The psychobiology of early fatherhood: exploring the neural and hormonal aspects

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VRIJE UNIVERSITEIT

THE PSYCHOBIOLOGY OF EARLY FATHERHOOD: EXPLORING THE NEURAL AND HORMONAL ASPECTS

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door

Anna Marlijn Lotz

geboren te Wageningen

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Chapter 1

General Introduction

In the past decades an increase of fathers' participation in infant caregiving has been observed (Bakermans-Kranenburg et al., 2019; Cabrera et al., 2000; Cowan & Cowan, 2019). Research suggests that this change is beneficial, as fathers' involvement and sensitive parenting behavior are associated with positive child development, attachment security, and well-being of the child (Barker et al., 2017; Brown et al., 2012; Cabrera et al., 2000; Deans, 2020; Lucassen et al., 2011; Pleck, 2012; Rodrigues et al., 2021). Higher levels of fathers' involvement and sensitive parenting behavior are thus favorable for the infants' development.

Interestingly, little research focused on the onset of parental behavior and its possible underlying biological mechanism in men becoming a father. There are some indications that fathers experience physical and emotional changes around the birth of their first infant. For example, men report to experience changes in their work and social life (e.g., Genesoni and Tallandini, 2009), changes in their own body (e.g., coevade syndrome, Brennan et al., 2007), and their own thoughts as they change in their representation of their infant (Vreeswijk et al., 2014). The underlying biological system that potentially triggers these changes is still largely unknown, but there are some indications that the neuroendocrine system may be involved as changes in hormone levels and the brain are observed when studying men transitioning to fatherhood (Bos, 2017; Bos et al., 2018; Edelstein et al., 2015, 2017; Gettler, McDade, et al., 2011; Storey et al., 2000). The current thesis will focus on the associations between neuroendocrine system and parenting behavior in fathers (Figure 1.1).

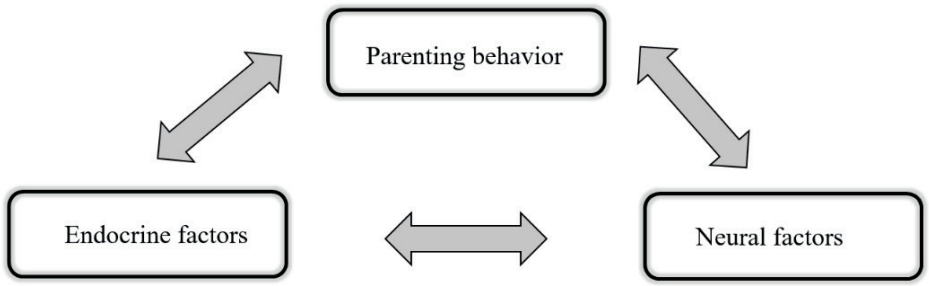

Figure 1.1

The three factors described in the context of first-time fathers

The dimensions of paternal behavior

Fathers parenting behavior can be studied based on different behavioral dimensions. First of all, paternal behavior can be studied in the context of parental sensitivity (Chapter 4). Parental sensitivity is defined as parents' ability to perceive, accurately

interpret, and appropriately and promptly react to infants' signals (Ainsworth, Bell, & Stayton, 1974) and has been studied extensively in parenting research using a variety of behavioral observation settings and coding systems, for example, via a (semi-structured) free play between parent and infant. When no interaction between parent and infant is possible, for instance in the case of an unborn infant, parental thoughts and feelings about their child and about the relationship with their child measured via the Five Minute Speech Sample (FMSS, Lambregtse-van den Berg et al., 2013; Magaña et al., 1986; Weston et al., 2017) may be a suitable alternative. Namely, some previous research indicates that Expressed Emotion, the overall outcome of the assessment, might be associated with parenting style, the quality of the parent–child relationship and the wellbeing of the child (Sher-Censor, 2015; Weston et al., 2017). In this thesis, expressed emotion as a possible correlate of sensitive parenting behavior (Chapter 3) is examined in first-time fathers to be.

Secondly, paternal behavior can be studied in terms of protective behavior. This behavior focusses on parental protection of infants from diseases, accidents and stranger violence which is vital for infant survival during pregnancy and after birth (Bakermans-Kranenburg & Van IJzendoorn, 2017; Hahn-Holbrook et al., 2011). Although this behavior is an essential aspect of parenting behavior, this behavioral dimension has rarely been studied in humans. The current thesis aims to extend the knowledge about paternal protective behavior by introducing two new measurement paradigms for observed and self-reported protective behavior (Chapter 5).

Endocrine factors related to paternal behavior

One of the biological factors that may trigger or regulate the above described dimensions of paternal behaviors is the endocrine system. Evidence points towards changes in fathers' endocrine system already before the birth of the infant. For example, previous research indicated that amongst others men's basal testosterone (T) and estradiol (E2) levels may decline during the course of the pregnancy (Edelstein et al., 2015; Saxbe et al., 2017). In addition, it has been shown that basal levels of T and cortisol (CORT) might change around the birth of their infant (Berg & Wynne-Edwards, 2001; Storey et al., 2000). Moreover, between-subject comparisons revealed that fathers had lower T levels than non-fathers (Grebe et al., 2019; Meijer et al., 2019), although this effect might be confounded by relationship status (Grebe et al., 2019).

Besides the reported hormonal changes during the course of the pregnancy, circulating hormones were studied in relation to parenting behavior as well. For example, lower levels of T are reported to be associated with higher levels of paternal involvement and parenting quality (Meijer et al., 2019). In contrast, higher basal CORT levels in the early postnatal period predicted greater involvement in direct and indirect infant care

measured a few months later (Kuo et al., 2018). In the context of sensitive parenting behavior, basal levels of oxytocin (OT), vasopressin (AVP) and T were reported to be associated with fathers' sensitive behavior (e.g., Apter-Levi et al., 2014; Feldman et al., 2011, 2010; Gordon et al., 2017; Weisman et al., 2014), and administration studies revealed that OT nasal spray led to higher paternal response structuring and less hostility towards the infants (Naber et al., 2010; Naber et al., 2013). Interestingly, only limited research reports on the link between fathers' sensitive behavior and hormone reactivity. Feldman and colleagues observed that fathers with higher levels of stimulatory contact showed an increase in OT after father-infant interaction (Feldman et al., 2010). Both T and CORT seem to decrease after holding or interaction with their infant (Bos et al., 2018; Kuo et al., 2018; Storey et al., 2011). No studies reporting on AVP reactivity were found.

In the context of protective parenting behavior, no previous studies have focused directly on the relation between basal hormone levels and fathers' protective behavior towards their infant. However, when studying the exposure to infant stimuli, e.g., infant cry or infant pictures, there are indications that AVP might be involved in the processing of infant stimuli in (prospective) fathers (Alyousefi-Van Dijk et al., 2019; Atzil et al., 2012; Cohen-Bendahan et al., 2015; Thijssen et al., 2018). In terms of hormone reactivity, T and AVP might have a specific role in the activation of paternal protective behavior as presented in the Steroid/Peptide Theory of Social Bonds (Van Anders et al., 2011), although empirical evidence is limited. A previous study has shown that cry sounds increase salivary T levels in men when no nurturing response is possible (Van Anders et al., 2012), but no studies are available for AVP reactivity.

In sum, there are several studies addressing the possible relation between baseline hormone levels and hormone reactivity in the context of paternal behavior. However, how these endocrine and behavioral factors are related is still largely unknown. The current dissertation aims to enhance our knowledge about the relation between the endocrine system and parenting behavior, focusing specifically on OT, AVP, T and CORT in the context of paternal sensitivity (Chapter 3 and 4) and protective behavior (Chapter 5).

Remarkably, when reporting on the possible role of hormones in context of paternal behavior, most research focus on isolated hormones. However, it should be noted that the situation that hormones act on their own is an exception (Bos, 2017; Feldman & Bakermans-Kranenburg, 2017; Rajhans et al., 2019). For example, studies point towards a relation between OT, AVP and T levels as OT nasal spray administration increased salivary AVP and T levels (Weisman et al., 2014; Weisman, Schneiderman, et al., 2013). Second, it is suggested that several hormones are biologically or functionally related. This is for example illustrated by the fact that OT and AVP have very similar chemical

constructs and AVP receptors are sensitive to both OT and AVP (Carter, 2017; Carter et al., 2020). Moreover, there are indications that T and CORT are related as salivary levels of these hormones were found to be positively associated (Bos et al., 2018; Gettler, Mcdade, et al., 2011), and the HPA-axis and HPG-axis may influence each other (Viau, 2002). Lastly, evidence states that the OT-AVP system might interact with the HPA-axis (e.g.,Carter et al., 2020; Weisman et al., 2013b). Besides the influence of hormones on each other, the interaction between hormones on their effects on behavior is an essential aspect to incorporate in paternal studies (Bos et al., 2018; Gordon et al., 2017; Mehta & Prasad, 2015). In the current dissertation the unique, combined and interactive effects of several parenting hormones are studied, focusing on basal hormone levels (Chapter 4 & 5), hormone reactivity to infant interaction (Chapter 4) and hormone administration (Chapter 3).

Neural factors related to paternal behavior

Another biological factor that has been studied in the light of fatherhood is the neural system. Some studies have focused on the structural changes that might occur in the brain during the transition to fatherhood (e.g..,Hoekzema et al., 2017; Kim et al., 2014), but most studies have focused on fMRI paradigms exposing participants to visual and auditory infant stimuli (Feldman, 2015). Combining these fMRI results, reviews point towards the existence of a parental brain (Feldman, 2015; Rilling & Mascaro, 2017), which include several networks associated with mirror simulation, empathy, mentalizing, motivation and reward, emotion regulation and avoidance (Feldman, 2015; Rilling & Mascaro, 2017). Moreover, evidence points towards the presence of a neural model for infant cry perception (Witteman et al., 2019) and a possible functional network associated with infant protection (Hahn-Holbrook et al., 2011; Van 't Veer et al., 2019). Indeed associations have been observed between neural responses to infant stimuli and (expectant) fathers' parenting behavior (e.g., Alyousefi- van Dijk et al., 2020; Kuo et al., 2012; Mascaro et al., 2014; Van 't Veer et al., 2019), and this supports the idea that neural activity might be a proper correlate for parenting behavior. In chapter 5, we aimed to further explore the neural responses associated with infant protection and the relation with observed and self-reported protective behavior.

Combining hormonal and neural factors

Based on previous research, it can be suggested that neural activity may be modulated by hormones. More specifically, it is proposed that variation in the sensitivity of the brain to central hormone levels might result in inter-individual differences in the neuro-endocrine system and thereby might be related to the observed variability in parenting behavior (for review see Bos, 2017). This theory is supported by hormone administration studies and correlational studies that point towards a possible link between hormone levels and neural activity in fathers (to-be) (Atzil et al., 2012;

Khoddam et al., 2020; Thijssen et al., 2018), although other studies did not find these effects (Li et al., 2017; Mascaro et al., 2014). In chapter 5, we assessed the relation between neural responses to infant-threatening situations and basal T and AVP levels. Moreover, we aimed to explore whether the associations between T and AVP levels and protective behavior would be mediated by neural responses to infant threat in brain areas involved in the parental care network, visual processing, and threat detection.

Research project Father Trials

Data reported in the current dissertation is collected in the research project Father Trials; a project focusing on hormonal and behavioral experiments on prenatal and postnatal parenting (Bakermans-Kranenburg, 2014). Data reported in the third chapter was collected via a double blind randomized controlled within-subject design. Twenty-five prospective fathers were invited for two assessments during pregnancy, with an intervening period of 7 days, and a follow-up assessment after the birth of their child. In the first two assessments, participants self-administered a dose of either 20 IU AVP or a placebo. In the follow-up all participants received placebo. Chapters 4 and 5 focus on data collected in the study 'Baby Dichtbij', a randomized controlled intervention study focusing on men in the early postnatal phase of fatherhood. Seventy-nine first-time fathers were invited for three assessments, with a behavioral intervention focusing on close physical proximity between the first two assessments. The current dissertation describes the data from the first assessment, the baseline measurement.

Outline of the dissertation

Chapter 2 consists of a review article, focusing on the first 1000 days of fatherhood. We discussed social-cultural, behavioral, hormonal and neural aspects of fatherhood in the context of previous literature. Moreover, a biobehavioral model of the emergence of fatherhood incorporating the relation between these four aspects in the prenatal, perinatal and early postnatal phases of fatherhood is proposed. The subsequent chapters zoom in on parts of this model with the overall aim of unraveling the possible endocrine and neural correlates of paternal behavior in first time fathers (see Figure 1.2). In Chapter 3, we focused on one of the factors that may influence paternal sensitivity and involvement, in particular in the period around the birth of the first child, namely fathers' thoughts and feelings regarding their child and their relationship with the child. The study aimed to explore the effect of AVP administration on fathers-to-be Five Minute Speech Sample-based expressed emotion (Daley et al., 2003; Lambregtse-van den Berg et al., 2013; Magaña et al., 1986), emotional content (De Smedt & Daelemans, 2012), and emotional prosody (Banse & Scherer, 1996). Moreover, the influence of the transition to fatherhood on these three parameters was explored. In Chapter 4, we studied father's sensitive parenting behavior in the early postnatal phase of fatherhood. We explored the role of endocrine factors by focusing on (1) the

separate and combined associations of basal OT, AVP, T and CORT levels with sensitivity, and (2) the associations between paternal sensitivity and OT, AVP, T and CORT reactivity following father-infant interactions. Additionally, we explored whether interactions between the various basal hormone levels could predict paternal sensitivity. In Chapter 5, we focus on another dimension of parental behavior. We studied protective parenting behavior and its possible hormonal and neural correlates by introducing three new paradigms, i.e., a newly developed questionnaire 'Paternal Protection Questionnaire', a new behavioral paradigm 'the Auditory Startling Task', and an adapted version of an fMRI threat task (Van 't Veer et al., 2019). In Chapter 6, I provide a summary of the findings and discuss them in light of previous literature. Moreover, I discuss the limitations of the current studies and provide suggestions for future research.

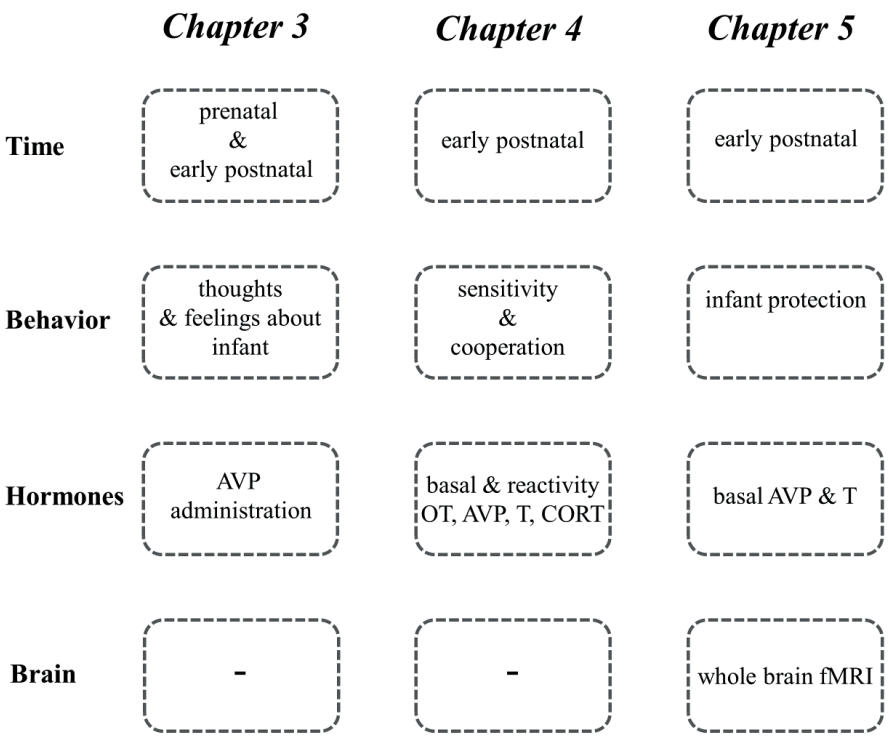

Figure 1.2

Overview of behavioral, hormonal, and neural factors studied in each empirical chapter

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Chapter 2

Birth of a father: Fathering in the first 1,000 days

Bakermans-Kranenburg, M.J., Lotz, A., Alyousefi-van Dijk, K., & van IJzendoorn, M. (2019). Birth of a Father: Fathering in the First 1,000 Days. *Child Development Perspectives*, 13 (4), 247-253. DOI: 10.1111/cdep.12347

Abstract

As a result of societal changes, fathers participate more actively in child care than they used to. In this article, we propose a context-dependent biobehavioral model of emergent fatherhood in which sociocultural, behavioral, hormonal, and neural factors develop and interact during the first 1,000 days of fatherhood. Sociocultural factors, including different expectations of fathers and varying opportunities for paternal caregiving through paid paternal leave, influence paternal involvement. Levels of hormones (e.g., testosterone, vasopressin, oxytocin, cortisol) predict fathers' parenting behaviors, and involvement in caregiving in turn affects their hormones and brain responses to infant stimuli. The birth of the first child marks the transition to fatherhood and may be a critical period in men's lives, with a smoother transition to fatherhood predicting more optimal involvement by fathers in subsequent years. A focus on prenatal and early postnatal fathering may pave the way for developing interventions that effectively support fathering during pregnancy and in the first years of their children's lives.

Keywords: Fathers, Parenting, Hormones, Imaging

Introduction

Fathers matter. The publication of Michael Lamb's book, *The Role of the Father in Child Development*, in 1976 marked growing awareness of fathers' role in the development of their offspring. Since its publication, fathers' involvement in childrearing has increased substantially, at least as documented in Western, industrialized countries. In 1970, fathers in such countries (Belgium, France, the German Democratic Republic, and the United States) worked 50.5 hr per week on average (Roby, 1975). On workdays, they spent an average of 11.8 min on child care (e.g., reading to, playing with, educating, supervising, or traveling with a child), and this doubled to an average of 25.3 min per day on the weekend. As a result of societal changes in these countries, including the increased participation by women and mothers in the labor force, this situation began to change between 1970 and 1980 and men became more active participants in child care. One generation later, in 2010, fathers in five countries (Australia, Denmark, France, Italy, and the United States), spent 34.5 hr per week on average on paid work, and on both weekdays and weekend days, they spent an average of 1.2 hr a day on childcare (Craig & Mullan, 2010), a three- to six-fold increase over what their own fathers typically did. Unfortunately, we know less about such changes in non-Western and less industrialized countries.

Accumulating knowledge points to fathers' role in early child development and highlights neurobiological changes in the transition to parenthood. In this article, we review this literature from the perspective of a biobehavioral model of emergent fatherhood (see Figure 2.1), starting from pregnancy with the transition to parenthood that marks the birth of the father through the first few years after birth. We focus on this phase because researchers and policymakers alike consider the first 1,000 days after conception critical for the child's ability to grow, learn, and thrive (e.g., Berg, 2016 ; https://thousanddays.org; https://publications.parliament.uk/pa/cm201719/cmselect/cmhealth/1496/1496.pdf). In a similar vein, we suggest that the transition to fatherhood is a critical period in men's lives, with a smoother transition to fatherhood predicting more optimal involvement of fathers in subsequent years. Longitudinal descriptive and experimental studies are needed to test this hypothesis; here, we propose a model with components essential for such studies (see Figure 2.1).

A biobehavioral model of emergent fatherhood

The transition to fatherhood is a major developmental milestone for men. Inspired by Bronfenbrenner's bio-ecological perspective (Bronfenbrenner & Ceci, 1994), we propose a model of the transition to fatherhood that considers many levels, including the sociocultural level with respect to different expectations of fathers, childrearing attitudes, and involvement with infants. This level may influence the types of behavior

fathers engage in with their infants (see Figure 2.1). As Figure 2.1 also shows, we propose bidirectional relations between fathering behaviors and hormonal and neural components in the prenatal, perinatal, and postnatal phases. We discuss each of these areas to show how they affect and are affected by the transition to parenthood. Research has described these transitions in mothers more frequently than in fathers, but the effects of fathering on child development, in and of itself and in interaction with maternal behavior, have also been shown (Dagan & Sagi-Schwartz, 2018). Therefore, we need a complementary focus on fathers.

