and precuneus showed greater neural responding to pictures of their infants), so these findings are consistent with other studies suggesting that prenatal prolactin may help to prepare men for fatherhood.

Our finding that mother's and father's prenatal prolactin levels were correlated aligns with prior research on hormonal linkage in cohabiting couples (Saxbe et al., 2017; Timmons et al., 2015). In previous research using the same sample featured in the current study, we have reported synchrony in prenatal cortisol and testosterone levels (Khaled et al., 2021; Cardenas et al., under review), but this is the first study to our knowledge to report on within-couple linkage in prolactin. Mother's prolactin naturally increases during pregnancy before dropping steeply during the postpartum window (Biswas & Rodeck, 1976). However, fathers' prolactin remains relatively consistent over time, including during the peripartum period (Storey, 2000). Therefore, while mothers naturally secrete greater prolactin during pregnancy in preparation for lactation and childbirth, there may be an association between partners' prolactin levels that is independent of pregnancy stage. In general, this coheres with prior work on hormonal synchrony that suggests romantic partners' emotional and physical proximity predicts shared endocrine profiles (Schneiderman et al., 2014; Timmons et al., 2015) and that hormonal linkage can be found within couples in the perinatal period (Saxbe et al., 2015; Khaled et al., 2021; Cardenas et al., under review). However, this finding contrasts with Storey's (2000) examination of the correlation between mothers' and fathers' prenatal prolactin levels. Storey did not find any association between partners'

prolactin in a sample of 20 couples. It is possible that Storey's null results are due to relatively lower statistical power, given that the current sample is more than four times larger. In any case, the mechanisms underlying hormonal linkage in romantic partners warrant continued investigation, although interpersonal processes such as conflict, dyadic coping, and behavioral synchrony offer possible explanations (see Saxbe et al., 2018 for a review).

At three months postpartum, men who showed higher prolactin levels during pregnancy reported lower parenting stress and were more likely to endorse an attunement-oriented style of parenting (e.g., believing that infants benefit from parents responding to their in-the-moment cues). This is consistent with existing research on prolactin levels in new fathers, suggesting that prolactin is associated with paternal caregiving behavior (Hashemian et al., 2016). These findings also dovetail with other studies examining fathers' neurobiological preparation for caregiving during the prenatal period. For example, a previous study from our lab featuring the MRI sample found that expectant fathers who showed greater neural activation in mentalizing and emotion regulation regions while engaging in a theory of mind neuroimaging task subsequently reported greater postpartum endorsement of attuned parenting styles (Cardenas et al., 2021). Our findings further suggest that expectant fathers' neurobiology may provide insight into their postpartum caregiving cognitions and attitudes.

The current study is the first, to our knowledge, to test links between prenatal prolactin and both prenatal and postpartum self-reported father-infant bonding-related outcomes. As predicted, fathers with greater prenatal prolactin levels reported stronger prenatal paternal bonding with their unborn infant and enjoyed interacting more with their baby at three months following birth. The pleasure-in-interaction subscale measures fathers' satisfaction, feelings of pleasure, and competence while engaging in "hands-on" interactions with their infant. This subscale also reflects the father's desire to prolong their involvement in their interactions with their baby, their positive anticipation of the interaction, and their reluctance to end the interaction. However, prenatal prolactin did not predict facets of father-infant bonding such as patience and tolerance or affection and pride for the infant. These findings make sense given that prenatal increases in prolactin levels have been found to prepare fathers for immediate paternal interactive behaviors such as coordinated play (Gordon et al., 2010), but not necessarily more global positive feelings toward their infant.

While the relationship between stress and prolactin has been established (Lennartsson & Jonsdottir, 2011; Sobrinho, 2003), research into the relationship between prolactin and parenting-related stress is more limited. To our knowledge, this is the second study to examine this relationship. Our finding that prolactin levels were negatively associated with stress in new fathers contrasts with a study by Gordon and colleagues, which found no association (Gordon et al., 2010). Of note, Gordon et al. (2010) examined fathers' prolactin and stress at two and six months postpartum while we examined prolactin during the partner's pregnancy. Future work in this area can clarify the relationship between prolactin, stress, and time by examining fathers' prolactin across the transition to parenthood in tandem with parenting stress across the postpartum period.