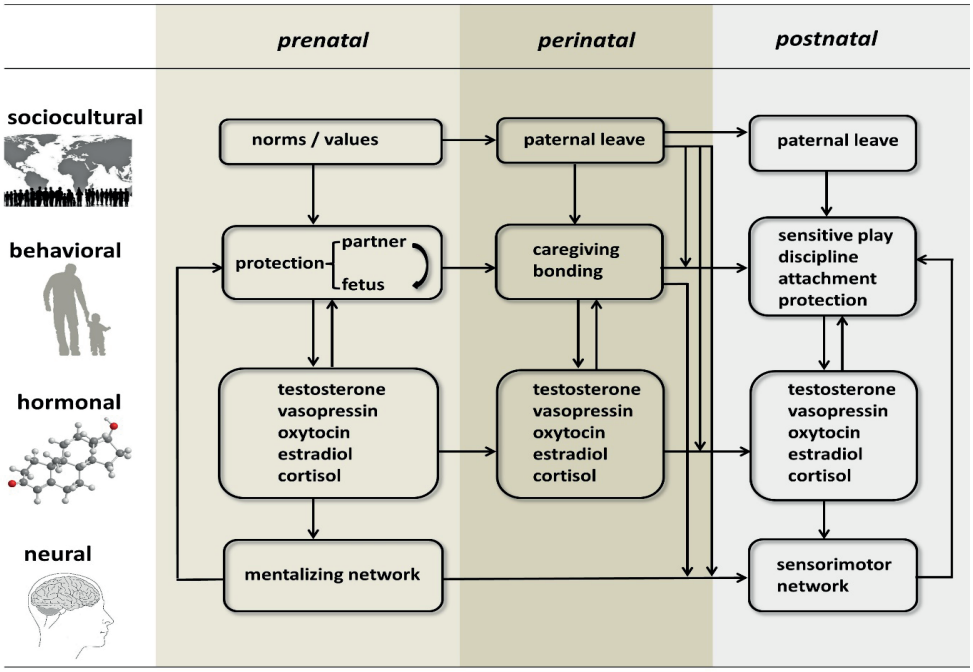

Figure 2.1

A biobehavioral model of emergent fatherhood

Note. The transition to fatherhood varies at many levels: sociocultural, behavioral, hormonal, and neural. Bidirectional relations exist between fathering behaviors and hormonal and neural components in the prenatal, perinatal, and postnatal phases. For example, expectations of fathers in the sociocultural level may influence their bonding and involvement in caregiving behaviors, which may in turn influence but may also be influenced by hormonal and neural processes.

Sociocultural factors

Sociocultural norms and values with regard to fathers' involvement in child care have changed over time, affecting fathers' personal norms and behaviors. Along with these changes, paid paternity leave has become more accessible, increasing opportunities for paternal caregiving that in turn may lead to hormonal and neural changes in fathers (see Figure 2.1). But significant differences in parental leave create disparities in opportunities for fathers' involvement in infants' care. Of the 186 countries examined by one study (Heymann & McNeill, 2013), 179 provided paid maternity leave, and 81 countries extended paid leave to new fathers through parental leave that could be taken by either parent, or through paternity leave specific to fathers. The United States is one of the few industrialized countries without any statutory national paid family leave provisions for either parent. On the other end of the continuum, Sweden allows parents 540 days of paid parental leave per child, of which 90 days are nontransferable for each parent, with the right to return to employment. Not all fathers use the opportunities for paid leave, and in general, fathers take leave less frequently than mothers.

Why do couples use more maternal leave than paternal leave? First, breastfeeding favors the mother's proximity to the infant, particularly during the first 6 months of the infant's life. Second, because of income differences between men and women, it is often economically less feasible for fathers to reduce their working hours than it is for mothers. Third, work-related and social expectations may push mothers into the role of primary caregivers and fathers into the role of secondary caregivers. Fourth, mothers may be (unconsciously) reluctant to delegate caregiving responsibilities to their partners (maternal gate-keeping; Gaunt, 2008). As a result, fathers spend less than half as much time in direct one-on-one interaction with their children as mothers, especially in early childhood (Wood & Repetti, 2004). Although quantity of time invested in parenting is considered less important than quality (Ainsworth, 1967), it takes time to get to know infants, become aware of their preferences, and read their (attachment) signals. Time spent in direct responsibility for infant care is related linearly to connectivity between parenting-related brain areas in fathers (Abraham et al., 2014), showing that sociocultural norms that affect paternal involvement (indexing the behavioral level of our model) also affect the neural level indirectly.

Paternal behavior

For at least two reasons, it is important to realize that fathering starts during pregnancy. First, the prenatal environment has far-reaching consequences for child development (Glover, O'Donnell, O'Conner, & Fisher, 2018), and fathers can influence that environment positively (e.g., by quitting smoking) and negatively (e.g., by engaging in partner violence). Behaviors that protect the pregnant partner, such as ensuring

that she gets sufficient rest and avoids pathogenic food, protect the infant and benefit the baby's development. Whether and how interindividual and intraindividual variance in such behaviors is related to hormonal and neural variation, and to variation in postnatal parenting behavior, remains to be determined.

Second, expectant fathers may experience somatic pregnancy symptoms, known as the couvade syndrome, including nausea, leg cramps, appetite and mood changes, and weight gain (Mason & Elwood, 1995). Estimates of incidence range from 11% to 79%, depending on what criteria studies use for inclusion. In nonindustrialized societies, the couvade syndrome may be a ritualization of the transition to fatherhood (e.g., in some cultures, the father remains in bed and is nurtured after the birth of the baby, while the mother resumes work), but it may also be related to typical physiological processes in fathers that eventually lead to parental responsiveness (Mason & Elwood, 1995). In one study, fathers with more couvade symptoms had a greater decrease in testosterone after exposure to infant cues (Storey, Walsh, Quinton, & Wynne-Edwards, 2000). Thus, the symptoms may be observable phenomena resulting from underlying hormonal changes that also predict dimensions of caregiving. Researchers have not yet related the couvade syndrome to the quality of postnatal caregiving.

In the first year of an infant's life, establishing an attachment relationship is an important developmental milestone. Although attachment theory has sometimes been criticized for emphasizing the traditional role of mothers as sole caregivers, both Bowlby (1969/1982) and Ainsworth (1967) made explicit that fathers were common and capable attachment figures. In fact, Bowlby argued, based on Harlow's (1958) experiments with fur and wired rhesus monkey mothers, that (breast-)feeding was not essential for the infant-parent relationship and that fathers could be capable caregivers of young infants. Indeed, the first study of the Strange Situation Procedure with fathers and mothers showed similar proportions of secure attachment with both parents (Main & Weston, 1981).

Parental responses to infants' interactive behaviors are generally rated in terms of sensitivity or emotional support. Similar to the pattern of associations for mothers, higher levels of paternal sensitivity predict generally more favorable child outcomes. In correlational and experimental research, mothers' sensitivity is associated modestly but robustly with secure infant-mother attachment ($r = .24$-$.35$; Verhage et al., 2016). For fathers, this meta-analytic association is weaker ($r = .12$; Lucassen et al., 2011), with fathers' observed sensitivity sometimes similar to but often lower than mothers' sensitivity (e.g., Volling, McElwain, Notaro, & Herrera, 2002). Indeed, it is not uncommon for studies to report that fathers are substantially less sensitive and less involved than mothers, but that similar proportions of children are securely attached

to these fathers and mothers (e.g., Lickenbrock & Braungart-Rieker, 2015). This might suggest that the sensitivity or attachment measures used with mothers are less valid when used with fathers, or that different dimensions of parenting predict infant-father attachment (Grossmann et al., 2002). Given that the intergenerational transmission of attachment is similar in strength for fathers and mothers (Verhage et al., 2016), the search for paternal behavior underlying this transmission should get more attention. Stimulatory play and support of (cognitive) exploration may be paternal behaviors that promote secure infant-father attachment. Limit-setting has also been suggested as specific although not exclusive dimension of the father-child relationship (Grossmann et al., 2002).

Just like with mothers' parenting, fathers' parenting may be hampered by feelings of depression in the postnatal period. The prevalence of perinatal depression in fathers is 4-10% (Paulson, Bazemore, Goodman, & Leiferman, 2016), and fathers' depression has been associated with problem behavior in children (Ramchandani, Stein, Evans, & O'Connor, 2005) and subsequent depression in the children themselves (Gutierrez-Galve et al., 2018). Paternal perinatal depression influences the father-child relationship and is related to less optimal relationships between couples as well as to maternal depression (Paulson et al., 2016), doubling the risk for unfavorable child outcomes. As in mothers, in fathers, hormonal imbalances may be related to postpartum depression (Saxbe et al., 2018), but lack of sufficient sleep may also play a role: 35% of parents with children under age 2 report that they get only 5-6 hr of sleep per night (Krueger & Friedman, 2009). Identifying risk factors for paternal perinatal depression is an important step towards prevention, ideally before the baby is born.

Hormones

When women get pregnant, they experience hormonal changes. Oxytocin levels increase during pregnancy, as do levels of estradiol, testosterone, and cortisol (Edelstein et al., 2017). After a peak in oxytocin and cortisol around childbirth, levels decrease in the postpartum period. Do any hormonal changes prepare men for fatherhood?

Over the course of pregnancy, testosterone and estradiol decline in men, and in one study, men with greater declines were more involved in child care after birth (Edelstein et al., 2017). Indeed, testosterone is generally considered favorable to mating and unfavorable to parenting efforts, and in primary studies (e.g., Gettler, McDade, Feranil, & Kuzawa, 2011) and meta-analyses, fathers tend to have lower levels of testosterone than nonfathers, but the effect size is modest (r = .11; Meijer, Van IJzendoorn, & Bakermans-Kranenburg, 2019); this is probably because downregulation of testosterone levels depends on fathers' actual involvement in child care and the presence or absence of other competitive demands. In one study, fathers' lower basal testosterone in the

immediate postnatal period predicted more involvement in childcare 2-4 months later (Kuo et al., 2018). Fathers with lower basal testosterone levels tend to engage higher-quality parenting (meta-analytic effect size r = .07; Meijer et al., 2019). However, testosterone may prepare fathers for caregiving; for example, exposure to cry stimuli increases fathers' testosterone levels (Fleming, Corter, Stallings, & Steiner, 2002; Van Anders, Tolman, & Volling, 2012).

Monogamous male prairie voles have elevated levels of the hormone vasopressin after mating, leading to territoriality and partner protection (Winslow, Hastings, Carter, Harbaugh, & Insel, 1993). Similar preparatory mechanisms, including enhanced sensitivity to vasopressin, may be found in humans. Administering vasopressin to expectant fathers promoted attention to virtual baby-related avatars (Cohen-Bendahan, Beijers, Van Doornen, & de Weerth, 2015), and affected neural and behavioral responses to sounds of infant crying (Alyousefi-Van Dijk et al., 2019; Thijssen et al., 2018), pointing to a role for vasopressin in responding to infant distress. Moreover, vasopressin levels may be related to fathers' stimulatory interaction with their infants (Abraham & Feldman, 2018).

Levels of oxytocin, another hormone related to parenting (Feldman & Bakermans-Kranenburg, 2017), increased over the first 6 months of fatherhood and after stimulatory play (Abraham & Feldman, 2018), while experimentally increased oxytocin levels led to more stimulatory play in fathers (Naber, Van IJzendoorn, Deschamps, Van Engeland, & Bakermans-Kranenburg, 2010). This experimental study was also the first to show that administering oxytocin to fathers affected fathers' behavior.

Cortisol may also play a role in fathers' parenting. In mothers, higher levels of cortisol when babies are 2-24 months old are related to lower maternal sensitivity (Finegood, Blair, Granger, Hibel, & Mills-Koonce, 2016), but directly after birth, high levels of cortisol are associated with more affectionate infant-directed behavior (Fleming, Steiner, & Corter, 1997). In fathers, cortisol levels increase in response to infant crying (Fleming et al., 2002), and decrease when they hold their newborn (Kuo et al., 2018) or interact with their toddler (Storey, Noseworthy, Delahunty, Halfyard, & McKay, 2011). The distinction between basal cortisol levels and cortisol reactivity may be essential. Cortisol reactivity may be functional in responding to stressors such as the birth experience or infant distress, but (chronic) high cortisol levels may not be conducive to sensitive parenting. Indeed, in one study, fathers' higher prenatal cortisol levels predicted lower quality of parenting 6 weeks postnatally (Bos et al., 2018). Moreover, cortisol may interact with testosterone in relation to parenting behavior. During prenatal care of a life-like infant doll, cortisol was negatively associated with quality of caregiving in fathers with high testosterone levels (Bos et al., 2018).

In summary, hormonal changes in the transition to fatherhood seem related to parenting behavior bidirectionally (See Figure 2.1). Moreover, hormonal changes may induce or accompany changes in brain structure and functioning. Next, we turn to this issue.

Neural networks

In mothers, reductions in grey matter volume in brain areas related to parenting have been observed from before to after pregnancy, while no such changes were apparent in the fathers (Hoekzema et al., 2016). However, changes in fathers' grey matter volume in the postnatal period (between 2–4 weeks and 12–16 weeks postpartum) have been seen (Kim et al., 2014). In animals, grey matter volume increased in brain regions involved in the detection of salient infant cues and regulating parenting behavior, and that are especially sensitive to oxytocin and vasopressin through high densities of the pertinent receptors. Structural brain changes in new mothers can be induced by endocrine changes around pregnancy and childbirth, or by caregiving experiences after birth that may differ between mothers (who are often primary caregivers) and fathers (who are often secondary caregivers). To disentangle these two factors, and focusing on neural responses rather than morphology, one study compared primary caregiving mothers, secondary caregiving fathers, and primary caregiving (homosexual) fathers after the birth of their first child (Abraham et al., 2014). When watching themselves interact with their infant, primary caregiving fathers were similar to secondary caregiving fathers in the activation of their superior temporal sulcus (STS), the social understanding network, but similar to mothers in the activation their amygdala, the emotional processing network. This points to the influence of caregiving experiences on brain functionality, which is corroborated by the finding that the connectivity between the STS and the amygdala increased linearly with time spent directly responsibility for infant care.

In a meta-analysis of brain responses of 350 people, 95 of whom were fathers, to sounds of infants' cries, men showed more activity than women in the right inferior frontal gyrus (IFG), extending into the temporal pole and left angular gyrus (Witteman et al., 2019). The right IFG is involved in mentalizing, while the angular gyrus is involved in semantic processing. This suggests that men may preferentially activate a mentalizing network when processing infant cries. Women showed more activity in the insula (involved in emotional processing). The meta-analysis also compared parents and (partnered) nonparents. Compared to adults without children, parents shifted towards more activity in a sensorimotor network including the insula, pre- and postcentral gyrus, and the right putamen, enabling the integration of emotional information with somatosensory and motor information, and paving the way for behavioral responses (see Figure 2.1).

A study of processing threat to infants looked at the neural basis for protective parenting before and after the birth of the fathers' first child (Van 't Veer, Thijssen, Witteman, Van IJzendoorn, & Bakermans-Kranenburg, 2019). In this imaging study, fathers viewed videos of an infant in danger and matched control videos without such danger, and were told to imagine that the infant was their own or someone else's. Neural responses in bilateral motor areas, possibly indicating preparation for action, were stronger when fathers-to-be imagined that the threatened infant was their own rather than someone else's, but after the birth of their baby, the distinction between responses to one's own and someone else's infant faded (Van 't Veer et al., 2019). This suggests that protective mechanisms present during pregnancy may broaden to include other babies after the experience of having an infant.

Directions for research and intervention: The father-to-be

After decades during which men and infants were often perceived as inhabiting different worlds, their worlds have met. The transition to fatherhood is a major life event that may predict parenting involvement and child development through toddlerhood and middle childhood into adolescence. In our review, we focused on fathering in the first 1,000 days, and father-infant interaction can be supported as early as pregnancy. In our lab, we tested a prenatal Video-feedback Intervention program using ultrasounds between the 21st and 30th week of the pregnancy. Each father is invited to interact with the fetus, verbally or by softly massaging the infant through the mother's abdominal wall. The baby's response is seen through ultrasound, a safe and noninvasive way to watch and wonder about the unborn child. The interaction is videotaped and reviewed with the father in three sessions, focusing on (a) infant's attachment versus exploration signals, (b) speaking for the baby (e.g., *she seems really relaxed when you sing that song for her*), and (c) sensitivity chains (movement of the fetus, parental response, potential response of the fetus). The parenting coach doing the intervention uses the video fragments to illustrate each theme. Seeing the infants respond to their fathers singing or reading to them is a moving experience, one that hopefully creates a head start for fathers.

Prenatal fathering experiences like this may support and extend the increased involvement of fathers in childrearing that we have seen in the past 50 years. Since involvement in caregiving affects fathers' hormonal and neural functioning, such effects on fathers may be lasting, but this issue requires further research. The question of how changes in men's behavior, and in their hormonal and neural functioning in the prenatal period are related to each other and to sociocultural factors warrants more attention. Sociocultural norms and expectations regarding fathers' involvement during pregnancy may set the stage for fathers' involvement after birth. Given the effects of

fathering on child development, researchers and policymakers should give a more prominent place to fathers during pregnancy and the early postnatal period for the sake of the child and the family.

Author contribution (CRediT)

MJB-K: Conceptualization, Writing- Original Draft, Supervision, Project administration. AL: Writing – Review & Editing, Visualization. KA-vD: Writing- Review & Editing. M-vIJ: Conceptualization, Writing- Review & Editing.

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Chapter 3

Vasopressin and parental expressed emotion in the transition to fatherhood

Lotz, A.M., Rijlaarsdam, J., Witteman, J., Meijer, W., van Dijk, K., van IJzendoorn, M.H., & Bakermans-Kranenburg, M.J. (2020). Vasopressin and parental expressed emotion in the transition to fatherhood, *Attachment & Human Development*, DOI: 10.1080/14616734.2020.1719427

Abstract

In the last decades, parenting researchers increasingly focused on the role of fathers in child development. However, it is still largely unknown which factors contribute to fathers' beliefs about their child, which may be crucial in the transition to fatherhood. In the current randomized within-subject experiment, the effect of nasal administration of vasopressin (AVP) on both Five Minute Speech Sample-based (FMSS) expressed emotion and emotional content or prosody was explored in 25 prospective fathers. Moreover, we explored how the transition to fatherhood affected FMSS-based parameters, using prenatal and early postnatal measures. Analyses revealed that FMSS-based expressed emotion and emotional content were correlated, but not affected by prenatal AVP administration. However, child's birth was associated with an increase in positivity and a decrease in emotional prosody, suggesting that the child's birth is more influential with regard to paternal thoughts and feelings than prenatal AVP administration.

Keywords: Five Minute Speech Sample, Vasopressin, Paternal Sensitivity, Emotional Prosody

Introduction

Parenting research has long focused on mothers and their role in child development. This is not surprising given that mothers are generally the primary caregivers within families (Cabrera, Tamis-Lemonda, Bradley, Hofferth, & Lamb, 2000). However, over the last decades a change in family life has occurred, with an increasing role for fathers in caregiving, as also reflected in research on fathers (see Cowan & Cowan, 2019, in a special issue of *Attachment and Human Development* on fathers; Cabrera et al., 2000). This is considered to be a positive development since paternal involvement and sensitivity, reflecting the quantity and quality of fathers' caregiving investments, contribute to positive development and well-being of the child (Barker, Iles, & Ramchandani, 2017; Brown, Mangelsdorf, & Neff, 2012; Cabrera et al., 2000; Pleck, 2012). Indeed, both paternal involvement and paternal sensitivity have been associated with father-child attachment security (Brown et al., 2012; Lucassen et al., 2011). In the current study, we explore one of the factors that may influence paternal sensitivity and involvement, in particular in the period around the birth of the first child, namely fathers' thoughts and feelings regarding their child and their relationship with the child, using the Five Minute Speech Sample.

The transition to fatherhood is often perceived as a life-changing event. During the first few weeks to months after their child's birth, first-time fathers experience changes in the relationship with their partner, as well as difficulties in finding a new work-family balance. In addition, they may be confronted with their unrealistic expectations of fatherhood and frustrations about their paternal (in-)competence (e.g., Deave & Johnson, 2008; Genesoni & Tallandini, 2009; Goodman, 2005; May & Fletcher, 2013). Within this time-window, most new fathers have to adapt their ideas about fatherhood and consider what type of father they want to be. This regulation of paternal emotions, thoughts, and behaviors might facilitate or hamper an emotionally rewarding feeling when being with the child (Goodman, 2005).

The neuroendocrine system might be involved in the regulation of paternal behavior. In the past decades, neuroendocrine research has provided ample evidence that the parent - child interaction and caregiving behaviors are influenced by neuropeptides and hormones, including oxytocin (OT), vasopressin (AVP), testosterone (T), and prolactin (Prl) (e.g., Abraham & Feldman, 2018; Feldman & Bakermans-Kranenburg, 2017; Rilling & Mascaro, 2017). Although the vast majority of this work focused on mothers, there is evidence that hormonal levels are associated with paternal behavior and father-child interactions. More specifically, multiple studies have shown a relation between OT and typical paternal behavior observed during father-child interactions, such as responsive structuring and stimulatory touch (e.g., Feldman, Gordon, Schneiderman, Weisman, &

Zagoory-Sharon, 2010; Naber, Poslawsky, Van IJzendoorn, Van Engeland, & Bakermans-Kranenburg, 2013; Naber, van IJzendoorn, Deschamps, van Engeland, & Bakermans-Kranenburg, 2010). Furthermore, lower salivary T levels have been associated with increased participation of fathers in child care and quality of caregiving, both prenatally (Bos et al., 2018; Edelstein et al., 2017) and postnatally (Bos et al., 2018; Gettler, McDade, Feranil, & Kuzawa, 2011).

The neuroendocrine system might play a role in the transition to fatherhood as well. Although the hormonal changes in fathers during pregnancy are not as pronounced as those of mothers, Prl was found to increase in first-time fathers during the course of pregnancy (Storey, Walsh, Quinton, & Wynne-Edwards, 2000), T was found to decrease during pregnancy and thereafter (Edelstein et al., 2015; Storey et al., 2000), and was reported to remain significantly lower during fatherhood (Gettler et al., 2011). As suggested by Bos (2017), inter-individual variation in the endocrine system may be related to variability in parenting style, due to variation in peripheral and central hormone levels and variation in the sensitivity of the brain and peripheral nodes of endocrine axes for these hormones. Most endocrine research has focused on OT and T, and the potential role of AVP has been somewhat neglected. To address this gap in the literature, the current study focused on the role of AVP in first-time fathers.

Research in non-monogamous and biparental mammals indicates that AVP is involved in the development of paternal behavior. For example, central administration of AVP in non-monogamous male meadow voles that were pup-unresponsive activated paternal behavior (Parker & Lee, 2001). Furthermore, in biparental male prairie voles, AVP injections in the lateral septum dose-dependently increased paternal behavior while AVP-induced paternal behavior decreased after blocking the $V1_a$ receptor with an antagonist (Wang, Ferris, & De Vries, 1994). Moreover, in both male and female prairie voles, an increase of AVP mRNA was observed after birth of offspring (Wang, Liu, Young, & Insel, 2000). In humans, there is evidence that AVP is involved in paternal behavior, as well. Apter-Levi, Zagoory-Sharon, and Feldman (2014) showed that plasma AVP was positively related to observed stimulatory contact in parent - child interactions for both mothers and fathers (Apter-Levi et al., 2014). However, in a sample of fathers Atzil, Hendler, Zagoory-Sharon, Winetraub, and Feldman (2012) observed a negative relation between plasma AVP and brain areas involved in empathy and social cognition in response to short video clips of own infant versus an unfamiliar infant. In the same vein, Abraham et al. (2017) found that AVP might be associated with a negative co-parenting style. Thus, AVP has not always been shown to support sensitive (co-)parenting.

Nevertheless, experimental manipulation of AVP levels through nasal administration revealed that AVP might promote orientation towards babies (Cohen-Bendahan, Beijers, van Doornen, & de Weerth, 2015) and is involved in the processing of auditory infant stimuli (Thijssen et al., 2018) in first-time fathers-to-be. Furthermore, it might be suggested that AVP is involved in distinguishing between own and unknown infant (Alyousefi-van Dijk et al., 2019). Interestingly, no effect of AVP administration was observed in the neural response to infant stimuli in fathers of toddlers (Li, Chen, Mascaro, Haroon, & Rilling, 2017). It may thus be the case that AVP is particularly relevant during the transition to parenthood (Alyousefi-van Dijk et al., 2019).

Parental sensitivity, defined as the parent's ability to perceive, adequately interpret and react to infants' signals in an accurate way (Ainsworth, Bell, & Stayton, 1974), is usually studied during parent-infant interactions. Obviously, alternative approaches should be considered when investigating dimensions of parenting in prospective first-time fathers, who are transitioning to parenthood. When parenting sensitivity cannot easily be assessed because of the absence of a baby, parental thoughts and feelings about their child and about the relationship with their child may be relevant. One of the possibilities to measure these is the Five Minute Speech Sample (FMSS), which has been adapted for use with expectant fathers (Lambregtse-van den Berg et al., 2013). Originally, the FMSS had been developed by Magaña et al. (1986) as a psychiatric research tool; relatives of a psychiatric patients were interviewed to assess the quality of their relationships with the patient and relatives' feelings about the patient (Magaña et al., 1986; Vaughn & Leff, 1976). During the last decades, the FMSS has been adapted for parenting research and implemented in the field of parenting and developmental research, both focusing on healthy families and families in which the parent or child suffers from a psychiatric disorder (Weston, Hawes, & Pasalich, 2017). Parents are asked to respond to one or two general questions and to talk for 5 min about their future or current child and the relationship with their child. The overall outcome of the assessment is referred to as Expressed Emotion (EE), indicating positive and negative thoughts and feelings about the child and the relationship with the child. Some previous research indicate that EE might be associated with the quality of parent – child relationship and the wellbeing of the child (Sher-Censor, 2015). For example, it has been shown that parental EE and the constituting constructs, criticism (CRIT) and emotional over-involvement (EOI), are associated with the child's lower emotional and physical well-being (reviewed by Sher-Censor, 2015). One study found a significant link between mothers' EE and children's disorganized attachment at 6 years of age (Jacobsen, Hibbs, & Ziegenhain, 2000), but another study failed to find such an association (Gravener et al., 2012). Furthermore, positive and negative associations are found between the EE and observed positive and negative parenting, respectively (Weston et al., 2017). Moreover, it has been shown that the FMSS coding system can be used for prenatal

assessments (Lambregtse-van den Berg et al., 2013), and that prenatal EE might predict postnatal parental sensitivity of both mothers and fathers, up to several years after birth (Lucassen et al., 2015).

Hormones in general, and AVP in particular, might influence the emotional content of parental descriptions of their child (i.e., *what* they are saying, also called emotional semantics) as well as *how* parents talk about their offspring (i.e., emotional prosody). Given the rapid developments in computerized text analysis in the past 20 years, automatic computer coding of the FMSS recordings might reveal response patterns that are meaningfully related to respondent's FMSS-based expressed emotion, as coded by trained raters. Such automatic coding enables sentiment analysis, with ratings for subjectivity (objective vs subjective) and polarity (positive vs negative) of the content of the text in a standardized manner. In addition to content analysis, automatic coding can be used to determine the emotional prosody of the responses. Previous research has shown that emotional prosody is expressed acoustically primarily in fundamental frequency, the energy distribution of the frequency spectrum, and the temporal domain (Banse & Scherer, 1996). For example, it has been shown that the fundamental frequency is higher in recordings characterized by anger, fear and joy, while it is lower in recordings characterized by sadness (Pittam & Sherer, 1989). Thus, automatic coding may provide additional information about the FMSS.

The current study aims to explore (i) the extent to which coder-rated expressed emotion and computer-coded emotional content are associated, (ii) the effect of AVP administration on FMSS-based expressed emotion, emotional content and emotional prosody, and (iii) the effect of the transition to fatherhood on FMSS-based expressed emotion, emotional content, and emotional prosody. Concerning the first question, we speculate that ratings by human coders and computer-coded variables will be (at least partly) associated because polarity, positive comments and critical comments are all based on indicators of positivity and negativity in the speech sample. Due to the absence of research on the role of AVP or the baby's birth in fathers' speech about their baby, no a priori hypotheses are presented for the effects of AVP and the transition to fatherhood on the FMSS variables.

Methods

Participants

Twenty-five prospective fathers participated in the study. They were recruited through midwives and ads on Leiden University affiliated webpages. All participants cohabitated with their pregnant partners, spoke Dutch fluently, were in good physical and mental

health (i.e., had no psychiatric, neuroendocrine or neurological diagnosis), and had no significant intake of alcohol or drugs. At the time of the first assessment, the mean age of the participants was 31.92 years (SD=4.30) and educational levels were high, with 80% of the fathers having obtained a higher education degree, and 20% having completed only secondary school. The mean gestational age of the unborn infants was 27.02 weeks (SD = 4.91) at time of the first assessment. At the time of the postnatal assessment (n = 20), 29 weeks (SD = 5.27) after the first assessment, the mean age of the infants was 15.66 weeks (SD = 2.36). Average birth weight of the child was 3586.30 grams and reported health of the child was very good; with 90% reported as excellent or very good, 5% reported as good, and 5% reported as moderate. All children except one were born full-term, one child was born after 36 weeks gestational age. Fifteen infants were male, nine were female, and the sex of one infants was not reported. The study was approved by the Ethics Committees of the Institute of Education and Child Studies at Leiden University and the Leiden University Medical Centre, as well as the Central Committee on Research Involving Human Subjects. All participants signed informed consent.

Procedure

Participants were invited for two assessments during the pregnancy (n = 25), with an intervening period of 7 days, and a follow-up assessment after birth (n = 20). All assessments took place at the Leiden University Medical Centre (LUMC). Briefly, each assessment consisted of three parts: 1. nasal spray administration; 2. neural measures with (f)MRI; and 3. behavioral measures, including the Five Minute Speech Sample (FMSS). More detailed descriptions about the other measures can be found elsewhere (Thijssen et al., 2018; van 't Veer, Thijssen, Witteman, van IJzendoorn, & Bakermans-Kranenburg, 2019). Following all assessments, participants completed some online and e-dairy questionnaires at home.

During the first two assessments, participants self-administered a dose of either 20 IU vasopressin (AVP, Vasostrict, Par Pharmaceutical) or a placebo (PL, Chlorobutanol, LUMC pharmacy) using Syringe MAD-nasal devices (Teleflex, Morrisville), with equal distribution across both nostrils, under supervision of a research assistant. The order of receiving either AVP or PL nasal sprays during the first and second assessment was counterbalanced and unknown to both participant and researchers. During the follow-up (postnatal) assessment, all participants self-administered a placebo. The average time between the administration of the nasal spray and the FMSS was 155 min (*SD* = 10) for PL, 154 min (*SD* = 8) for AVP, and 153 min (*SD* = 9) in the postnatal assessment.

Measures

Five Minute Speech Sample (FMSS)

We used an adaptation of the original FMSS paradigm (Daley, Sonuga-Barke, & Thompson, 2003; Lambregtse-van den Berg et al., 2013; Magaña et al., 1986). Participants were instructed to talk for 5 min about their unborn child (first two visits) and their newborn child (third visit); "What do you hope or expect your child will be like and how would you like to relate to your child?". To prevent prolonged silences, we asked an additional question 3 min later: "What do you think it will be like when your child has grown up?". Recordings were performed using a TASCAM DR-05 digital recorder (TASCAM, division of TEAC America, Montebello California) at 16 bit resolution and a 44.1 khz sampling rate. The recordings were subsequently transcribed using PRAAT software (Boersma & Weenink, 2018) for automated acoustic and text analysis as well as manual coding of content. A random sample of 12% of the prenatal transcripts was transcribed by two raters, allowing for an automatic inter-rater reliability analysis using the F1 metric, the harmonic mean of recall and precision ranging between 0 and 1, after each pair of transcripts was aligned using the Needleman-Wunsch algorithm. This procedure was performed initially on a selection of transcripts to improve the transcription protocol and for the final reliability analysis (Garrard, Haigh, & de jager, 2011). Interrater-reliability of FMSS transcripts as measured with the mean F1 metric was .77, which is adequate (Garrard et al., 2011). A third rater was trained to transcribe the postnatal recordings. Two transcripts were manually compared with the transcripts of the two other raters and showed adequate reliability.

To score FMSS-based expressed emotions, two FMSS coding manuals developed for prospective parents (Lambregtse-van den Berg et al., 2013) and new parents (Daley et al., 2003) were combined to match our study population of fathers in the transition to parenthood. The resulting coding system consisted of six scales: initial statement, warmth (with three subscales, tone of voice, spontaneity, and concern & empathy), relationship, emotional over-involvement, critical comments, and positive comments. For critical comments as well as positive comments, the frequencies were coded. Critical comments were scored when high expectations were set, e.g. "I hope my child will be very smart and athletic, otherwise, I would be very disappointed". Positive comments were coded when the participant talked about his child with praise, approval, or appreciation, e.g., "I will love my child whatever it will be like". The other scales were rated on 3-point rating scales as either 1 = low, 2 = moderate, 3 = high (or 1 = negative, 2 = neutral, 3 = positive).

High Expressed Emotions (EE) was scored when at least one of the following scales was rated as 1 (negative or low): initial statement, warmth, relationship, and emotional over-involvement, *and* more critical comments than positive comments were observed.

A borderline EE score was assigned if only one of these two criteria was met. Raters were trained by two of the authors (JR, AL) and inter-rater reliability was assessed based on 10 transcripts. Following previous research inter-rater reliability was assessed based on the EE scores, however, due to limited variation in EE scores no ICC could be calculated. We additionally assessed the coding reliability for each of the six scales. Only for positive comments and critical comments, adequate reliabilities were achieved (positive: ICC ≥ .89; critical: ICC ≥ .60). Although the low ICCs may be attributable to a low number of speech samples in the training set or limited variance in scores, we took a conservative approach by only analyzing the number of positive and critical comments. In case of disagreement, consensus scores were used in further analyses.

To score FMSS-based emotional content and prosody, the emotional content and the acoustic parameters reflecting emotional prosody of the FMSS were analyzed using automated analyses with python and PRAAT, respectively. Firstly, using the sentiment analysis module of the PATTERN package (De Smedt & Daelemans, 2012) the polarity score and the subjectivity score of each text were calculated. Polarity scores were calculated by matching content words against a dictionary containing positivity ratings of each word and subsequently standardizing the total score between -1, indicating a maximally negative content of the text, and +1, indicating a maximally positive content of the text. Subjectivity scores were calculated based on the total number and degree of subjectivity of each word (matched against a dictionary with subjectivity scores for each adjective as rated by human raters) and standardized between 0 and 1. For example, the phrase "He will join the soccer team" would be rated low on subjectivity, whereas the phrase "I would find it amazing when he would join the soccer team" would be assigned a high subjectivity score. One subject yielded a total word count of < 100 for the PL condition and was excluded from the emotional content analysis since low word count may compromise the reliability of the polarity and subjectivity scores.

Furthermore, acoustic parameters implicated in emotional prosody (Banse & Scherer, 1996) were analyzed for each total FMSS recording (excluding silences, noise and utterances produced by the interviewer). Acoustic parameters included the median of fundamental frequency (F_0), the standard deviation of F_0, the median of the first formant (F_1,), the standard deviation of intensity, spectral slope and speaking rate (number of words per minute). Fundamental frequency corresponds perceptively to pitch, while the first overtone (formant) corresponds to openness of the mouth. Spectral slope (the degree of attenuation of larger frequencies) corresponds perceptively to 'timbre' of the voice, and intensity to loudness.

Covariates

We assessed potentially confounding effects of the current mood of the participants, as assessed by the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988). Participants filled in this questionnaire on average 36 min before the start of the FMSS (PL: Δ*t* = 36 min, *SD* = 4 min; AVP: Δt = 36 min, *SD* = 3 min; postnatal assessment: Δt = 31 min, *SD* = 3 min). Internal consistency of the positive (POS) and negative (NEG) scales were adequate to high in all conditions (Placebo POS *M* = 31.96, *SD* = 7.52 , α = .92; NEG *M* = 13.32 , *SD* = 2.98, α = .66; AVP POS *M* = 32.04, *SD* = 6.56, α = .88; NEG *M* = 13.96, *SD* = 3.63, α =.71; postnatal assessment POS *M* = 29.55, *SD* = 6.70, α = .88; NEG *M* = 14.95, *SD* = 3.53, α = .66). Participant mood was not affected by AVP administration (POS AVP vs PL: *Z* = -0.07, *p* = .95; NEG AVP vs PL: *Z* = -0.55, *p* =.65) or birth (POS PL vs post: *Z* = -1.81, *p* = .07; NEG PL vs post: *Z* = -1.36, *p* = .19). Moreover, as shown in Table3.1, positive comments and critical comments were not related to positive and negative affect scores in all three conditions. Therefore, current mood of the participant was not taken into account as covariate in the main analyses.

Table 3.1

Spearman correlations between the Five Minute Speech Sample variables and Positive and Negative Affect Schedule (PANAS) measured in the placebo, vasopressin and postnatal condition

FMSS	Positive affect PL	Negative affect PL	Positive affect AVP	Negative affect AVP	Positive affect post	Negative affect post
Positive comments	.01	.15	-.18	-.18	-.01	-.19
Critical comments	.01	-.33[1]	-.13	-.01	-.08	.15

Statistical analysis

The analyses proceeded in four steps. In the first step, we examined possible relations between demographic variables and FMSS-based expressed emotion (positive comments, critical comments), emotional content (i.e., subjectivity, polarity) and emotional prosody variables. Furthermore, associations between FMSS-based expressed emotion and current mood status were examined. For correlations with demographic variables, both parametric and non-parametric tests were performed since the sample size was relatively small and not all variables met the normality assumption. Pearson correlations are reported when Spearman correlations revealed the same outcome. These analyses were performed using data from the PL condition. Differences in emotional status and talkativeness related to AVP administration or the birth experience were examined with separate Wilcoxon Matched-Pairs Tests. Possible correlations for positive comments and critical comments across the two prenatal assessments were calculated with both

1 Statistics slightly deviate from published article

Pearson and Spearman correlations. Pearson correlations are reported when Spearman correlations revealed the same value. In the second step, we tested the extent to which coder-rated expressed emotion and computer-coded emotional content were associated, checking both Pearson – and Spearman correlations. In the third step, we examined the effect of AVP administration on the FMSS variables. Effects on positive comments, critical comments, and emotional content were examined using Wilcoxon matched-pairs tests. Although the distribution of emotional content met the parametric assumptions, we report non-parametric tests to enable a comparison with the positive comments and critical comments variables. The effect of AVP administration on emotional prosody was analyzed using multivariate repeated measures ANOVA with condition (PL or AVP) as within-subjects factor and the acoustic parameters as dependent variables. In the final step, we explored the effect of the transition to fatherhood on both FMSS-based expressed emotion and emotional content. Effects on positive comments, critical comments, and emotional content were examined using Wilcoxon matched-pairs tests comparing data from the prenatal PL condition and the postnatal assessment. A multivariate repeated measures ANOVA was performed to test the effect on emotional prosody. To this end, the first prenatal assessment and the postnatal assessment were compared as an effect of time (first vs second assessment), and no effect of AVP administration was found.

All analyses were carried out with the software IBM SPSS Statistics version 23. Given the explorative nature of the study, we used non-corrected significance levels of $p < 0.05$, and two-way exact p-values are reported for all Wilcoxon matched-pair tests.

Results

Descriptive statistics

To assess possible associations with demographic variables and current mood, bivariate correlations were performed. In the PL condition, correlations of FMSS-based expressed emotion (positive comments, critical comments) and emotional content (i.e., subjectivity, polarity) and emotional prosody variables with demographic variables were small to moderate in magnitude (see Table 3.2). Paternal age was negatively correlated to subjectivity, and positively correlated to F_0 SD and spectral slope. The age of the child at the postnatal assessment was positively correlated to father's subjectivity as assessed in the FMSS. The total number of words spoken in the FMSS was not affected by AVP administration or birth (effect of hormone: $Z = -0.07$, $p = .96$; effect of birth: $Z = -0.24$, $p = .82$), and not taken into account in further analyses. The correlations for positive and critical comments at the two prenatal assessments were $r = .23$ ($p = .28$) and $r = .54$ ($p < .01$), respectively.

Table 3.2

Pearson correlations between the Five Minute Speech Sample variables measured in the placebo prenatal and postnatal condition and demographics

FMSS	Age	Education	Pregnancy Duration	Age of Child
Positive comments	-.05	.23	-.22	.35
Critical comments	.27	.20	.36	.16
Subjectivity	-.41*	-.01	-.18	.63**
Polarity	-.29	-.09	-.14	.25
Intensity SD	-.04	-.15	.20	-.06
Fo median	-.34	.13	-.21	.20
Fo SD	.46*	.10	.28	.09
F1 median	-.35	-.04	-.17	.13
Spectral slope	.56**	.20	-.09	-.27
Speak rate	.03	.35	-.22	-.11

Note. Correlations between FMSS variables and participant age, education and pregnancy duration in the prenatal placebo condition, and age of child in the postnatal session. Spearman correlations did not differ from the Pearson correlations shown above.
*p<0.05, **p<0.01.

Associations between Expressed Emotion and Emotional content

The number of positive comments was positively related to polarity (r = .32, p = .13; r_s = .45, p = .03) and subjectivity (r = .48, p = .02) in the placebo condition. The number of critical comments was negatively related to polarity (r = -.45, p = .03) and subjectivity (r = -.47, p = .02). These correlations did not remain significant after AVP administration for positive comments (polarity: r = .31, p = .14; subjectivity: r = -.04, p = .86) and critical comments (polarity: r = -.01, p = .97; subjectivity: r = .21, p = .34). Spearman correlations did not significantly differ from Pearson correlations, except for the association between positive comments and polarity (as shown above).

The influence of AVP

As shown in Table 3.3, analyses revealed that the numbers of positive comments (Z = -1.37, p = .18, d = 0.34) and critical comments (Z = -1.33, p = .20, d = 0.25) in the speech sample were not affected by administration of AVP. Moreover, hormone administration had no effect on polarity (Z = -1.06, p = .30, d = 0.23) or subjectivity (Z = -0.06, p = .97, d = 0.01)[2]. Lastly, multivariate repeated measures ANOVA did not reveal an effect of AVP administration on emotional prosody (F[6,19] = 0.68, p = .67, η^2 = .18)[1].

2 p - value deviates from published article, where we reported one-tailed significance.