Our findings linking prenatal prolactin with perinatal grey matter volume changes in fathers are somewhat consistent with prior findings showing grey matter volume reductions in men during the transition to parenthood that are linked with men's neural responses to their infants (Kim et al., 2014; Martínez García et al., 2022; Paternina-Die et al., 2020). Researchers have interpreted changes in grey matter to potentially indicate a refinement or specialization of neural circuits (Paternina-Die et al., 2020; Selemon, 2013). For example, a study by Hoekzema and colleagues found that mothers with greater volume reductions in ventral striatum, a region involved in reward, across the transition to parenthood were more likely to show greater neural responses to images of infant cues (Hoekzema et al., 2020). Similarly, a study by Kim and colleagues found that decreases in orbital frontal cortex volume in new fathers were associated with greater paternal intrusiveness, which may be related to more stimulatory caregiving behavior (Kim et al., 2014). However, our study is the first to find a link between prolactin and grey matter volume changes during the transition to fatherhood. Only two correlations out of 10 survived correction for multiple comparisons, suggesting that these results should be interpreted with caution. However, it is interesting that the posterior cingulate was one of the structures that was linked with prolactin given that it has previously been associated with the transition to fatherhood (Paternina-Die et al., 2020). Moreover, the nucleus accumbens, another structure that was linked with prolactin, is associated with reward and motivation, which is consistent with our finding that higher prolactin predicted fathers' reports of greater pleasure when interacting with their infants. It is also interesting that all of the structures that were linked with prolactin were on the left side of the brain. A recent study examining functional connectivity in mothers focused only on left-lateralized structures based on a review of the parenting brain literature, which tended to report that left- vs. right-lateralized structures, including the posterior cingulate and nucleus accumbens, were more consistently linked with parenting-relevant variables (Orchard et al., 2023).

4.1 Strengths and Limitations

This study contributes to the literature as the largest and most comprehensive investigation of prenatal prolactin as a predictor of adaptation to parenthood in first-time human fathers. This is the first study, to our knowledge, to test prenatal prolactin levels as a predictor of brain remodeling across the transition to parenthood, and to also examine associations between men's prolactin levels, their partners' prolactin levels, and parenting-relevant constructs such as pre- and postnatal bonding, attunement, and parenting stress. Our results further the understanding of prolactin as a hormone that may have implications for fathering, and highlight the importance of fathers' prolactin levels in pregnancy as a potential marker of preparation for parenthood in males.

This study had a number of limitations. Our sample size (91 men who provided prenatal prolactin, with smaller numbers of men who had complete partner data and self-report data available) was small, although larger than any other longitudinal studies of prolactin in human fathers. Our MRI sample (32 fathers with both prenatal prolactin data and prenatal and postpartum scan data) was particularly small, and both the size of the longitudinal MRI sample and the timing of postpartum scan collections was adversely affected by the COVID-19 pandemic. Our ability to compare fathers who were scanned before or

during the COVID-19 was also constrained by low power given the small number of fathers in each group. It is possible that there were structural differences between fathers who were and were not exposed to pandemic lockdowns, but given our small sample, we were underpowered to test this possibility thoroughly. Moreover, we only collected prolactin once during pregnancy, during an in-lab visit in mid-to-late pregnancy. Multiple measures of prolactin across the visit or at multiple timepoints across pregnancy would have enhanced our ability to not just look at prolactin in conjunction with brain and parenting measures, but also to look at change in prolactin over time. We also did not collect pre-conception prolactin measures, but it is possible that men's prolactin levels at puberty or in young adulthood are particularly meaningful for shaping his later entry into parenthood. Prolactin measurement was standardized across fathers in terms of timing (e.g., late afternoon) and the format of the visit (three to four hours spent in the presence of the pregnant partner, including several structured interaction and discussion tasks), but fathers did not undergo any experimental manipulations that have been specifically linked with changes in prolactin (e.g. holding an infant or a soft-bodied doll). Data for this study was drawn from a longitudinal study that began in 2013, before pre-registration was widely practiced. Therefore, we did not pre-register the hypotheses reported on here. Our sample was socioeconomically and racially/ethnically diverse, but fathers tended to have high educational attainment and to be in stable cohabiting couple relationships, meaning that our findings cannot be generalized to all men transitioning to parenthood. Despite these limitations, this study advances the literature on prolactin and the neurobiology of the transition to first-time fatherhood in human males.