Table 3.3

The effect of vasopressin administration on Five Minute Speech Sample parameters

		Mean (SD) PL	Mean (SD) AVP	Test statistic parametric	*p*-value	Effect size (d)	Test statistic non-parametric (Z)	*p*-value
Word count		711.36 (201.77)	705.76 (207.20)				-0.07	.96
Positive comments		2.28 (2.25)	3.04 (2.26)			0.34	-1.37	.18
Critical comments		0.52 (1.00)	0.80 (1.29)			0.25	-1.33	.20
Polarity		0.21 (0.09)	0.19 (0.08)			0.23	-1.06	.30
Subjectivity		0.66 (0.07)	0.66 (0.05)			0.01	-0.06	.97
Emotional prosody				0.68	.67	.16		
	F_0 median	93.29 (10.50)	93.85 (12.03)					
	F_0 SD	60.10 (15.24)	57.36 (11.00)					
	F_1 median	1.10 (0.12)	1.10 (0.13)					
	Intensity SD	8.54 (1.34)	8.79 (1.98)					
	Spectral slope	-0.01 (0.00)	-0.01 (0.00)					
	Speak rate	2.32 (0.66)	2.31 (0.69)					

Note. Only the comparison in emotional prosody was tested parametrically with a multivariate repeated ANOVA and effect size is calculated in η^2. All other comparisons are examined with separate Wilcoxon Matched-Pairs Tests. Mean and SD for parameters included in emotional prosody are shown separately.

The influence of birth

Table 3.4 shows the effects of the birth of the child on positive and critical comments, emotional content (i.e., polarity and subjectivity), and emotional prosody parameters. The number of positive comments (Z = -2.17, p = .03, d = 0.49), but not the number of critical comments (Z = -0.78, p = .51, d = 0.22) differed after the birth of the first child, with an increase in positivity after birth. Polarity (Z = -0.20, p = .86, d = 0.07)[2] and subjectivity (Z = -0.40, p = .71, d = 0.01)[1] were not influenced by the birth of the child. However, as shown in Table 3.4, emotional prosody parameters changed after the birth of the child (F[6,14] = 4.62, p = .01, η^2 = .66)[1]. Post hoc analyses revealed that variation in intensity decreased from pre-birth (M = 9.63, SD = 1.46)[1] to post-birth (M = 8.69, SD = 1.27); F(1,19) = 6.02, p = .02, η^2 = .24. Furthermore, first formant decreased from pre-birth (M = 1.17, SD = 0.13) to post-birth (M = 1.08, SD = 0.11); F(1,19) = 27.07, p < .01, η^2 =. 59. A trend was observed for decreased speak rate after birth (pre: M = 2.21, SD = 0.67; post: M = 2.26, SD = 0.63)[1]; F(1,19)= 3.65, p = 0.07, η^2 = .16.

Discussion

In the current study, we investigated the effect of vasopressin on FMSS characteristics in men in the transition to fatherhood, and the influence of the birth of the child on paternal speech about their infant and their relationship with the infant. Furthermore, we explored whether computerized coding was meaningfully related to traditional rater-based coding of FMSS variables. Analyses revealed that rater-based FMSS expressed emotion (positive comments and critical comments) and automatically coded emotional content (polarity and subjectivity) were correlated. No effect of AVP was observed on FMSS-based variables, but the birth of the child influenced both FMSS-based expressed emotion and emotional prosody parameters.

Starting with the associations between coder-rated and computer-rated FMSS variables, we can conclude that computerized coding is a promising addition to traditional coding. Higher numbers of positive comments and lower number of critical comments were associated with higher polarity and subjectivity. These meaningful associations point to automatic computer coding of the FMSS recordings as a valuable addition to the traditional Expressed Emotion coding of the FMSS coding in both clinical and research settings. At this point, the modest correlations do not suggest that the traditional EE coding of the FMSS could be replaced by automatic coding, given the remaining substantial non-overlap between the measures. Future studies relating the distinct FMSS ratings to observed parenting behavior may reveal what part of the variance in parenting can be explained by the traditional and computerized coding procedures separately and in tandem.

Table 3.4

The influence of birth on Five Minute Speech Sample parameters

		Mean (SD) PL	Mean (SD) post	Test statistic parametric (F)	p-value	Effect size (d)	Test statistic non-parametric (Z)	p-value
Word count		711.36 (201.77)	688.60 (195.22)				-0.24	.82
Positive comments		2.28 (2.25)	4.05 (3.00)			0.49	-2.17	.03
Critical comments		0.52 (1.00)	0.80 (1.06)			0.22	-0.78	.51
Polarity		0.21 (0.09)	0.21 (0.07)			0.07	-0.20	.43
Subjectivity		0.66 (0.07)	0.67 (0.06)			0.01	-0.04	.71
Emotional prosody				4.62	.01	.66		
	F_0 median	93.29 (10.50)	94.08 (10.77)					
	F_0 SD	60.10 (15.24)	65.29 (15.85)					
	F_1 median	1.10 (0.12)	1.08 (0.11)					
	Intensity SD	8.54 (1.34)	8.69 (1.27)					
	Spectral Slope	-0.01 (0.00)	-0.01 (0.00)					
	Speak rate	2.32 (0.66)	2.26 (0.63)					

Note. Only the comparison in emotional prosody was tested parametrically with a multivariate repeated ANOVA and effect size is calculated in η^2. All other comparisons are examined with separate Wilcoxon Matched-Pairs Tests. Mean and SD for parameters included in emotional prosody are shown separately.

Moreover, AVP administration did not influence the FMSS-based variables. Speech style and content during the FMSS may be independent of paternal AVP levels, although AVP has been related to other fathering dimensions in the past (e.g., Abraham & Feldman, 2018; Thijssen et al., 2018). Alternative explanations for the absence of the expected associations are the following. First, a training effect might have influenced the results. That is, participants performed the FMSS in the AVP and placebo conditions in a relatively short time-window, which may have resulted in memorized answers. To our knowledge, this is the first study using a small time-window of 7 days between two FMSS recordings, and indeed, scores of the two sessions were correlated. Future research should address the effect of the duration of the intervening period between two assessments of the FMSS. Second, it might argued that the intranasally administered AVP did not reach or could not affect the neurobiological systems involved in FMSS responses of prospective fathers. However, intranasal administration of AVP has been shown to result in increased AVP concentrations in both cerebrospinal fluid and blood plasma of healthy adult men and women within 10 minutes, with effects still present after 80 min (Born et al., 2002). Furthermore, studies have shown that neurobiological systems involved in the processing of cry sounds (Thijssen et al., 2018), processing of infant-related visual stimuli (Cohen-Bendahan et al., 2015) and the activation of protective parenting (Alyousefi-van Dijk et al., 2019) are affected by the AVP nasal administration in prospective fathers. However, it remains unknown what specific neurobiological effects are evoked by AVP administration. Third, the time-window between administration of AVP and the start of the FMSS might play a role. In the current study, the FMSS started on average 155 min after AVP administration. This time-window is relatively large compared to previous AVP studies: ranging between 45 – 150 min (Alyousefi - Van Dijk et al., 2019; Cohen-Bendahan et al., 2015; Li et al., 2017; Thijssen et al., 2018) and might have resulted in attenuation of the effect of AVP administration. Finally, it should be noted that the sample size was limited, and thus the statistical power to find effects was modest. The current sample consisted of men with a relatively high educational level, co-habiting, and living in a Western country. This small exploratory and hypothesis-generating study should be replicated in larger samples and in non-Western cultures to examine the replicability and generalizability of the results.

The birth of the first child, however, did influence several FMSS-based variables. Specifically, we observed an increase in the number of positive comments and a decrease in emotional prosody. The increase of positive FMSS content could be due to the experience of fathering, as the paternal emotions, thoughts and behavior may facilitate emotional rewarding feelings about the child (Goodman, 2005), although no influence of birth on the reported positive or negative affect states were observed in the current study. The observed changes in emotional prosody variables after birth

might well be due to decreased parental sleep; increased tiredness may affect prosody (Hagen, Mirer, Palta, & Peppard, 2013; McGlinchey et al., 2011). Moreover, possible maturation effects on the voice (see e.g. Lortie, Rivard, Thibeault, & Tremblay, 2017) that might affect emotional prosody cannot be excluded since no control non-father group was included. Future studies should explore possible influences of depressive mood and sleep quality on emotional prosody. Interestingly, in contrast to the observed influence on positive comments, no effect of birth was observed on the emotional content variables. Future research should address this discrepancy.

In order to study FMSS-based expressed emotion in men transitioning into fatherhood, we combined two FMSS coding manuals that were originally developed for prospective parents (Lambregtse-van den Berg et al., 2013) and new parents (Daley et al., 2003), respectively. Following previous research, we aimed to assess the EE scores of the FMSS recordings. However, different configurations of the individual scale scores may lead to similar overall EE scores, at the cost of meaningful variation. Indeed, in some studies, this underlying variation and additional speech sample information that could be missed in the dichotomous EE scale have been used. For example, Daley et al. (2003) successfully used all preschool subscales in their study of mothers of preschool children. Moreover, Baker, Heller, and Henker (2000) and Wamboldt, O'Conner, Wamboldt, Gavin, and Klinnert (2000) related adjusted scale scores for positive affect and worry, emotional overinvolvement, and number of positive remarks to self-reported parental functioning and observed parent-child interactions and found diverging predictions for individual scales, which support their predictive validity as separate scales (Baker et al., 2000; Wamboldt et al., 2000).

In the current study, we explored paternal thoughts and feelings via the FMSS. One of the reviewers suggested that it might be interesting to examine whether indicators of indirect parenting, such as statements about provisioning and protection (e.g., for protection see Bakermans-Kranenburg & van IJzendoorn, 2017), can be measured with the FMSS. We explored post hoc whether such statements were present in our current dataset, and indeed we found evidence for the presence for these dimensions of indirect care (e.g. "I hope we are able to set apart some money for her"; "I hope we can prevent that she is being bullied"), suggesting that future research could include these indicators for indirect care in the FMSS.

Unfortunately, scoring these individual scales is not always straightforward, and after thorough training, we achieved inter-coder reliability for two of them. This might be due to differences in the study population compared to other studies. Future research should examine for more individual scale scores whether they can be trained

to reliability, maybe with a more detailed coding manual, and whether the scales (combined and uniquely) are associated with observed parental sensitivity, infant-father attachment quality and paternal indirect care.

In summary, the current study is the first to examine the effect of AVP on FMSS-variables in men in the transition into fatherhood, a unique time-window characterized by changes in the regulation of parental emotions and behaviors. Based on our findings, it may be concluded that FMSS-based variables may be independent of AVP in prospective fathers. Moreover, we explored the possibility of using a computerized assessment of possible correlates of sensitivity and identified meaningful relations between traditionally rated expressed emotion and computer-rated emotional content and emotional prosody. Our findings suggest that such automatic coding of the speech samples provide useful additional information and can be used to develop less time-consuming and more reliable coding procedures of the FMSS.

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Chapter 4

Exploring the role of endocrine factors in paternal sensitive parenting

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Abstract

Parental sensitivity has been studied extensively in parenting research. Recently, there has been increasing attention to endocrine factors that may be related to parental sensitivity, such as oxytocin, vasopressin, testosterone, and cortisol. Although hormones do not act in isolation, few studies integrated multiple hormones and examined their combined associations with parental sensitivity. The current study aimed to explore the hormonal correlates of paternal sensitivity by examining in 79 first-time fathers of young infants (2 – 4 months old) (1) the separate and combined associations of basal oxytocin, vasopressin, testosterone, and cortisol levels with sensitivity, and (2) the associations between paternal sensitivity and oxytocin, vasopressin, testosterone, and cortisol reactivity following father-infant interactions. We additionally explored whether interactions between the various basal hormone levels could predict paternal sensitivity. Saliva for the quantification of fathers' hormone levels was sampled before and after an interaction with their infant to determine basal levels and reactivity. Results revealed no significant associations between sensitivity and basal hormone levels or reactivity. However, results indicated that cortisol and testosterone interacted in their effects on paternal sensitive parenting, such that there was a stronger positive association between testosterone and sensitivity for fathers with lower cortisol levels. These findings suggest that variations in parental sensitivity might be better explained by interactions between hormones than by single hormone levels.

Keywords: Fathers, Sensitivity, Oxytocin, Vasopressin, Cortisol, Testosterone

Introduction

Parental sensitivity, defined as parents' ability to perceive, accurately interpret, and appropriately and promptly react to infants' signals (Ainsworth, Bell, & Stayton, 1974), has been studied extensively in parenting research, using a variety of behavioral observation settings and coding systems. The interest in parental sensitivity is not remarkable, as sensitive parenting behavior is related to positive child outcomes such as cognitive development, socio-emotional functioning (Deans, 2020; Rodrigues et al., 2021) and infant attachment security, both with mothers (De Wolff and van IJzendoorn, 1997; Posada et al., 2016) and fathers (Brown et al., 2012; Lucassen et al., 2011). Recently, there has been increasing attention to endocrine factors that may be related to parental sensitivity (e.g., Feldman & Bakermans-Kranenburg, 2017). Moreover, research suggests that several hormones, including oxytocin (OT), vasopressin (AVP), testosterone (T) and cortisol (CORT) are associated with human paternal caregiving behavior (e.g., Bos, 2017; Rajhans et al., 2019; Rilling & Mascaro, 2017). However, few studies integrate multiple hormones and examine their simultaneous associations with parental sensitivity. The current study aimed to explore the hormonal correlates of paternal sensitivity by (1) examining the separate and combined associations of basal OT, AVP, T, and CORT levels with sensitivity in fathers of young infants, and (2) studying associations between paternal sensitivity and OT, AVP, T, and CORT reactivity following father-infant interaction. In a post-hoc analysis, it was additionally explored whether interactions between the various basal hormone levels could predict paternal sensitivity.

A widely studied hormone in the context of the study of parental sensitivity is OT (Feldman and Bakermans-Kranenburg, 2017). Concerning basal OT levels, several studies showed that OT positively relates to sensitive parenting behavior. For example, higher basal OT levels have been associated with more parental affectionate contact, but not stimulatory contact, towards infants during a parent-infant interaction task (Apter-Levi et al., 2014). Interestingly, studies that distinguish between mothers and fathers show that basal OT levels are positively related to affectionate contact in mothers (Feldman et al., 2010), whereas in fathers, OT levels are positively related to stimulatory contact (Feldman et al., 2010, but see Gordon et al., 2017 for non-significant findings in fathers). Higher paternal basal OT levels have also been associated with more positive engagement, affect synchrony and positive communicative sequences between father and infant (Feldman et al., 2011). Moreover, studies that focused on intranasal OT administration, showed that OT administration led to higher paternal responsive structuring and less hostility towards the infants (Naber et al., 2010; Naber et al., 2013), although no effects were observed on paternal sensitivity and non-intrusiveness. Less is known about the relation between paternal sensitivity and OT

reactivity to interaction with infants, but one study found that for fathers who showed higher levels of stimulatory contact, OT increased after father-infant interaction (Feldman et al., 2010). This finding suggests that paternal sensitive behavior may be positively related to OT reactivity.

A neuropeptide that is biologically related to OT is AVP (Carter, 2017; Carter et al., 2020). Research on AVP in relation to parental caregiving behavior is scarce, however, some research indicates that AVP is involved in specific parental behaviors during parent-infant interactions. Apter-Levi et al. (2014) showed that, in contrast to their observation for OT, mothers' and fathers' basal AVP levels were positively associated with observed stimulatory touch, although not with affectionate touch. Moreover, parents with high basal AVP levels, compared to low basal AVP levels, provided more stimulatory touch and tended to respond more to infant social cues with gaze at an object or stimulatory touch. These results might suggest that basal AVP might have a similar role in positive parenting behavior as paternal OT, however, to draw firm conclusions further research is needed. Focusing on fathers specifically, previous studies showed that AVP might be linked to the processing of infant cues in fathers (to be) (Alyousefi-Van Dijk et al., 2019; Atzil et al., 2012; Cohen-Bendahan et al., 2015; Thijssen et al., 2018), but not to the thoughts and feelings fathers have about their unborn child (Lotz et al., 2020a). Interestingly, no previous studies have focused on AVP reactivity. However, as AVP is biologically related to OT (Carter, 2017; Carter et al., 2020) and previous literature indicates that father-infant interaction may lead to changes in OT, it is important to study whether fathers' sensitivity is associated with changes in AVP during interaction with their infant.

A steroid hormone that has been linked to paternal behavior is T. T has been previously studied in the context of paternal involvement and parenting quality, and lower levels of basal T were found to be associated with higher involvement and parenting quality, with small to medium combined effect sizes (see for meta-analyses Grebe et al., 2019; Meijer et al., 2019). Observational studies that focused specifically on sensitivity during father-infant interactions found negative associations between basal T levels of fathers and their affectionate and stimulatory touch, and between basal T levels and the average duration of infant-directed vocalization, i.e., motherese (Gordon et al., 2017; Weisman et al., 2014). In the same vein, the delay in infant-directed speech was positively associated with basal T levels of fathers (Weisman et al., 2014). In the context of hormonal reactivity, one study found that paternal salivary T levels decrease after a caregiving interaction with their infant (Bos et al., 2018). A similar decrease in T of fathers was observed in reaction to an infant doll's cries when coupled with nurturing responses (van Anders et al., 2012). This might indicate that T reactivity is related to

paternal caregiving behavior. Moreover, there is some evidence that hormone reactivity induced by father-infant interactions might predict positive parenting behavior in a subsequent task (de Vries et al., 2019; Kuo et al., 2016).

Another steroid hormone that is associated with parenting behavior is CORT. For example, it was shown that in both fathers and mothers basal CORT measured a few days after the birth of their infant was positively associated with parental behavior (Fleming and Steiner, 1987; Kuo et al., 2018). Specifically for fathers, higher basal CORT levels in the early postnatal period, i.e., first two days after birth, predicted greater involvement in direct and indirect infant care measured a few months later (Kuo et al., 2018). Interestingly, the relation between basal CORT levels and positive parenting seems to be reversed (i.e., negative) when CORT is measured several months after birth in both fathers (Bos et al., 2018) and mothers (Finegood et al., 2016; Gonzalez et al., 2012). As the infants in the current study are around eight weeks old, we expect to observe a negative association between basal CORT levels and paternal sensitivity. Concerning CORT reactivity, a significant decline in paternal CORT was observed after holding or interacting with their infant (Bos et al., 2018; Kuo et al., 2018; Storey et al., 2011). However, how this decline in CORT is related to the quality of paternal behavior is still unclear.

There are many indications that hormones act in concert, rather than acting in isolation (Feldman and Bakermans-Kranenburg, 2017; Rajhans et al., 2019). For example, OT might interact with T and AVP, as OT nasal spray administration increased salivary T levels (Weisman et al., 2014) and salivary AVP levels (Weisman et al., 2013). In addition, salivary T and CORT are found to be positively associated (Bos et al., 2018; Gettler et al., 2011). Moreover, hormones may interact in their effects on paternal behavior. For instance, OT and T may interact in their effect on paternal sensitivity as it was shown that T levels moderated the association between OT and affectionate touch (Gordon et al., 2017). In addition, salivary T and CORT might interact in their effects on behavior. For instance, the dual hormone hypothesis states that associations of T with behavior depend on individuals' CORT levels (Mehta and Prasad, 2015). In the context of parenting behavior, Bos et al. (2018) found a stronger negative association between CORT and sensitivity for fathers high in T, suggesting that a combination of high T and high CORT levels is associated with lower sensitivity scores. Taken together, previous research and theory suggest that studies of hormonal correlates of parenting behavior may be more informative when examining several hormones simultaneously, as the combined associations and interplay between these hormones may be more informative in their associations with parenting than each of them separately.

In the current study, we explored whether baseline levels of OT, AVP, T and CORT were associated with paternal sensitivity in first-time fathers. Moreover, we studied whether paternal sensitivity during observed father-infant interaction was associated with changes in OT, AVP, T and CORT. Finally, we explored post-hoc whether interactions between the various basal hormone levels could predict paternal sensitivity. By focusing on multiple hormones and their combined associations with paternal sensitivity, rather than only studying parenting hormones in isolation, we aimed to enhance our knowledge on the role of endocrine factors in sensitive parenting behavior in fathers.

Methods

Participants

Seventy-nine first-time fathers were recruited via municipal records, infant welfare centers, midwife practices and social media (See Supplementary Material Figure 4.1 for a recruitment overview). Participants were first-time fathers in the early postnatal phase of parenthood, all but one were the biological father of their child, spoke Dutch fluently, and cohabitated with their partner (and biological mother of the child). Children were healthy full-born infants (except for one infant that was born at 36 weeks and six days, but was considered healthy). See Table 4.1 for an overview of demographic variables.

Before inclusion, fathers were screened for psychiatric, endocrine, neurological diagnosis, medication use, alcohol/and or drug abuse, and possible MRI contraindications (e.g., metallic foreign objects in participant's body). Moreover, fathers were excluded when they had an upper torso injury that could affect the use of a baby carrier or reported to use a baby carrier more than five hours per week, which was relevant for the full study procedure that included the use of a baby carrier. To maximize the sample size, we decided to deviate from a priori stated inclusion criteria in seven cases (Birth < 37 weeks n = 1, endocrine disorder n = 1, cardiovascular disease n = 1, neurodevelopmental disorder and psychotropic medication use n = 1, and MRI contraindications n = 3). The study was approved by the Ethics Committees of the Leiden University Medical Centre (LUMC) and of the Department of Education and Child studies at Leiden University. The study was carried out in accordance with the declaration of Helsinki and all participants gave written informed consent.

Procedure

Depending on participant's preference and possible MRI contra-indications, the data reported in the current paper was collected either at the Leiden University Medical Centre (n = 65) or at the participant's home (n = 14). Each assessment consisted of the

following measures: saliva and hair sampling for hormonal measurements (Lotz et al., 2020b; Manenschijn et al., 2011); behavioral measurements, including a 10-minute Free play; a handgrip force paradigm (Alyousefi-Van Dijk et al., 2019); the Five Minute Speech Sample (Lotz et al., 2020a); and questionnaires about e.g., health, medication use and current mental state. Additionally, when the assessment took place at the LUMC, the Free Play was immediately followed by the Auditory Startling Task (AST; Lotz et al., 2020b) and neural measurements were conducted. Following the assessments, participants and partners completed online questionnaires at home.

Table 4.1

Sample Characteristics

N = 79		**M(SD)/N(%)**	**Range**		
Participant age (years)		33.10(5.36)	25.06	–	56.50
Education (years past primary education)[a]		8.28(1.85)	3.00	–	10.00
Country of birth[a]	The Netherlands	72(92)			
	Other	6(8)			
Race	Caucasian	73(92)			
	Other	6(8)			
Infant age (weeks)		11.62(3.37)	7.57	–	21.57
Infant sex	male	42(53)			
Baseline oxytocin[b] (pg/mL)		1.38(0.46)	0.00	–	2.18
Baseline vasopressin[b] (pg/mL)		1.63(0.47)	0.87	–	2.67
Baseline cortisol[b] (nmol/L)		1.53(1.63)	0.09	–	8.14
Baseline testosterone[b] (pg/mL)		44.52(35.80)	2.14	–	216.96
Post-interaction[c] Oxytocin (pg/mL)		1.36(0.45)	0.65	–	2.80
Post-interaction[c] vasopressin (pg/mL)		1.65(0.50)	0.80	–	2.52
Post-interaction[d] cortisol (nmol/L)		1.13(1.01)	0.17	–	5.11
Post-interaction[d] testosterone (pg/mL)		43.59(39.43)	2.88	–	196.14
Oxytocin reactivity[b]		-0.00(0.99)	-2.33	–	3.48
Vasopressin reactivity[b]		0.00(0.99)	-2.63	–	2.37
Cortisol reactivity[b]		0.00(0.99)	-2.27	–	2.70
Testosterone reactivity[b]		0.01(0.96)	-3.50	–	2.49
Observed sensitivity		5.73(1.48)	3.00	–	8.50
Observed cooperation		4.47(1.56)	2.00	–	8.00

Note. Sample characteristics are calculated based on complete cases data. Participants' race was coded by researchers based on videotapes of fathers and was defined as Caucasian or other. Hormonal reactivity was calculated with a residualized change score, i.e., post-interaction samples were residualized by corresponding baseline samples. For testosterone and cortisol reactivity levels, the baseline and post-interaction samples of testosterone and cortisol levels were log transformed.

[a] $N = 78$, [b] $N = 75$, [c] $N = 76$, [d] $N = 77$

Measures

Paternal sensitive parenting

Paternal positive parenting behavior was observed from a videotaped 10-minute free play session. Before the start of the recordings, fathers were instructed to play with their infant as they would normally do. To ensure that both father and infant were visible on the video at the start of the recording, participants were asked to lay their infant on a play mat and take a seat next to their infant. During the first five minutes, father and infant played without toys, after which the experimenter provided a standard set of age-appropriate toys (e.g., a ball and a music toy) to play with for another five minutes. Videos were rated for paternal sensitivity and cooperation using the 9-point Ainsworth Sensitivity Scales (Ainsworth et al., 1974), in which higher scores indicate higher levels of sensitivity and cooperation. Five coders were trained by an expert coder (MBK) and interrater reliability with the expert coder was established. ICCs (single measure, absolute agreement) based on 20 videos were adequate, ranging between .68 and .76 (*M* = .73) for sensitivity and between .64 and .79 (*M* = .70) for cooperation.

Hormones

Hormones were measured in saliva. Salivary samples were obtained at the beginning of the assessment (Baseline, *M* = 03:25 pm, *SD* = 3:13 hr, range = 09:15 am – 07:39 pm) and ten minutes after the end of the free play (post-interaction sample, *M* = 04:11 pm, *SD* = 3:14 hr, range = 09:50 am – 08:29 pm). Participants were instructed not to engage in physical exercise or consume any alcoholic drinks during the 24 hours prior to the assessment. Moreover, participants were instructed not to drink any caffeinated drinks on the day of the assessment, and not to smoke, chew gum, eat or drink (other than water) 30 minutes before the start of the appointment. Before the start of each saliva collection participants rinsed their mouth with water. After collection, samples were stored at -20 ˚C as soon as possible. When samples could not be stored in the freezer immediately, samples were placed on ice. Baseline samples of one participant were not stored adequately immediately after collection, and they were therefore excluded from further analyses. Hormonal reactivity was calculated with a residualized change score, i.e., post-interaction sample levels were residualized by baseline sample levels.

Steroid hormones. For the quantification of T and CORT, saliva was collected using the passive drool method. Participants collected approximately 1.5 ml saliva in a 2 ml cryogenic vial (SalivaBio, Salimetrics), either by drooling directly into the vial or by using a saliva collection aid (SalivaBio, Salimetrics). Before drooling, participants were asked to swallow once and to bent slightly forward. To stimulate saliva production, participants were recommended to move their jaws, to look at pictures of food, or to think about something sweet or sour. On average, it took 9.29 (*SD* = 5.71) min to complete the collection. T and CORT levels were quantified at Dresden LabService

GmbH (Germany) by Luminscence immunoassay (IBL International GMBH), e.g., see Alvergne et al., (2009) for a detailed description of the procedure for T. All samples were analyzed in the same assay run (14 plates total) and 30% of the samples were randomly selected and analyzed in duplicate. For the samples ran in duplicate, a mean value was calculated and used in further analyses. Fifty µL of each sample was used for the quantification of T. The limit of detection was 1.8 pg/mL. Inter-assay variability was 10% and intra-assay variability was 5%. Cross-reactivity with other substances tested $\leq$ 0.01 %. T values are reported in pg/mL. For the quantification of CORT, 20 µL of each sample was used. Detection limit was 0.012 µg/dL. Inter-assay variability was 8% and intra-assay variability was 7%. Cross-reactivity with other substances tested $\leq$ 1 %. CORT values are reported in nmol/L

Neuropeptides. For the quantification of AVP and OT, saliva was collected using a cotton swab (Salivette, Sarstedt). Participants were instructed to chew lightly on a cotton swab for 60 s and slightly move the swab around in their mouth. AVP and OT were quantified using radioimunnoassay at RIAgnosis (Sinzing, Germany, see for detailed description Kagerbauer et al., 2019). Salivettes were centrifuged at 4 degrees Celsius for 30 minutes with ca. 5000 g centrifugal force, after which 0.6 ml of saliva was pipetted into a vial (0.3 ml for the analysis of AVP and 0.3 ml for the analysis of OT). All samples were analyzed simultaneously in the same assay run. The detection limit for AVP and OT was in the 0.1 pg sample range. Intra-assay and inter-assay variability were < 10%. There was no significant cross-reactivity with other neuropeptides (< 0.7%). AVP and OT values are reported in pg/mL.

Data-analyses

Data Distribution

Distribution of the data was inspected in SPSS version 23. Shapiro Wilk tests showed that the distribution of all collected variables, except for baseline OT levels, did deviate significantly from a normal distribution. However, based on the skewness and kurtosis of the distributions, only baseline and the post-interaction samples of CORT and T levels did not approach normal distributions. These variables were Log-transformed for further analyses and hormone reactivity was calculated based on the Log-transformed CORT and T values as well. All four hormonal reactivity variables were normally distributed. Next, outliers were inspected. Inspection of Z-values revealed five outliers ($Z < -3.29$ or $Z > 3.29$): one for T reactivity, one for OT reactivity, one for the participants' age, and two for participants' BMI. All outliers were winsorized (Tabachnick & Fidell, 2007). Lastly, assumptions for multiple linear regressions were inspected. Variance inflation factors (VIF) ranged between 1.03 - 1.53, indicating absence of multicollinearity. Scatterplots revealed that the data was homoscedastic and normal P-P plots indicated that residuals were normally distributed. Durbin-Watson tests ranged between 2.00

– 2.14 and indicated independent error-terms. Visual inspection of Cook Distances indicated multivariate normality of the data and Mahalanobis Distances indicated the absence of multivariate outliers.

Covariates

We examined whether time of saliva collection (e.g., Berg & Wynne-Edwards, 2001; Dabbs Jr., 1990), participant age (Van Anders et al., 2014) and recent caffeine intake (e.g., Lovallo et al., 2006) significantly correlated with baseline levels of all four hormones. Additionally, age of the infant was a examined as a significant covariate for both T and CORT baseline levels. Specifically for CORT baseline levels, BMI was examined as possible covariate (Fraser et al., 1999). As the Free Play was immediately followed by the AST (Lotz et al., 2020b) during LUMC visits but not the home visits, the possible relation between the administration of the AST and hormone reactivity levels was tested. For observed sensitivity and cooperation, the age of the infant was explored as possible covariate because infant development might affect the interaction between father and infant. Correlations were tested via a two-sided Pearson correlation and significance was set at $p < .05$. For baseline hormone levels, significant correlations were observed between T and infant age ($r = .29$, $p = .01$), and between CORT and time of collection ($r = -.33$, $p = .00$). Spearman correlations revealed similar outcomes.

Analyses

Firstly, bivariate Pearson correlations were computed for the associations between baseline hormone levels, hormone reactivity, observed sensitivity, and observed cooperation based on the full cases dataset. Significance was set at $p < .05$. Secondly, Structural Equation Model (SEM) analyses were computed to explore the main research questions. In a first step, a SEM was computed that explored whether baseline hormone levels together predicted the latent construct Sensitivity (i.e., based on observed sensitivity and cooperation). A second SEM was computed to explore whether Sensitivity predicted hormonal reactivity (i.e., OT, AVP, CORT, and T). In a final SEM, it was explored whether hormonal reactivity predicted Sensitivity. SEM analyses were performed with the package Lavaan (Rosseel, 2012) in R (R Development Core Team, 2013). Infant age was included as a covariate for baseline T, and time of saliva collection was included as a covariate for baseline CORT. For each model, the fit was checked with the χ^2-statistic, the Comparative Fit Index (CFI), and the Root Mean Square Error of Approximation (RMSEA). CFI values greater than .90 and RMSEA values smaller than .08 indicate acceptable model fit (Hu & Bentler, 1999). Four percent of the data was missing (range = 0 – 5). Little's MCAR test (Little, 1988) indicated that the data was missing completely at random ($\chi^2(34) = 42.61$, $p = .15$). Therefore, Full Information Maximum Likelihood (FIML) was used to handle missing data.

Finally, we explored whether interactions between basal hormone levels predicted Sensitivity using the rFSA package (Lambert et al., 2018) in R. The rFSA package identifies interaction terms that are most optimal solutions to explain variance in the dependent variable. The algorithm starts with a random combination of two predictors and then exchanges one of the two variables of the interaction term and the corresponding main effect. After each change, the fit of the model was evaluated (Lambert et al., 2018). Baseline levels were centered and the analysis was based on 50 random starts. The average of the standardized scores for observed cooperation and sensitivity was used as dependent variable.

Results

Preliminary results

As shown in Table 4.2, analyses revealed correlations with small to large effect sizes (Cohen, 1988). Pearson correlations indicated a strong positive association between the observed sensitivity and cooperation scales. Furthermore, baseline T was positively associated with baseline CORT. The negative correlations between baseline OT and baseline T and baseline OT and baseline CORT felt short on significance, but showed small to medium effect sizes (respectively, $r(72) = -0.23$, $p = .05$; $r(72) = -0.22$, $p = .06$). Moreover, correlations between hormone reactivity levels indicated that T reactivity was significantly positively associated with CORT reactivity. Additionally, cooperation was negatively correlated with baseline OT levels and baseline AVP levels were positively associated with CORT reactivity. Finally, there was a trend for the negative association between baseline T levels and OT reactivity ($r(72) = -0.23$, $p = .05$).

Structural models (SEM)

Baseline hormone levels and sensitivity

The first SEM with baseline hormone levels controlled for infant age and saliva collection time, as predictors of Sensitivity showed a perfect fit: $\chi^2(5) = 2.65$, $p = .75$; CFI = 1.00; RMSEA= 0.00 (Figure 4.1). Standardized factor loadings were high, 0.73 and 0.91 for respectively observed sensitivity and cooperation, indicating an underlying latent variable Sensitivity. Parameter estimates revealed no significant associations with the latent construct Sensitivity, although a trend was observed for baseline OT levels ($\beta = -0.23$, SE = 0.32, $p = .09$). The observed perfect fit in combination with non-significant parameter estimates indicates that the power to reject the null hypothesis that the predicted model and observed data are equal was insufficient. We therefore fit a more parsimonious model with only baseline OT levels as predictor of Sensitivity. A negative residual variance was observed for observed cooperation. This might indicate that the model is not appropriate for our data. For this reason, the individual estimates

Table 4.2

Correlations Between Baseline Hormone Levels, Hormone Reactivity and Observed Sensitivity and Cooperation.

Variable	Baseline OT	Baseline AVP	Baseline CORT	Baseline T	Reactivity OT	Reactivity AVP	Reactivity CORT	Reactivity T	Sensitivity	Cooperation
Baseline OT	x	-	-	-	-	-	-	-	-	-
Baseline AVP	-.018	x	-	-	-	-	-	-	-	-
Baseline CORT	-.224†	-.033	x	-	-	-	-	-	-	-
Baseline T	-.229†	-.063	.539**	x	-	-	-	-	-	-
Reactivity OT	-.010	-.157	-.026	-.229†	x	-	-	-	-	-
Reactivity AVP	.063	.000	.024	.053	-.132	x	-	-	-	-
Reactivity CORT	-.104	.245*	.000	-.130	-.127	-.040	X	-	-	-
Reactivity T	-.181	.118	-.028	.004	.178	-.101	.423**	x	-	-
Sensitivity	-.136	.080	.141	.163	.188	.003	-.145	-.112	x	-
Cooperation	-.234*	.131	.087	.117	.121	-.022	-.169	-.126	.667**	x

Note. Bivariate Pearson correlations are calculated on full cases dataset. Hormone reactivity is calculated by residualizing post-interaction hormone levels with baseline hormone levels. Baseline and post-interaction CORT and T levels are log-transformed.

** $p < .01$, * $p < .05$, † $p < .1$

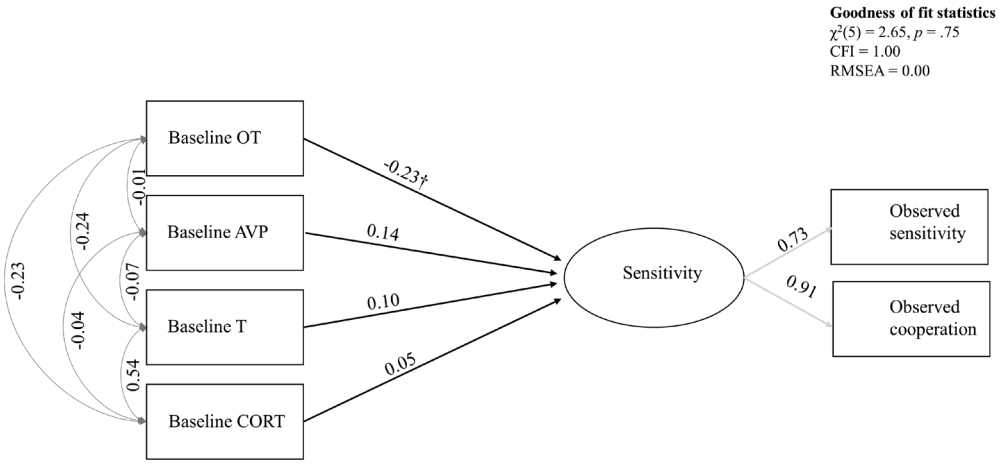

Figure 4.1

SEM model with baseline hormone levels as predictors of Sensitivity

Note. Path coefficients are standardized parameter estimates. Black arrows indicate standardized β's. Dark grey arrows indicate correlation coefficients between the predictors. Light grey arrows indicate standardized factor loadings for latent construct Sensitivity. Predictors are controlled for infant age and time of saliva collection.

† $p < 0.1$

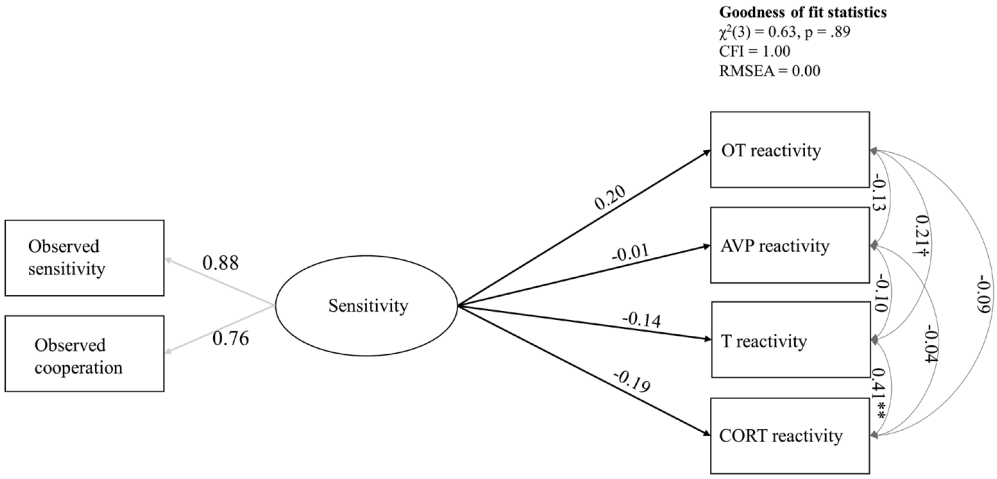

Figure 4.2

SEM model with Sensitivity as predictors of hormone reactivity

Note. Path coefficients are standardized parameter estimates. Black arrows indicate non-significant standardized β's. Dark grey arrows indicate correlation coefficients between the dependent variables. Light grey arrows indicate standardized factor loadings for latent construct Sensitivity.

† $p < .1$ ** $p < .01$

were not further interpreted. Finally, as the correlation matrix revealed that baseline OT levels were significantly correlated with observed cooperation, we performed a multiple linear regression analysis with cooperation as dependent variable. Results revealed no significant association between observed cooperation and baseline hormone levels, controlling for infant age and time of saliva collection (range β: -0.22 – 0.13; range SE: 0.37 – 0.56; $p \geq .06$), although the association between observed cooperation and baseline OT levels was almost significant (β = -0.22, SE = 0.40, $p = .06$).

Sensitivity and hormonal reactivity

Next, we conducted a SEM examining the latent construct Sensitivity as a predictor of hormone reactivity levels. This model also indicated a perfect fit: $\chi^2(3) = 0.63$, $p = .89$; CFI = 1.00, RMSEA = 0.00 (Figure 4.2). Standardized factor loadings for the latent variable Sensitivity were high, 0.88 and 0.76 for respectively observed sensitivity and cooperation. There were no significant associations between Sensitivity and hormone reactivity (range β: -0.19 – 0.20; range SE: 0.10 – 0.11; $p \geq .13$), indicating that variation in sensitive parenting was not related to variation in hormonal reactivity. Additionally, we explored whether hormone reactivity levels predicted Sensitivity (See supplementary material Figure 4.2). Again, a perfect fit was observed $\chi^2(3) = 0.63$, $p = .89$; CFI = 1.00, RMSEA = 0.00 and factor loadings for the latent variable were high (above .75). No significant associations were observed between hormone reactivity levels and Sensitivity (range β: -0.14 – 0.21; range SE: 0.17 – 0.20; $p \geq .14$), indicating that hormonal reactivity does not predict fathers' sensitive behavior.

Interaction between baseline hormone levels

rFSA analysis revealed that the interaction term between baseline CORT and T, in combination with the main effects of baseline CORT and T as predictors provided the optimal solution for the fit of the data (adjusted $R^2 = 0.06$, $F(3,71) = 2.58$, $p = .06$). A post-hoc multiple regression analysis revealed that the interaction between CORT and T significantly predicted the average of the standardized scores for cooperation and sensitivity (β = -0.27, SE = 0.61, $p = 0.02$). To further examine this interaction conform the dual hormone hypothesis (Mehta & Prasad, 2015), we performed a median split creating a low and high CORT group and assessed the relation between T and Sensitivity for both groups separately (see Figure 4.3). For fathers with low CORT levels, baseline T was more positively related to Sensitivity than for fathers with high CORT levels. However, it should be noted that neither the slope for the low CORT group nor the slope for the high CORT group was significantly different from zero (Low CORT: β = 0.24, SE = 0.45, $p = .15$; High CORT: β = -0.06, SE = 0.45, $p = .73$).