4.2 Conclusion

The current study is an important early step in elucidating prolactin's role in supporting the transition to parenthood in human fathers. Further work is needed to replicate and extend the findings reported here, and to better clarify the mechanisms of paternal prolactin in human fathers. Specifically, future studies can combine more dynamic measures of prolactin beginning before as well as across pregnancy and the postpartum period with some of the same self-report measures of parenting attitudes that are included in the current study. Future studies can also include observational measures of parenting behavior to supplement self-reports. Larger prospective neuroimaging studies of the paternal brain are also needed in order to more precisely delineate how paternal hormones might affect the perinatal remodeling of the male brain. It would also be valuable to investigate what drives individual differences in men's prolactin levels (e.g., mechanisms such as genetic influences, lifestyle factors, proximity to the pregnant partner, early life stress, sleep and circadian rhythms). However, these results provide exciting initial evidence that prenatal prolactin may be an important marker of men's preparation for, and subsequent adaptation to, first-time fatherhood. Understanding the neurobiological underpinnings of men's motivation to engage in parenting is an important public health research priority with far-ranging implications for child welfare and societal well-being.

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Data availability statement:

All data used in the current manuscript are available upon request.

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Highlights:

- Prolactin in expectant fathers positively correlated with antenatal bonding to the infant
- Men's prolactin levels were positively correlated with their pregnant partners'
- Paternal prenatal prolactin predicted more positive parenting attitudes at three months postpartum
- Paternal prenatal prolactin predicted perinatal grey matter volume reductions in parenting brain regions