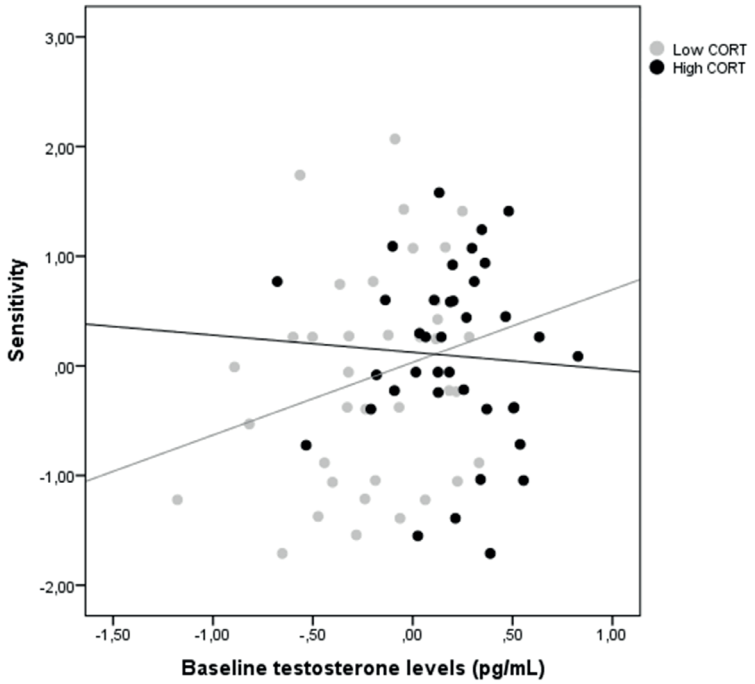

Figure 4.3

The interaction between testosterone and cortisol on sensitivity

Note. This figure demonstrates the interaction between testosterone and cortisol on sensitivity. A median split based on cortisol levels was performed to define High CORT and Low CORT groups. Sensitivity was calculated by averaging the standardized scores for observed cooperation and sensitivity. All three variables are centered and cortisol and testosterone Log-transformed.

Sensitivity analyses

As we obtained perfect fit for each SEM model, suggesting a lack of statistical power to reject the null hypothesis, we performed sensitivity analyses to explore whether multiple linear regression analyses resulted in similar (standardized) estimates. For this purpose, standardized scores for sensitivity and cooperation were averaged. Sensitivity analyses with multiple linear regression analyses revealed similar (standardized) estimates for all three SEM models (see supplementary material Table 4.1 a-c).

Moreover, sensitivity analyses were performed for the three SEM models excluding two participants that had an endocrine disorder or reported to have used medication potentially interfering with the endocrine system on the day of the assessment, as this might affect participants' hormone levels. The SEM with baseline hormone levels as predictors of the latent construct Sensitivity showed a perfect fit: χ^2 (5) = 2.75,

p = .74; CFI = 1.00; RMSEA= 0.00. Parameter estimates revealed no significant associations with the latent construct Sensitivity (range β: -0.21 – 0.12, p > .12), and the beta corresponding to the association between baseline OT and Sensitivity was within the range of 10% from the beta from the main analyses. The SEMs focusing on hormone reactivity levels indicated both perfect fit and revealed similar outcomes as the main analyses.

Discussion

In the current study, the relation between parenting hormones and sensitive parenting behavior was studied in first-time fathers in the early postnatal phase. We explored associations between basal OT, AVP, T, and CORT (separate and combined) on the one hand and paternal sensitivity on the other hand, as well as associations between paternal sensitivity and OT, AVP, T, and CORT reactivity. Finally, we explored the interactions between various basal hormone levels in the prediction of paternal sensitivity. Results revealed no significant associations between sensitivity and hormone baseline levels or reactivity, however, analyses indicated that the interaction between CORT and T significantly predicted paternal sensitive parenting.

As possible correlates of paternal sensitive behavior, we focused on the baseline levels and hormone reactivity of two neuropeptides and two steroid hormones that have previously been associated with parental sensitivity, namely OT, AVP, T and CORT. To test whether baseline hormone levels together are proper predictors of paternal sensitivity, and whether paternal sensitivity predicts hormonal reactivity, we performed SEM analyses with observed sensitivity and cooperation as a latent construct (Sensitivity). Both the SEM model including basal hormone levels, and the SEM model including hormonal reactivity revealed a perfect fit, suggesting a lack of power to reject the null hypothesis that the predicted model and the observed data are equal (Muthen, 2013). Nonetheless, as multiple regression sensitivity analyses revealed similar regression parameter estimates, we are able to interpret the individual regression parameters. Concerning basal hormone levels, none of the bivariate associations between hormones and Sensitivity were significant, suggesting that basal hormones were no suitable correlates of paternal sensitivity in the current study. These findings are not in line with previous literature that reported significant associations between single baseline hormone levels and positive parenting behavior (see e.g., Apter-Levi et al., 2014; Feldman et al., 2010; Kuo et al., 2018; Meijer et al., 2019). Concerning hormone reactivity, no associations with Sensitivity were observed, suggesting that paternal sensitivity does not relate to fathers' hormonal responses to interacting with their infants. Although no previous research examined associations of

AVP and CORT reactivity with paternal caregiving behavior, some previous studies did suggest an association between OT and T reactivity and quality of caregiving (Feldman et al., 2010; van Anders et al., 2012). The current findings did not confirm the limited available previous findings on the link between paternal sensitivity and hormone reactivity.

The discrepancy between the current non-significant associations and previously observed relations might be explained by several reasons. First, the perfect fit of the SEM analyses and the non-significant regression estimates might indicate that the current study was underpowered. This might be due to a relatively small sample size and on average low correlations between hormone levels and observed parenting behavior (Muthen, 2013). Notably, several effect sizes for the regression estimates were around .20 (i.e., the association between baseline OT and Sensitivity, Sensitivity and OT reactivity, and Sensitivity and CORT reactivity) and a trend was observed for the negative association between basal OT and Sensitivity. These might indicate promising findings for further exploration in larger samples.

Second, differences between previous studies and the current study in the operationalization of parental sensitivity may have led to different findings. In the current study, we used the Ainsworth Sensitivity Scales (Ainsworth et al., 1974), reflecting parents' ability to perceive, accurately interpret, and appropriately and promptly react to infants' signals (sensitivity) and the extent to which parents' behavior interferes with the infants ongoing activity (cooperation). A different coding scheme that has been used in previous studies focusing on the endocrine correlates of parental sensitivity is the biobehavioral synchrony model (Feldman, 2012). This model includes amongst others the amount of parental affectionate contact and stimulatory contact (Feldman et al., 2010). Interestingly, although the synchrony model incorporates affectionate behavior that might sooth the infant, the aspect of prompt and appropriate responses to infant signals is not incorporated in the coding scheme. Moreover, stimulatory play can be more or less cooperative, depending on whether the action interferes with the baby's ongoing activity. This difference in coding schemes might explain that we observed reversed (negative) associations between the basal OT and cooperation and between OT and Sensitivity in the current dataset, compared to previous findings of Feldman et al. (2010). Future research is necessary to further examine the similarities and differences between the coding systems to be able to compare previous findings on the associations between fathering behavior and endocrine measurements.

Last, contrary to previous research, we included four hormones that had been associated with parenting behavior, thereby incorporating their shared variance. Including several hormones might be a more suitable method as previous literature indicates that hormones act in concert rather than in isolation (e.g., Feldman & Bakermans-Kranenburg, 2017; Rajhans et al., 2019.

Indeed, in the current study we found that the interaction between CORT and T predicted Sensitivity. The finding that CORT and T interacted in their effects on parenting behavior aligns with the dual hormone hypothesis (Mehta & Prasad, 2015) and previous research (Bos et al., 2018). In the current study, the association between T and sensitivity was positive and stronger for fathers low in CORT than for fathers high in CORT, although in neither group the association between T and sensitivity was significant. Based on the current findings, we suggest that the combinations low CORT and low T levels on the one hand and high CORT and high T levels on the other hand are not related to optimal levels of paternal sensitivity. The latter is in line with previous findings by Bos et al. (2018) who observed lower sensitivity in fathers with high T and high CORT. Future research is clearly needed to elaborate on the associations between hormone systems and parenting behavior. Specifically the interaction between CORT and T seems an important candidate to explore; their interplay might provide a more relevant correlate for positive parenting behavior than hormone main effects.

The current study has several limitations that should be discussed. First, we have single measurements of basal hormone levels, reactivity, and paternal sensitivity. Future research is encouraged to use repeated measurements collected on several consecutive days as this approach may provide more robust indications about the associations between hormones and behavior. Second, we cannot draw conclusions about longitudinal or causal relations between hormones and behavior based on the current study. Although there is time-ordering in the current measures (i.e., the basal hormone sample was collected before the father-infant interaction, and the post-interaction sample was collected 10 minutes after the interaction), the measures were assessed in close temporal proximity. Manipulation of hormones or parenting behavior may be needed to assess any causal effects. Last, as already mentioned above, the current analyses might be underpowered due to the relatively modest sample size. Future research should aim for larger samples to test the associations between hormonal systems and sensitive parenting behavior.

In sum, the current study was the first to explore the separate and combined associations between OT, AVP, T and CORT, and fathers' sensitive parenting behavior. Our results indicate an absence of associations between paternal sensitivity on the one hand and basal levels of hormone activity and reactivity on the other hand. However,

basal CORT and T interacted in their prediction of sensitive parenting behavior. This might indicate that variations in parental sensitivity might be better explained by interactions between hormones than by single hormone levels. As sensitive parenting behavior is related to a number of positive child outcomes including cognitive and socio-emotional development (Deans, 2020) and infant attachment security (Brown et al., 2012; Lucassen et al., 2011), further examination of the association between hormones and behavior might be important to better understand the contributing factors of paternal sensitivity.

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Author contribution (CRediT)

AML: Methodology, Validation, Formal analysis, Investigation, Data curation, Writing-original draft, Visualization, Project administration. RSMB: Methodology, Formal analysis, Writing – review & editing, Visualization, Supervision. KA-vD: Investigation, Writing – review & editing. AMW: Investigation, Writing- review & editing. MJB-K: Conceptualization, Methodology, Formal analysis, Data curation, Writing – review & editing, Supervision, Funding acquisition. MWFTV: Methodology, Formal analysis, Data curation, Writing – review & editing, Visualization, Supervision.

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Chapter 5

Exploring the hormonal and neural correlates of paternal protective behavior to their infants

Lotz, A.M., Verhees, M.W.F.T., Horstman, L.I., Riem, M.M.E., van IJzendoorn, M.H., Bakermans-Kranenburg, M.J., Buisman, R.S.M. (2020). Exploring the hormonal and neural correlates of paternal protective behavior to their infants. *Developmental Psychobiology*, 00,1–12. https://doi.org/10.1002/dev.22055

Abstract

Infant protection is an important but largely neglected aspect of parental care. Available theory and research suggest that endocrine levels and neural responses might be biological correlates of protective behavior. However, no research to date examined associations between these neurobiological and behavioral aspects. This study, preregistered on https://osf.io/2acxd, explored the psychobiology of paternal protection in 77 new fathers by combining neural responses to infant threatening situations, self-reported protective behavior, behavioral observations in a newly developed experimental set-up (Auditory Startling Task), and measurements of testosterone and vasopressin. fMRI analyses validated the role of several brain networks in the processing of infant-threatening situations and indicated replicable findings with the infant-threat paradigm. We found little overlap between observed and reported protective behavior. Robust associations between endocrine levels, neural responses and paternal protective behavior were absent.

Keywords: Brain Imaging, Fathers, Hormones, Parental Care, Protection

Introduction

An important aspect of parental care, but largely neglected in parenting research, is infant protection (Bakermans-Kranenburg & Van IJzendoorn, 2017). Parental protection of infants from diseases, accidents and stranger violence is vital for infant survival during pregnancy and after birth (Hahn-Holbrook et al., 2011). In addition, experiences with protective parents may enhance children's trust in parent's availability to help and protect them in times of danger or distress, promoting secure attachment (Bowbly, 1982). Despite the clear importance of parental protection by both parents, protective behavior, and its neurobiology has been mainly studied in mothers (Hahn-Holbrook et al., 2011). Since fathers have an increasing role in childcare in modern Western societies (Bakermans-Kranenburg et al., 2019), research into fathers' caregiving and paternal protection is timely. For this reason, this study aims to explore the psychobiology of protective behavior in fathers.

Studies in both biparental mammals and humans have examined the psychobiology of paternal protective behavior in a variety of paradigms. In mammals, for example, pup retrieval and attacking intruders as examples of parental protection have been studied (Abraham & Feldman, 2018; Wynne-Edwards & Timonin, 2007). The neural basis of this behavior might be linked to the endocrine system, with an important role for steroids and neuropeptides (reviewed by Bales & Saltzman, 2016, but see Wynne-Edwards & Timonin, 2007 for a critical note on the suggestion of a causal link between behavior and the endocrine system). In humans, men's behavioral, hormonal and neural responses have been studied during exposure to infant crying, an indicator for a possible threatening situation (e.g., Alyousefi-Van Dijk et al., 2019; Khoddam et al., 2020; Li, Chen, Mascaro, Haroon, & Rilling, 2017; Thijssen et al., 2018; Van Anders, Tolman, & Volling, 2012), during exposure to video fragments of infant-threatening situations, and via self-report on daily life situations (e.g., Van 't Veer, Thijssen, Witteman, Van IJzendoorn, & Bakermans-Kranenburg, 2019). Several literature reviews described a neuro-endocrine basis for paternal behavior (Abraham & Feldman, 2018; Hahn-Holbrook et al., 2011; Rilling & Mascaro, 2017), indicating that specific hormones such as testosterone (T) and vasopressin (AVP), and specific neural activations might be proper correlates or even activators of observed protective behavior. However, only few studies combined the various aspects of the psychobiology of human paternal protective behavior, and no studies to date integrated all three aspects (hormonal, neural, and behavioral). This study aims to fill this gap by combining neural responses to infant threat, behavioral measures of protective behavior in daily life and in an experimental set-up, and measurements of T and AVP.

The potential roles of T and AVP in protective parenting have been incorporated in the Steroid/Peptide Theory of Social Bonds (Van Anders, Goldey, & Kuo, 2011). This model is mostly based on nonhuman mammalian literature, although it includes human research as well. First, the model implies that low levels of T might be linked to parental contexts that are perceived as nurturing. This idea is in line with previous research in humans showing that lower salivary T is associated with increased participation of fathers in child care and enhanced quality of caregiving, both prenatally (Bos et al., 2018; Edelstein et al., 2017) and postnatally (Bos et al., 2018; Gettler et al., 2011; Weisman et al., 2014), although combined effect sizes are small (for a meta-analysis see Meijer, Van IJzendoorn, & Bakermans-Kranenburg, 2019). Additionally, the Steroid/Peptide Theory of Social Bonds implies that high levels of T are associated with parental contexts that involve a need for protective responses. Indeed, research has shown that cry sounds increase salivary T levels in men when no nurturing action is possible (Van Anders et al., 2012). Additionally, T levels in fathers-to-be are positively associated with neural activation in brain areas involved in social cognition, arousal, and reward learning when listening to infant cry sounds (Khoddam et al., 2020), although it should be noted that another study did not reveal such a relation in fathers of infants between 1 and 2 years old (Mascaro et al., 2014). Moreover, T administration increases men's neural responses to facial threat cues in brain areas associated with threat processing (Goetz et al., 2014). On the basis of these findings, we expect that baseline T levels are positively associated with protective behavior and neural reactivity to infant-threatening stimuli.

Second, the Steroid/Peptide Theory of Social Bonds assigns a specific role to AVP reactivity in protective parenting, with increases of AVP positively related to protective aggression (Van Anders et al., 2011). A number of studies suggest that paternal protection might be associated with AVP. For instance, it has been shown that in father-to-be's administration of AVP increases orientation towards baby avatars (Cohen-Bendahan et al., 2015), increases excessive handgrip force while looking at an image of an unknown infant compared to an image of their own infant (Alyousefi-Van Dijk et al., 2019), and increases activation in several brain areas in response to emotionally versus neutrally labeled infant cry sounds (Thijssen et al., 2018). Moreover, basal AVP levels in fathers have been shown to be negatively related to neural activity in brain areas involved in empathy and social cognition when viewing neutral or positive videos of own infant versus other infant (Atzil et al., 2012). The authors interpreted this as a possible AVP-dependent vigilance towards strangers. In contrast, other studies showed that AVP administration did not increase fathers' neural processing of infant cry and the subjective cry rating (Li et al., 2017), and no correlation between basal AVP levels and explicit and implicit infant caregiving was observed in prospective fathers (Cohen-Bendahan et al., 2015). Thus, mixed findings for both basal and reactive AVP levels in protective behavior have been documented. However, no studies to date specifically

looked at AVP in relation to protective paternal behavior and neural processing of infant threat. Based on previous findings and the Steroid/Peptide Theory, it could be predicted that higher basal levels of AVP are associated with more paternal protective behavior and stronger neural responses to infant threat.

As mentioned above, very little research has examined the relation between brain responses and behavior in the context of protective behavior. To our knowledge, only one study to date has focused on the relation between paternal protective behavior and its neural correlates (Van 't Veer et al., 2019). In that study, on a different sample than this study, several brain networks known to be associated with the parental care network, visual processing and threat detection were shown to be involved in the processing of videos depicting infant-threatening situations. Moreover, father's reported protective behavior in daily life was linked to stronger brain activation in the frontal pole while watching their own (versus an unknown) infant in threatening (versus neutral) situations. Based on these findings, activation of a neural threat component might be positively associated with observed and reported protective behavior.

This study explores the psychobiological correlates of paternal protection. To this end, paternal protective responses were measured using behavioral observations during the exposure to a loud/alarming sound in a lab setting, self-reported protective behavior, and the neural processing of videos depicting infant-threatening situations. Moreover, basal salivary T and AVP levels were determined, and relations between neural, hormonal, and behavioral measures were examined. We hypothesized that these three measures would be positively related, for example, higher neural responses to infant threat in brain areas involved in the parental care network, visual processing areas and threat detection would be associated with higher basal hormone levels and more observed and self-reported protective behavior (see Figure 5.1a). Moreover, based on the previously reported hormone administration effects on neural processing (e.g., Goetz et al., 2014; Thijssen et al., 2018), we speculated that the associations between T and AVP levels and protective behavior would be mediated by neural responses to infant threat in brain areas involved in the parental care network, visual processing areas and threat detection (see Figure 5.1b).

Methods

Participants

Seventy-seven first-time fathers participated in this study. Participants were recruited via municipal records, infant welfare centers, midwife practices, and social media (see Figure S5.1 for an overview of the recruitment). To maximize sample size for the current

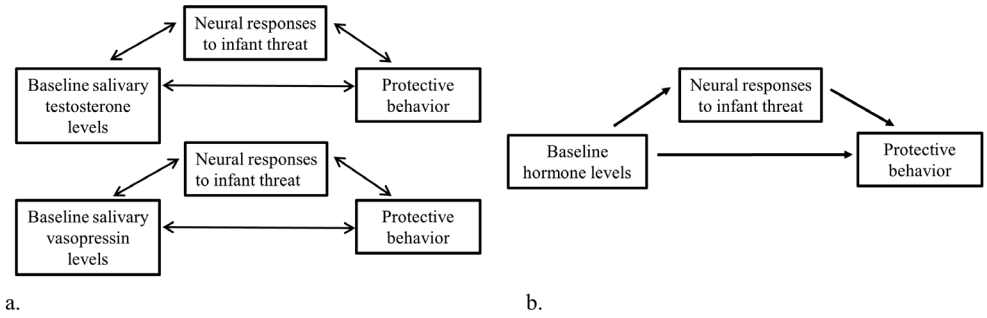

Figure 5.1

Visual overview of working hypotheses

Note. a. The planned associations between the three dependent variables. Protective behavior represented by either observed or reported protective behavior; b. Neural responses as a mediator in the relation between baseline hormone levels and protective behavior.

analyses, we decided to deviate from a priori stated inclusion criteria in nine cases (MRI contraindication $n = 5$, Cardiovascular disease $n = 1$, Use of medication potentially interfering with the endocrine system $n = 1$, Birth < 37 weeks $n = 1$, Not biological father $n = 1$). Participants who were not eligible to undergo an fMRI scan, for example due to diabetes or metallic foreign objects in body, were invited for a research visit at the participant's home. All but one participant were the biological father of the child. All participants cohabited with the biological mother of the child. Moreover, participants were in good mental and physical health (i.e., had no psychiatric, neuroendocrine or neurological diagnosis, and no upper torso injury that could affect the use of a baby carrier), except for four who reported a psychiatric, neuroendocrine, or cardio-vascular diagnosis, or had taken medication on the assessment day that could interfere with the endocrine system. Participants reported no significant intake of alcohol or drugs at the time of inclusion. Participants spoke Dutch fluently and reported not to use a baby carrier over 5 hr per week at time of inclusion, which was relevant for various research questions. All children, except for one (born after 36 weeks and 6 days), were born full-term (i.e., born after 37 week gestation) and all were in good health. See Table 5.1 for sample characteristics. The study was approved by the Ethics Committees of the Leiden University Medical Centre and of the Department of Education and Child studies at Leiden University. The study was carried out in accordance with the declaration of Helsinki and all participants gave written informed consent.