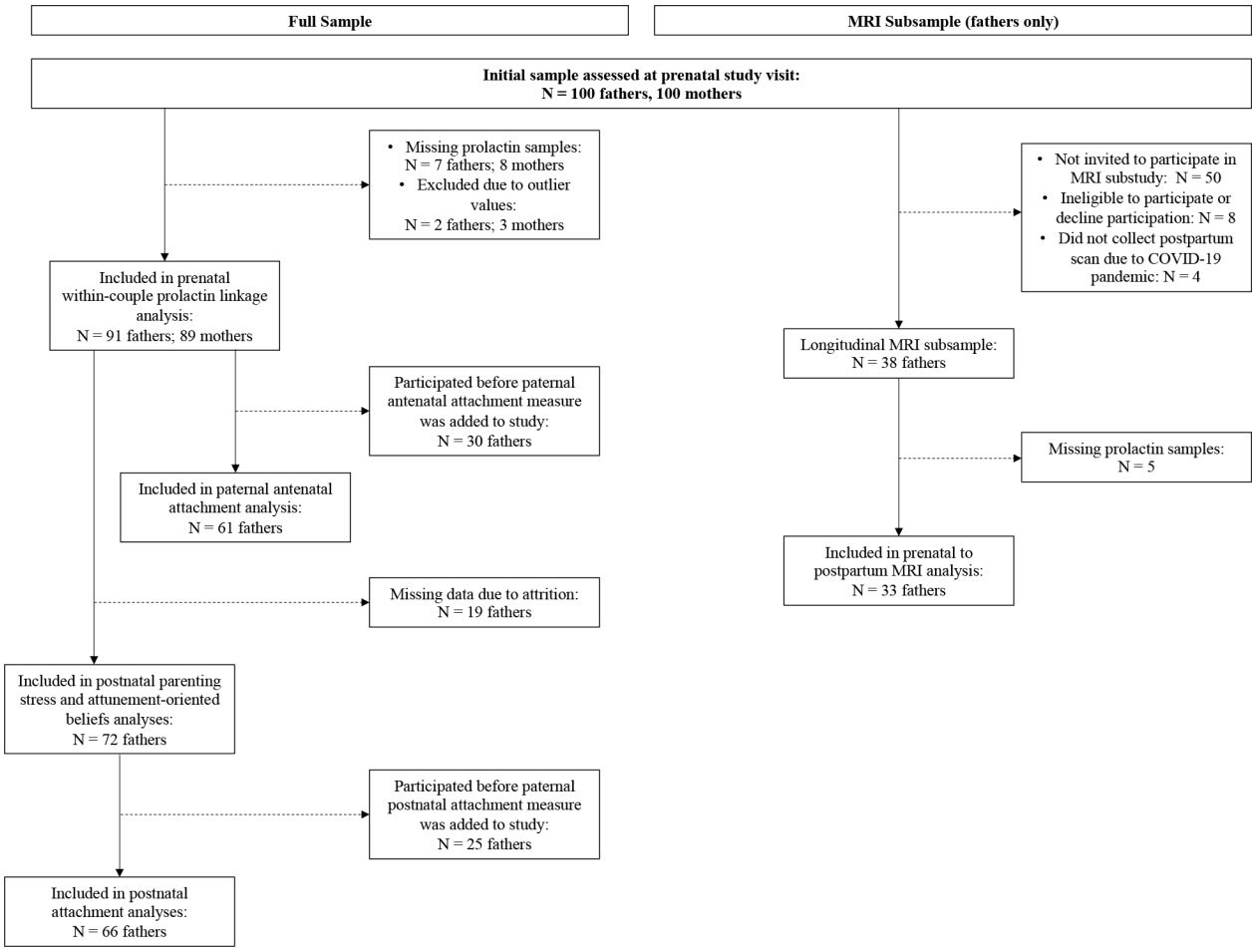
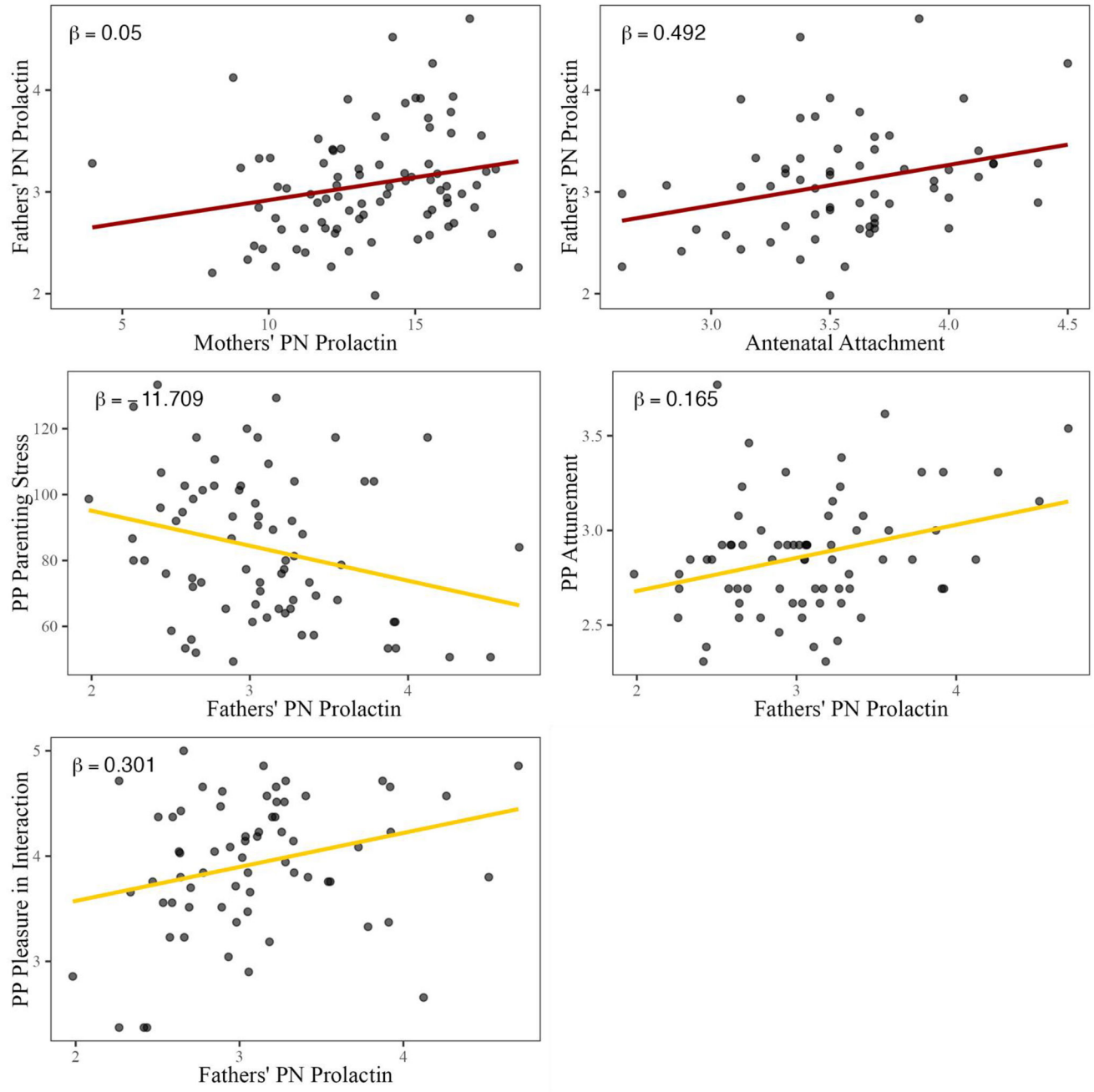