Procedure

The research visit was located either in the Leiden University Medical Centre or at the participant's home, depending on possible MRI contra-indications (e.g., diabetes, metallic foreign objects in participant's body) and preference of the participant. The assessment consisted of the following measures: Behavioral measurements, including a 10-min Free play (Witte et al., 2019), a handgrip force paradigm (Alyousefi-Van Dijk et al., 2019), and the Five Minute Speech Sample (Lotz et al., 2020); Saliva and hair sampling for hormonal measurements; and questionnaires about, for example, health, medication and current mental state. When the assessment took place in the LUMC, the Auditory Startling Task (AST, Witte et al., 2019) was performed and neural

Table 5.1

Sample Characteristics

		M(SD)/N(%)	Range
Participant age (years, *N* = 77)		33.14 (5.39)	25.06 – 56.50
Education (years past primary education, *N* = 76)		8.25 (1.86)	3.00 – 10.00
Country of birth (*N* = 76)	The Netherlands	70 (92%)	
	Other	6 (8%)	
Race (*N* = 77)	Caucasian	71 (92%)	
	Other	6 (8%)	
Infant age (weeks, *N* = 77)		11.40 (3.10)	7.57 – 21.43
Infant sex (*N* = 77)	male	41 (53%)	
	female	36 (47%)	
Testosterone (pg/mL, *N* = 75)		43.17 (35.15)	2.14 – 216.96
Vasopressin (pg/mL, *N* = 75)		1.64 (0.46)	0.87 – 2.67
AST (*N* = 59)		5.56 (1.70)	3.00 – 10.00
PPQ (*N* = 72)		3.46 (0.39)	2.29 – 4.00
fMRI cluster 1 (*N* = 64)		0.67 (0.96)	-2.15 – 2.53
fMRI cluster 2 (*N* = 64)		0.76 (0.97)	-1.98 – 2.90
fMRI cluster 3 (*N* = 64)		1.02 (0.95)	-1.04 – 2.94
fMRI cluster 4 (*N* = 64)		0.89 (0.78)	-0.79 – 2.62

Note. Sample Characteristics are calculated based on non-transformed complete cases data. Participants' race was coded by researchers based on videotapes of fathers and was defined as Caucasoid type or other. AST: protective behavior observed during the Auditory Startling task. PPQ: self-reported protective behavior measured with the Paternal Protection Questionnaire. fMRI cluster 1 – 4 are individual mean *z*-values based on the contrast threat > neutral. Cluster 1: left cuneal cortex, left lateral occipital cortex and left occipital pole. Cluster 2: right cuneal cortex, right lateral occipital cortex and right occipital pole. Cluster 3: left supramarginal gyrus, planum temporale, lateral occipital cortex, central opercular cortex, middle temporal cortex, parietal operculum cortex. Cluster 4: insular cortex, frontal orbital cortex, temporal pole, superior frontal gyrus, frontal operculum cortex, central operculum cortex, thalamus, putamen, precentral gyrus, right planum temporale, right supramarginal gyrus, right middle temporal gyrus, right inferior temporal cortex, right superior temporal gyrus, anterior cingulate gyrus, amygdala.

measurements were conducted with (f)MRI and DTI. Following the assessments, participants and partners completed some online questionnaires at home (including the Parental Protection Questionnaire, PPQ;Van 't Veer et al., 2019).

Measures

Protective Behavior

Auditory Startling Task. To observe paternal protective behavior, we applied the AST (Witte et al., 2019). During the AST, a short loud sound fragment was played "unexpectedly" by a hidden audio installation while the participant was videotaped playing with his infant. The sound consisted of white noise (80 dB) and was programmed for 10 s with short breaks. At the end of the sound fragment, the researcher entered the room and apologized for the sound, referring to technical problems (the purpose of the sound fragment was explained to the participants at the end of the study). Paternal protective behavior was coded from the video, as well as baby states 30 s before and during the sound fragment. The coding system was developed for the current study. The coding scheme for protective behavior consists of a 10-point scale, with higher scores reflecting more protective behavior, see Table S5.1. The coding scheme for baby states before and during noise was based on a 5-point scale (Mah, Bakermans-Kranenburg, Van IJzendoorn, & Smith, 2015), with one additional scale point: 1 = Drowsy or asleep, 2 = Quiet, 3 = Alert, 4 = Startled, 5 = Fussing, 6 = Distressed. When various states or responses were observed, the highest rating was assigned. Five raters were trained by one of the authors (AL). Interrater reliability was assessed based on a total of 20 videos. A first set of 10 videos was scored directly after the training. A second set of ten videos was coded after all raters coded several videos independently. All raters obtained good interrater reliability, ICC (single measure, absolute agreement) for Paternal protective behavior > .84, Baby state before noise ICC > .67, Baby state during noise ICC > .75).

Parental Protection Questionnaire. To measure father's protective behavior towards the child in daily life, fathers were asked to fill in the Parental Protection Questionnaire (PPQ, see Van 't Veer et al. (2019) for a prenatal version of this questionnaire) after the assessment. The partners reported on the participants' protective behavior as well. The questionnaire contains 12 items that were scored on the prevalence during the past month (1 = never, 2 = seldom, 3 = sometimes, 4 = often or always, 5 = not applicable). Examples of questions are: "I made sure that the baby's diaper was changed in time", or "I made sure that the living room was safe for the baby". Scores on items that were coded 5 were replaced with individual mean scores calculated over all other items. A one-factor exploratory factor analysis on participants' data revealed that the first factor explained 24.4% of the variance and seven items loaded > .40. These seven items ($\alpha_{participant}$ = .67 and $\alpha_{partner}$ = .80) were used to calculate mean scores for self-reported and partner-reported protective behavior.

Latent Construct 'Protective behavior'. Associations between participants' observed protective behavior and reported protective behavior (partner- and self-report) were examined in the full cases dataset, and indicated no underling latent construct for 'Protective behavior (range r = -.04 to .19, p >.16). Additionally, we explored a possible multi-informant component for self-reported protective behavior (Kraemer et al., 2003), combining both partner and participant PPQ scores on the seven EFA items. A PCA with varimax rotation did not reveal the presence of a multi-informant component. Observed and self-reported protective behavior were, therefore, separately examined in subsequent analyses.

Neural Responses to Infant Threat

fMRI Infant Threat Paradigm. To examine the possible neural basis for paternal protection, fathers participated in an fMRI task adapted from Van 't Veer et al. (2019). In the current protection task, as described in Witte et al. (2019), participants watched videos while lying in an MRI scanner. The videos depicted either a scenario in which an infant was in a threatening situation or a matched neutral video in which there was no threat to the infant. During the task, participants watched 12 different video pairs (see Table S5.2 for a description of the videos, videos available upon request). The video fragments were filmed using a gender-neutral lifelike baby doll. Fathers were instructed to imagine that the infant in the videos was their own infant. To ease the task of imagining their own infant in the videos, a picture of their infant was shown before the task. Moreover, the visibility of the doll's face and the faces of the actors in the videos was minimized.

Each video, 12 threatening video fragments and 12 matched neutral video fragments, was shown twice, resulting in a total of 48 videos. The duration of each video fragment was 6 s. The videos were shown in one of four pre-programmed semi-random orders. For each order, it was ensured that videos were equally distributed across the task: 12 neutral and 12 threatening videos were presented during the first half of the task as well as the second half of the task. To maximize the power of the design, inter stimulus interval (ISI) between videos was sampled using the web-based tool Neurodesign (Durnez et al., 2017). Videos were separated by an ISI of variable length ranging from 3.0 to 8.0 s, with a mean ISI of 4.5 s. The task was programmed in E-Prime software (version 2.0; Psychology Software Tools, Inc.).

Prior to the assessment, participants were asked to send a neutral picture of their own child. To ensure that each photo contained only the facial features of the infant, each photo was edited in Adobe Photoshop CS by adding a black-face contour to remove ears and most of the hair, and a black background. To make sure that all images contained approximately the same pixel ratio between the black background and face, images

were resized so that face length was set on 10 cm. Finally, a selection of the picture containing the face was copied to a new black image of 640 x 480 pixels. Participants were familiarized to the edited image and task design during a practice task prior to the MRI scan session with two pairs of neutral and threatening videos that were not included in the real task. At the onset of the real task, an edited picture of participants' own infant was shown with a written instruction to imagine that their own infant is displayed in the succeeding videos. The instruction and edited picture were shown again after each eight videos (thus six times in total). After a stimulus interval of 250 ms, the instruction screen advanced to one of the four pre-programmed semi-random order of 48 videos as described above.

fMRI Parameters. MRI scanning was performed on a 3 T Philips Achieva TXMRI system (Philips Medical Systems, Best, the Netherlands). For registration purposes, a T1-weighted anatomical scan was acquired (repetition time (TR)= 7.90 ms, echo time (TE) = 3.50 ms, flip angle = 8°, 155 transverse slices, ACQ voxel size 1.1 × 1.1 × 1.1 mm). The fMRI-task utilized a gradient-echo blood oxygen level dependent (BOLD) echo-planar imaging sequence with: TR = 2,200 ms, TE = 30 ms, flip angle = 80°, 38 transverse slices, and ACQ voxel size of 2.75 × 2.75 × 2.75 mm (including a default interslice gap). The duration of the fMRI paradigm was 10 min 53 s (290 volumes). Fieldmap corrections were performed using a multi-acquisition B0 map, performed directly after the end of the fMRI protection task.

fMRI Data Analyses. Data was structured following the Brain Imaging Data Structure (BIDS) (Gorgolewski et al., 2016) and preprocessed using *fMRIPrep* (version 1.5.2 (Esteban, Markiewicz, et al. (2018); RRID:SCR_016216)), which is based on *Nipype* 1.3.1 (Gorgolewski et al. (2011); RRID:SCR_002502), see supplementary material for details. Furthermore, in the FEAT module (Smith et al., 2004) of FMRI Expert Analysis Tool (FSL), spatial smoothing was performed using a Gaussian kernel with a full-width-at-half-maximum of 5 mm. High-pass filter cutoff was set at 90 s. First-level analyses of the participant for the contrast threatening videos > neutral videos and the reverse contrast threatening videos < neutral videos were performed using FEAT. Threatening and neutral videos as well as the instruction picture of own child were modeled separately as a square-wave function. Each predictor was convolved with a double gamma hemodynamic response function and temporal derivatives were added to the model, resulting in six regressors in each model. All first-level contrast images and the corresponding variance images were submitted to second level mixed-effects group whole-brain analyses. Group-level analysis was performed using FEAT to detect average activation for the contrast threat > neutral and the reverse contrast. Statistical maps were thresholded using clusters determined by $Z > 3.1$ and a cluster corrected significance threshold of $p < .05$. Masks were created for each significant cluster

resulting from the threat > neutral contrast and used as input for a featquery extracting the individual mean *z*-value values for each significant cluster. These individual *z*-values were used for further confirmatory analyses. Visual inspection of motion parameters flagged one participant with head motion between 1.4 and 3.0 mm, and sensitivity analysis for fMRI higher level analysis was performed.

Salivary testosterone and vasopressin

Salivary samples were obtained at the beginning of each assessment. Most assessments took place in the late afternoon, that is, after 15:00, or early evening (67%), however, visits were also scheduled during the morning (18%) or early afternoon (15%) (*M* = 15:38 hr, *SD* = 3.05, range = 09:15 – 19:39). Participants were instructed not to consume any alcoholic drinks or have excessive physical exercise during the last 24 hr prior to each assessment. Furthermore, participants were asked not to drink any caffeine-containing drinks on the day of the assessment, and not to smoke, chew gum, eat or drink (other than water) 30 minutes before the start of the appointment. Just before sampling participants rinsed their mouth with water. All samples were stored as soon as possible at -20 ˚C. Saliva samples collected at home were placed on ice for transportation. Samples of one participant were excluded from analyses since they were not frozen after collection.

Testosterone. Participants drool approximately 1.5 ml saliva into a 2 ml cryogenic vial (SalivaBio, Salimetrics), either directly into the vial or indirectly using a saliva collection aid (Saliva Bio, Salimetrics). Before drooling, participants were asked to swallow once and to bent slightly forward. To stimulate saliva production, participants were recommended to think about something sweet or sour, to move their jaws up and down, or to look at pictures of food that were provided. On average, it took 9.16 (*SD* = 5.64) min to complete the collection. T was quantified at Dresden LabService GmbH (Germany) by Luminscence enzyme immunoassay (IBL International GMBH), see Alvergne et al. (2009) for a description of the procedure. Fifty microliter of each sample was used for the immunoassay. The limit of detection was 1.8 pg/mL. Samples used for this article were quantified in the same assay run (12 plates in total). Duplicate analysis was performed for a random selection of 30% of the samples. For these samples, an average value was calculated and used in further analyses. Inter-assay variability was 10% and intra-assay variability was 5.22%. Cross-reactivity with other substances tested $\leq$ 0.01 %. T values are reported in pg/mL.

Vasopressin. Participants chewed on a cotton swab (Salivette, Sarstedt) for 60 s. Saliva for the quantification of AVP was collected using salivettes (Sarstedt). Participants were instructed to chew lightly on a cotton swab for 60 s and move the swab around in their mouth every now and then to boost saliva collection. Researchers kept track of the

time using a stopwatch. AVP levels were quantified by radioimunnoassay at RIAgnosis (Sinzing, Germany), as previously described in Frijling et al. (2015) and Kagerbauer et al. (2019). Salivettes were centrifuged at 4 for 30 min with ca. 5,000 *g* centrifugal force, after which 0.3 ml of saliva was pipetted into a vial for the analysis of AVP. The detection limit for AVP was 0.1 pg/ml. All samples were analyzed simultaneously in the same assay run. Intra-assay and inter-assay variability was < 10%. There was no significant cross-reactivity with other neuropeptides (< 0.7%). AVP values are reported in pg/mL.

Data-analyses

Data Distribution

Distribution of the full cases data was visually inspected and normality was tested using the Shapiro Wilk test in SPSS version 23. fMRI mean *z*-values were normally distributed. Basal AVP levels approached normal distribution. T levels were right skewed and were therefore log-transformed for further analyses. The distributions of self-reported and partner-reported protective behavior were left-skewed and were therefore transformed with reflective log to approach a normal distribution. The distribution of observed protective behavior was right-skewed, however, transformations did not improve the data distribution, thus nontransformed scores of observed protective behavior were used in further analyses. Sensitivity analyses with Spearman correlations were performed for variables with a non-normal distribution. Visual inspection of boxplots in combination with corresponding z-values (outlier > 3.29) indicated one outlier for the variable Age of the participant. The outlier was winsorized (Tabachnick & Fidell, 2007). Further analyses were conducted in SPSS version 23, unless stated otherwise.

Multiple Imputation

Nine percent of the data was missing (range: 0 - 25%). Little MCAR test (Little, 1988b) was not significant ($\chi^2(194) = 191.98$, $p = .53$), indicating that data was missing completely at random. Missing data were multiply imputed with the R package 'mice' (Van Buuren & Groothuis-Oudshoorn, 2011) in R (R Development Core Team, 2008). The missing data was imputed 50 times with 100 iterations, using predictive mean matching (PMM; Little, 1988a). For the construction of the prediction model, all variables of interest (observed – and self-reported protective behavior, basal T and AVP levels, individual mean *z*-values for fMRI clusters 1-4), all possible covariates and auxiliary variables (i.e., variables that are not part of the model but that are correlated with the variables in the model: age of the infant at time of the first assessment and scored baby state before AST noise) were taken into account. Autocorrelation function (ACF) plots (Azur, Stuart, Frangakis, Leaf, 2011) indicated that all imputations converged. Moreover, correlations between imputed variables (Table 5.2) were similar to the correlations between non-imputed variables (see Table S5.3). The imputed datasets were used for further confirmatory analyses.

Table 5.2

Correlations between neural, behavioral and hormonal measurements based on multiply imputed data

	1.	2	3.	4.	5.	6.	7.
1. testosterone	.						
2. vasopressin	-.06	.					
3. AST	-.07	-.20	.				
4. PPQ	-.06	-.06	.16	.			
5. fMRI cluster 1	.16	-.01	.02	.09	.		
6. fMRI cluster 2	.22†	.07	-.02	.08	.85**	.	
7. fMRI cluster 3	.14	-.08	.00	.03	.74**	.70**	.
8. fMRI cluster 4	.16	-.00	-.05	.01	.81**	.77**	.90**

Note. Bivariate Pearson correlations are calculated based on pooled multiply imputed data. AST: protective behavior observed during the Auditory Startling task. PPQ: reflective log transformed self-reported protective behavior measured with the Paternal Protection Questionnaire. fMRI cluster 1 – 4 are individual mean *z*-values based on the contrast threat > neutral. Cluster 1: left cuneal cortex, left lateral occipital cortex and left occipital pole. Cluster 2: right cuneal cortex, right lateral occipital cortex and right occipital pole. Cluster 3: left supramarginal gyrus, planum temporale, lateral occipital cortex, central opercular cortex, middle temporal cortex, parietal operculum cortex. Cluster 4: insular cortex, frontal orbital cortex, temporal pole, superior frontal gyrus, frontal operculum cortex, central operculum cortex, thalamus, putamen, precentral gyrus, right planum temporale, right supramarginal gyrus, right middle temporal gyrus, right inferior temporal cortex, right superior temporal gyrus, anterior cingulate gyrus, amygdala. Testosterone values were log transformed and corrected for time of collection. Spearman correlations did not differ significantly from Pearson correlations shown above.
** $p < .01$, † $p < .1$

Covariates

For the full-cases and pooled multiply imputed data, it was tested whether time of saliva collection, age of participant at time of first assessment, excessive physical exercise, recent alcohol and caffeine use were significantly correlated with basal hormonal levels. In addition, baby state during AST noise was examined as a significant covariate for observed protective response during the AST and number of days between the start date of the intervention and the date the PPQ was completed was examined as a significant covariate for the PPQ. Only a significant correlation between time of saliva collection and T was observed (r= -.23, p= .048; r_{pooled} = -.23, p = .046), therefore, T values were corrected for time of collection via residualizing. Spearman correlations revealed approximately similar outcomes.

Confirmatory Analyses

Pearson bivariate correlations were calculated to examine the relation between the neural, behavioral and hormonal measurements. Only neural clusters that included brain areas involved in the parental care network, visual processing areas or threat detection (as reported in Van 't Veer et al., 2019) were included in the current

confirmatory analyses. Significance was set at $p < .05$. Equivalence tests using a two one-sided tests (TOST) procedure, were performed to explore whether observed effects that failed to reach statistical significance were not caused by insufficient statistical power (Lakens et al., 2018). Lower and upper bounds were set to an effect size of $r = .08$, which was considered the smallest effect size of interest based on previous literature (Alyousefi-Van Dijk et al., 2019; Meijer et al., 2019).

Exploratory Analyses

Bivariate correlations between neural clusters activating on the reverse contrast neutral > threat, and behavioral and hormonal measurements were explored in the complete cases dataset. Significance was set at $p < .05$. A Benjamini-Hochberg correction was applied to control for multiple testing. When the confirmatory analyses revealed significant correlations between the neural, behavioral and hormonal measurements, mediating effects of neural responses on the relation between salivary hormone levels and observed and self-reported protective behavior were explored.

Sensitivity Analyses

We conducted three sensitivity analyses. First, a sensitivity analysis was performed for the fMRI higher-level data analysis, excluding one participant with head motion between 1.4 mm and 3.0 mm. Second, Spearman correlations were performed when analyses included variables that were not normally distributed. Third, sensitivity analyses were performed excluding nine participants based on the *a priori* stated exclusion criteria. To control for multiple testing, a Benjamini-Hochberg correction was applied to these sensitivity analyses.

Results

fMRI Results

Second level mixed-effect group whole-brain analyses revealed four significant clusters for the contrast threat > neutral (see Figure 5.2 and Table 5.3 for cluster information). Descriptive statistics reported below are based on pooled values from the multiple imputed dataset. The first cluster corresponded to the left cuneal cortex, left lateral occipital cortex and the left occipital pole. The average mean *z*-value for activation was 0.69 (*SD* = 0.95, range = -2.15 to 2.53). The second cluster consisted of the right cuneal cortex, right lateral occipital cortex and the right occipital pole. The average mean *z*-value for activation was 0.77 (*SD* = 0.95, range= -1.98 to 2.90). The third cluster included the left supramarginal gyrus, planum temporale, lateral occipital cortex, central opercular cortex, middle temporal cortex, parietal operculum cortex. The average mean *z*-value for activation was 1.03 (*SD* = 0.95, range = -1.04 to 2.94). The fourth

cluster corresponded to the bilateral insular cortex, bilateral frontal orbital cortex, bilateral temporal pole, bilateral superior frontal gyrus, bilateral frontal operculum cortex, bilateral central operculum cortex, bilateral thalamus, bilateral putamen, bilateral precentral gyrus, right planum temporale, right supramarginal gyrus, right middle temporal gyrus, right inferior temporal cortex, right superior temporal gyrus, bilateral anterior cingulate gyrus, bilateral amygdala. The average mean *z*-value for activation was 0.89 (*SD* = 0.77, range = -0.79 to 2.62).

Second-level mixed-effect group whole brain analyses revealed 14 significant clusters for the contrast neutral > threat (see Table S5.4 and Figure S5.2 for cluster information).