Figure 1.
Sample Size Flowchart



Abbreviations: PN, prenatal; PP, postpartum

Figure 2.

Scatterplots and regression lines of cross-sectional and longitudinal associations between square-root transformed paternal prolactin and study measures.

Table 1.

Sample Demographics and Descriptive Statistics

Demographic/Study Measure	Mean	SD	Range
Father Age at PN Visit, years	33.35	5.59	22 – 57
Father BMI	26.63	4.49	18.75 – 43.93
Mother BMI	26.30	4.09	19.21 – 38.79
Days Pregnant at PN Visit	198.23	29.13	142.65 – 269.61
Baby Age at 3PP (weeks)	14.18	1.89	9.27 – 21.69
Father Plasma Prolactin (ng/mL)	9.69	3.41	3.93 – 22.11
Mother Plasma Prolactin (ng/mL)	187.03	69.06	15.80 – 343.20
PAAS	3.57	.41	2.62 – 4.50
PSI	83.67	21.77	49.33 – 133.33
BCQ: Attunement	2.87	.30	2.31 – 3.77
PPAS: Pleasure in Interaction	3.92	.64	2.37 – 5
PPAS: Patience and Tolerance	4.15	.63	1.99 – 5
PPAS: Affection and Pride	4.80	.35	3.08 – 5
Left Insula Grey Matter Change	.01	1.78	−4.09 – 3.40
Left PCC Grey Matter Change	−.49	1.64	−4.78 – 2.75
Left Nucleus Accumbens Grey Matter Change	.31	6.96	−8.85 – 20.33

	n	%
Current Smoking Status		
Smoker	68	74.7%
Non-smoker	23	25.3%
Race/Ethnicity		
White	45	49.5%
Black	6	6.6%
Hispanic/Latinx	19	20.9%
American Indian/Alaska Native	0	0%
Asian and Pacific Islander	16	17.6%
Other	4	4.3%
Declined to state	1	1.1%
Education		
High School or Equivalent	2	2.2%
Some College	11	12.1%
Associate Degree	2	2.2%
Bachelor’s Degree	43	47.3%
Master’s Degree	21	23.1%
Professional/Doctoral Degree	12	13.1%
Relationship Status		
Married or Domestic Partnership	76	83.5
Cohabitating	15	16.5

Abbreviations: PN, prenatal; PP, postpartum; BMI, Body Mass Index; PAAS, Paternal Antenatal Attachment Scale; PSI, Parenting Stress Index; BCQ, Baby Care Questionnaire; PPAS, Paternal Postnatal Attachment Scale

Table 2.

Zero-Order correlations of key measures

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Paternal Prolactin													
2. Maternal Prolactin	.22*												
3. PAAS	.28*	−.02											
4. PSI	−.26*	−.03	−.36**										
5. BCQ: Attunement	.33**	.25*	.16	−.13									
6. PPAS: Pleasure	.25*	.13	.61**	−.47**	.25*								
7. PPAS: Patience	.21	.06	.54**	−.68**	.09	.70**							
8. PPAS: Affection	−.01	.09	.43**	−.40**	.15	.55**	.53**						
9. Education	−.15	−.05	−.14	.18	−.04	−.22	−.15	−.05					
10. Smoking Status	.17	.00	−.01	.12	.15	−.07	−.08	−.22	.08				
11. BMI	.01	.03	.37**	−.10	.06	.31**	.30*	.37**	−.02	.06			
12. Days Pregnant	.13	.32**	.03	−.01	.00	.05	−.05	.14	.14	.10	.03		
13. Baby Age	.30**	.04	.07	−.02	.09	.06	.09	.09	−.22*	.16	−.24*	.15	
14. Father Age	−.01	−.22*	−.29*	−.03	.05	−.09	−.08	−.04	.14	−.18	−.08	.01	−.03

Abbreviations: PN, prenatal; PP, postpartum; BMI, Body Mass Index; PAAS, Paternal Antenatal Attachment Scale; PSI, Parenting Stress Index; BCQ, Baby Care Questionnaire; PPAS, Paternal Postnatal Attachment Scale

* $p < 0.05$

** $p < 0.01$

*** $p < 0.001$

Table 3.

Hierarchical regression analyses for prolactin and self-reported parenting measures

	Beta Estimates						
Step 1	**Model 1**	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**	**Model 7**
(Intercept)	2.298**	2.505***	89.705*	2.332***	2.789*	3.339***	2.634*
Days Pregnant	.002	.002					
Father's Age	.006	.004	−.266	.004	−.004	.000	−.003
Father's Education	−.074	−.080	3.123	−.008	−.079	.026	−.032
Father's Smoking Status	.216	.189	5.382	.105	−.131	−.244*	−.163
Father's BMI	−.001	.002	−.501	.005	.047**	.037***	.046**
Mother's BMI	.009						
Baby's Age			−.186	.012	.034	.046*	.052
Num.Obs.	88	90	80	80	73	73	73
R2	.069	.067	.057	.038	.147	.238	.132
Step 2	**Model 1**	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**	**Model 7**
(Intercept)	1.548	.739	101.295**	2.039***	2.316*	3.529***	2.177
Days Pregnant	.000	.003					
Father's Age	.016	.021	−.200	.003	−.005	.000	−.002
Father's Education	−.080	−.102	3.092	.010	−.056	.014	−.014
Father's Smoking Status	.308*	.173	7.985	.065	−.232	−.247*	−.217
Father's BMI	−.003	−.017	−.394	.003	.038*	.034***	.042*
Mother's BMI	.013						
Baby's Age			.888	.001	.025	.041	.034
Mother's Prolactin	**.050***						
Father's Antenatal Attachment		**.492***					
Father's Prolactin			**−11.709***	**.165***	**.301***	**.001**	**.251**
Num.Obs.	82	61	71	71	66	66	66
R2	.130	.202	.134	.109	.186	.259	.157
ΔR2	.123	.135	.077	.071	.039	.021	.025

Note:

* p < 0.05

** p < 0.01

*** p < 0.001

BMI = body mass index; Num. Obs. = total number of observations; PN = prenatal; Coefficients which test our hypotheses are **bolded.** Model 1, Paternal prolactin ~ maternal prolactin; Model 2, Paternal prolactin ~ antenatal attachment; Model 3, Postpartum parenting stress ~ paternal prolactin; Model 4, Postpartum attunement ~ paternal prolactin; Model 5, Pleasure in interaction ~ paternal prolactin; Model 6, Affection and pride ~ paternal prolactin; Model 7, Patience and tolerance ~ paternal prolactin

Table 4.

Associations between prenatal prolactin and prenatal-to-postpartum grey matter volume: Partial correlation table controlling for fathers' education and infant age at postpartum scan

	r	*p*
Left hippocampus	−.09	.632
Right hippocampus	.19	.312
Left amygdala	−.01	.997
Right amygdala	.08	.661
Left accumbens	−.49**	.005
Right accumbens	.30	.103
Left posterior cingulate	−.57***	<.001
Right posterior cingulate	.07	.726
Left precuneus	−.05	.791
Right precuneus	−.05	.810
Left insula	−.43*	.016
Right insula	.05	.774

* $p < 0.05$

** $p < 0.01$

*** $p < 0.001$