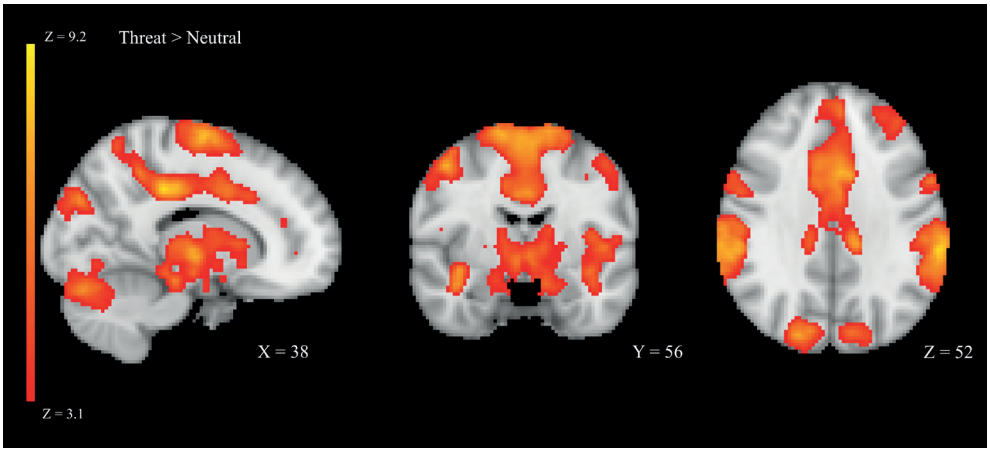

Figure 5.2

Neural activation for the contrast threat > neutral

Note. Activation is thresholded at Z > 3.2, $p < .05$.

Table 5.3

Brain coordinates of the peak average z-value for the contrast threat > neutral

Cluster index	voxels	region	x	y	z	Peak z	*p*
4	50297	L Insular cortex	-42	16	-8	8.89	0.00
3	6255	L Supramarginal gyrus	-64	-36	24	9.24	1.23e-36
2	828	R Lateral occipital cortex	20	-84	32	7.18	4.87e-9
1	556	L Cuneal cortex	-8	-82	30	5.76	8.94e-7

Note. L = left, R = right.

Associations between behavioral, neural, and hormonal measurements

As shown in Table 5.2, analyses revealed no significant associations between observed and self-reported protective behavior, neural reactivity, and T and AVP levels. Significant correlations were observed between the four fMRI clusters (range $r = .70$ - $.90$, $p < .01$), indicating that neural reactivity in the four clusters were strongly correlated. Equivalence tests were non-significant, indicating that the effect sizes were statistically equivalent (i.e., the observed effect sizes were not significantly different from the smallest effect size of interest, which was set at $r = .08$).

Exploratory Analyses

As shown in Table S5.5, analyses revealed no significant associations between the neutral > threat neural reactivity in the 14 clusters and basal hormone levels, observed- and self-reported protective behavior. Since the confirmatory analyses revealed no significant correlations between the neural, behavioral and hormonal measurements, mediating effects of neural responses on the relation between salivary hormone levels and observed and self-reported protective behavior were not examined.

Sensitivity Analyses

Analyses excluding one participant with excessive head motion revealed two significant clusters for the contrast threat > neutral. These two clusters contained the same brain regions as the four clusters in the group analysis reported above. One of these two clusters was very large (64,886 voxels) meaning that the calculated mean *z*-value for this cluster would be less specific for further interpretation. For this reason, it was decided to perform further analyses based on the four clusters. Second, Spearman correlations revealed approximately similar outcomes for the correlational analyses including variables that were not normally distributed. Third, analyses excluding nine participants who did not meet a priori stated inclusion criteria (see Table S5.6) revealed a negative association between AVP and observed protective behavior ($r = -.28$, $p = .03$) and a positive association between T and fMRI cluster 2 ($r = .26$, $p < .05$). These findings did not survive corrections for multiple testing.

Discussion

This study, preregistered on https://osf.io/2acxd, explored the psychobiological correlates of paternal protection in the early postnatal period. To this aim, protective behavior, neural responses to infant threat, and T and AVP levels were assessed in new fathers. Our main analyses revealed no significant associations between the behavioral, neural, and hormonal measures. Because significant associations were absent, the neural responses could not mediate the relation between salivary hormone levels and protective behavior.

Although protection is a crucial aspect of parenting, measures for parental protective behavior are scarce. The current study used a postnatal version of the PPQ (Van 't Veer et al., 2019) as an assessment of self-reported and partner-reported protective behavior. In addition, we introduced a new behavioral task to observe paternal protective behavior (the AST). Both measures aim to study the level of paternal precautionary behavior in real-life (Hahn-Holbrook, Holbrook, & Haselton, 2011) and obtained good reliability, but they were not significantly related. The measures may assess different aspects of paternal protection. Specifically, the PPQ examines behavior aimed at preventing possible harm to the infant, for example, focusing on hygiene and a safe environment, whereas in the AST an actual stressor, that is, a loud sound, is presented, calling for an immediate protective response. An alternative explanation could be that different response processes are involved in the two measures (Dang et al., 2020). The PPQ asks for participants' own perception of fathers' protective behavior in daily life situations during the past month, whereas in the AST, participants' actual behavior is assessed in a controlled unknown lab setting. Research indicates that reported and observational measures are often weakly correlated (Dang et al., 2020), especially in the realm of parenting (e.g., Voorthuis et al., 2013). In the AST, the majority of participants and infants showed a startle response in response to the sound, and a range of behaviors were observed, suggesting that the manipulation had the intended effect and inter-individual differences in protective behavior were observed. However, one could question whether the loud sound was experienced as a real threat for the infant. Due to ethical reasons, no stronger stressors could be used to trigger a paternal protective response. With these limitations in mind, we suggest that both the PPQ and the AST may be promising measures to assess different dimensions of protective behavior.

We did not find significant correlations between T and AVP levels and self-reported and observed protective behavior in our main analyses. These results did not support the hypotheses that T and AVP would be positively associated with protective behavior. Our hypotheses were based on the Steroid/Peptide Theory of Social Bonds (Van Anders et al., 2011), in which high levels of T and AVP are linked to parental contexts that involve a need for protective responses, particularly in the context of protective aggression. It should be noted that protective aggression is not directly measured in the PPQ or AST; the PPQ and AST are more likely to reflect child-focused behavior instead of parental aggression against the source of the danger the child is exposed to. Measuring child-focused behavior instead of source-focused protective aggression might explain the absence of an association between the hormonal and behavioral measurements. Furthermore, we focused on endogenous basal levels of T and AVP, rather than on reactivity or exogenous administration. This approach differs from that of several other studies (Cohen-Bendahan et al., 2015; Goetz et al., 2014; Thijssen et al., 2018; Van Anders et al., 2012), and might explain the diverging results.

Neural activation in response to infant threat was measured via an fMRI protection paradigm, adapted from Van 't Veer et al. (2019). In this paradigm, situations in which an infant is in immediate danger are shown; these are potential accidents that are likely to provoke a protective behavioral action when occurring in real life. In the current sample, whole brain analyses revealed four significant clusters for the contrast threat > neutral, and these clusters were strongly related to each other. The clusters comprised brain areas associated with visual processing (Grill-Spector & Malach, 2004), impulse control (Hu et al., 2016), empathy (Feldman, 2015; Rilling & Mascaro, 2017), mentalizing (Feldman, 2015), emotion regulation (Feldman, 2015) and threat detection, and reaction (Hahn-Holbrook et al., 2011; Swain & Ho, 2017). Brain areas involved in the latter four processes are associated with the parental caregiving network (Feldman, 2015; Rilling & Mascaro, 2017). These results align with those by Van 't Veer et al. (2019), who also found neural activation in brain networks associated with visual processing, threat detection, and the parental caregiving network, in first-time fathers (to-be) using a similar paradigm in an independent and smaller sample. This study thus validated the role of several brain networks in the processing of infant-threatening situations, and presents replicable findings with the infant-threat paradigm. Future fMRI studies may examine these replicated brain regions using a Regions of Interest (ROI) approach.

We did not find significant associations between neural responses to infant threat and basal T and AVP levels in our main analyses. The lack of associations between T, AVP and neural responses to infant threat was not in line with our predictions based on limited previous research that explored the relation between basal salivary T, AVP and neural responses (i.e., in areas involved in social cognition) to positive and negative infant stimuli (Atzil et al., 2012; Khoddam et al., 2020). For example, Khoddam and colleagues (2020) observed a positive correlation between T and neural responses to infant cry. Although infant cry can be an indicator of an infant-threatening situation, our infant-threat fMRI paradigm may represent a more direct measure for infant-threatening situations as infants in immediate danger are shown. Since no previous studies specifically focused on neural responses to the observation of infant-threatening situations, future studies should elaborate on (the lack of) associations between basal levels and reactive T and AVP, and neural responses to infant threat.

Additionally, no significant associations were observed between neural responses to infant-threatening situations and self-reported and observed protective behavior. This finding is not in line with those of a previous study (Van 't Veer et al., 2019), in which prenatally a positive relation was found between combined partner- and self-reported paternal protective behavior towards their unborn child in daily life and brain activation while watching threatening (versus neutral) situations concerning their own (versus an unknown) infant. The extent to which differences in study design, that is, inclusion of

a child familiarity factor and a focus on protective behavior towards the unborn child (and thereby their pregnant partner), might explain the discrepancy in findings with the current study remains to be explored by future research.

The following limitations of the current study should be mentioned. First, our sample size (N = 77), although relatively large compared to previous studies on indicators or correlates of paternal protection (with Ns ranging from 16 to 55), was insufficient to detect small effect sizes. Equivalence tests based on a priori determined smallest effects size of interest were non-significant, indicating that the null effects are as yet undetermined (Lakens, 2017) and replication studies with larger sample sizes are needed. This highlights the need for more research into paternal protective behavior. Second, a single hormone measurement was used to assess basal T and AVP levels. As a single assessment might not provide a sufficiently reliable estimate of basal hormone levels, results should be replicated. Future studies might consider using repeated measurements. Third, we did not incorporate the measurement of salivary cortisol levels in the current analyses. The hormone cortisol has been associated with parenting behaviors, especially in contexts of parental arousal (Bos, 2017). Previous studies revealed that the relation between T levels and caregiving behavior was dependent on cortisol levels (e.g., Bos et al., 2018; Voorthuis, Bakermans-Kranenburg, & van IJzendoorn, 2019). Future research studies into the psychobiology of paternal protection are advised to incorporate cortisol as well.

In sum, the current study was the first to look at the psychobiology of paternal protective behavior. We used observational as well as self-reported measures of protective parenting. Overall, this study replicated previously reported brain areas to be associated with paternal protection. However, we did not find robust associations between protective behavior, neural activation in response to infant-directed threat and T and AVP levels. Sensitivity analyses indicated a possible link between basal T levels and neural responses to infant-threatening videos, and suggested a negative association between basal AVP levels and observed protective behavior. Taking into account that these findings did not survive the correction for multiple testing and emerged in sensitivity analyses with a somewhat smaller sample size, these results should be interpreted carefully and await replication. Our understanding of the psychobiology of paternal protective behavior is thus still rather incomplete and needs more attention in future research on paternal behavior. Since accumulating knowledge points to fathers' important role in early child development (Bakermans-Kranenburg et al., 2019), further examination of the psychobiology of paternal protective behavior may contribute to a better understanding of the development of both paternal and child behavior.

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Author contribution (CRediT)

AML; Methodology, Formal analysis, Investigation, Data Curation, Writing - Original Draft, Visualization, Project administration. MWFTV; Methodology, Formal analysis, Data Curation, Writing - Review & Editing, Supervision. RSMB; Methodology, Software, Formal analysis, Data Curation, Writing - Review & Editing, Supervision. LH; Software, Formal analysis, Investigation, Data Curation, Writing - Review & Editing, Project administration MMEH-R; Methodology, Formal analysis, Data Curation, Writing - Review & Editing, Visualization. MHvIJ; Conceptualization, Methodology, Writing - Review & Editing, Supervision, Funding acquisition. MJB-K; Conceptualization, Methodology, Writing - Review & Editing, Supervision, Funding acquisition.

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Chapter 6

General Discussion

The overall aim of the current dissertation was to explore the psychobiology of fatherhood and to test the associations between the neuroendocrine system and parenting behavior in fathers. To this end, we reviewed previous literature and proposed a biobehavioral model of the emergence of fatherhood incorporating social-cultural, behavioral, hormonal, and neural aspects in the context of the prenatal, perinatal and early postnatal phases of fatherhood (Chapter 2). In the empirical chapters, we further explored these aspects in first-time fathers in the late prenatal and early postnatal phases of fatherhood. First, we examined the effect of vasopressin (AVP) nasal administration and the influence of birth on fathers' thoughts and feelings regarding their (unborn) infant (Chapter 3). Second, we explored the relation between endocrine factors and father's sensitive parenting behavior in the early postnatal phase of fatherhood (Chapter 4). Third, we explored possible hormonal and neural correlates of infant protection, a relatively neglected parenting dimension (Chapter 5).

In this final chapter, I provide an overview of the main findings per empirical study. Furthermore, these findings will be interpreted and discussed in light of the proposed biobehavioral model of the emergence of fatherhood (Chapter 2) and previous literature. Finally, limitations are considered and recommendations for future studies are presented.

Main findings of the empirical articles

In Chapter 3, '*Vasopressin and parental expressed emotion in the transition to fatherhood*', we focused on data collected within a double blind randomized controlled within-subject design. During two prenatal assessments, 25 participants self-administered a dose of either 20 IU AVP or a placebo and completed the Five Minute Speech Sample (FMSS) in which participants spoke for 5 min about their thoughts and feelings about the infant and the desired relationship. Analyses did not reveal a significant effect of AVP administration on FMSS-based expressed emotion, emotional content, and emotional prosody in the current study. These results suggest that fathers' thoughts and feelings about their unborn child might be independent of AVP. Additionally, we explored whether the birth of their infant influenced the content of the FMSS. Analyses showed that, on average, the fathers stated more positive comments about their infant after birth compared to when they were expecting. Moreover, a decrease in emotional prosody parameters was observed. Based on these results, it might be speculated that infant's birth is more influential with regard to fathers' expressed thoughts and feelings than AVP administration in the late prenatal phase of fatherhood.

In Chapter 4, '*Exploring the role of endocrine factors in paternal sensitive parenting*', we studied the separate and combined associations between AVP, oxytocin (OT), testosterone (T) and cortisol (CORT), and fathers' sensitive parenting behavior in the

early postnatal phase of fatherhood. Seventy-nine first time fathers of young infants (2-4 months old) participated in a 10-minute free play episode and paternal sensitivity was assessed based on observed sensitivity and cooperation levels (Ainsworth et al., 1974). Structural Equation Models did not reveal any significant associations between paternal sensitivity and basal hormone levels or hormone reactivity. Exploration of interaction effects of basal hormones on sensitivity indicated that the interaction T * CORT best predicted paternal sensitive parenting behavior. Conform the dual hormone hypothesis (Mehta & Prasad, 2015), we further assessed this relation by performing a median split based on CORT levels. Post-hoc analyses indicated a stronger positive association between T and sensitivity for fathers with lower CORT levels compared to fathers with higher CORT levels. These results suggest that observed variation in paternal sensitivity might be better explained by interactions between hormones than by single hormone levels.

In Chapter 5, '*Exploring the hormonal and neural correlates of paternal protective behavior to their infants*', we studied protective parenting behavior and its possible hormonal and neural correlates in the same sample of new fathers as described in Chapter 4. In order to study paternal protection, we introduced three new paradigms, that is, a newly developed questionnaire 'Paternal Protection Questionnaire', a new behavioral paradigm 'the Auditory Startling Task', and an adapted version of an fMRI threat task (Van 't Veer et al., 2019). Furthermore, both basal T and AVP levels were incorporated as these hormones are hypothesized to be important in the context of protective parenting behavior (Van Anders et al., 2011). Analyses revealed that the new paradigms for self-reported and observed protective behavior obtained good reliability. However, there was little overlap between observed and self-reported protective behavior. FMRI analyses revealed that we replicated and validated the role of several brain networks in the processing of infant-threatening situations previously observed by van 't Veer and colleagues (2019). Lastly, bivariate correlations revealed no statistically significant associations between basal T and AVP, neural responses and paternal protective behavior. Based on these findings, it may be concluded that both T and AVP baseline levels and neural responses to infant threatening situations may not be suitable correlates of paternal protective behavior in the early phase of fatherhood.

Integrating behavioral, hormonal and neural aspects of fathering

As mentioned above, we proposed a biobehavioral model of the emergence of fatherhood based on previous literature (Chapter 2). The model focuses on the first 1,000 days after conception, and incorporates the sociocultural, behavioral, hormonal and neural aspects of fathering within the prenatal, perinatal and early postnatal phases of fatherhood. For each of these three phases, bidirectional relations between paternal behaviors, hormonal and neural components are described. Moreover,

the model illustrates how sociocultural aspects may influence these behaviors and biological components. Lastly, unidirectional relations are proposed for each of the four levels throughout the different phases of fatherhood.

In the current dissertation, the bidirectional relations between paternal behaviors, hormonal and neural components were further explored to gain more insight in the proposed underlying psychobiological mechanisms in the emergence of paternal caregiving behavior.

In terms of the endocrine aspects of paternal behavior, we studied several parenting hormones (OT, AVP, T, and CORT) in isolation, in combination, and in terms of interactive effects. As already mentioned in previous chapters, there are several studies addressing the possible relation between hormone levels (basal and reactivity) and paternal behavior, especially the behavioral dimension sensitivity (e.g., Apter-Levi et al., 2014; Bos et al., 2018; Feldman et al., 2011, 2010; Gordon et al., 2017; Grebe et al., 2019; Kuo et al., 2018; Meijer et al., 2019; Naber et al., 2010, 2013; Storey et al., 2011; Weisman et al., 2014). Nonetheless, how these endocrine and behavioral factors are related is still largely unknown. Based on the empirical results presented in this dissertation, we cannot conclude that basal hormone levels and hormone reactivity are related to fathers' sensitive and protective behavior in the late prenatal and early postnatal phase of fatherhood. However, exploring interaction effects of basal hormones, analyses revealed that the interaction between T and CORT might be a potential predictor of paternal sensitive parenting behavior. This finding replicates previous findings of Bos et al. (2018) and is in line with the idea that hormones act in concert, rather than in isolation (Feldman & Bakermans-Kranenburg, 2017; Rajhans et al., 2019). These results suggest that observed variation in paternal sensitivity might be better explained by interactions between hormones than by single hormone levels. As CORT has also been associated with parental arousal (Bos, 2017), it would be an interesting addition for future psychobiological research to incorporate both T and CORT, and their interaction effect, when studying paternal protective behavior.

Several studies have focused on the possible relation between paternal caregiving behavior and neural responses (e.g., Alyousefi - van Dijk et al., 2020; Diaz-Rojas et al., 2021; Kuo et al., 2012; Mascaro et al., 2014; Van 't Veer et al., 2019). Again, based on the presented results, we cannot conclude that the neural clusters presented in Chapter 5 are related to behavioral components of infant protection in fathers. However, the observed neural responses align with previous findings of van 't Veer et al. (2019) and provided more insight in the neural mechanism potentially involved in the processing of infant- threatening situations.

Lastly, we did not observe any statistically significant association between the hormonal and neural aspects in the context of protective behavior. For this reason, we did not examine the potential mediating role of neural responses in the relation between basal hormone levels and protective behavior.

Possible explanations for the lack of evidence consistent with the expected psychobiological relations

The lack of evidence for relations between fathering behavior, hormones and neural responses in the presented articles might be explained in several ways. First, the possible underlying endocrine system is complex. Individuals can differ in the sensitivity of their endocrine system, for example, due to a different genetic make-up or early life experiences, possibly resulting in a variation in parenting behavior (Bos, 2017; Ellis et al., 2021). More specifically, in the current studies similar baseline hormone levels or doses of nasal hormone administration may have resulted in different degrees of protective or sensitive behavior, and thereby diminishing the expected relation between hormones and behavior. Future research focusing on the relation between fathering behavior, hormones and neural responses is recommended to take into account information about fathers' genetics and early life experiences.

Second, we still know very little about the relation between the transition to fatherhood and the endocrine system. In the current dissertation, we focused on (expectant) first-time fathers in the late prenatal phase and first few months after birth of their first infant as we expected that the suggested behavioral and physical changes would be most pronounced in these new fathers. Indeed, previous literature indicates that men's basal hormone levels change during the course of the pregnancy and around birth (Berg & Wynne-Edwards, 2001; Saxbe et al., 2017; Storey et al., 2000), and found associations between paternal caregiving behavior and the endocrine system in the first six months after birth (Apter-Levi et al., 2014; Bos et al., 2018; Feldman et al., 2010, 2011; Weisman et al., 2014). However, it is possible that around the first few months of birth, the relation between paternal caregiving behavior and the endocrine system still has to be established or can change across the first years after birth. For example, it has been found that the relation between CORT and parental behavior depends on infant's age and thus changes over time (Bos et al., 2018; Finegood et al., 2016; Fleming & Steiner, 1987; Gonzalez et al., 2012; Kuo et al., 2018). This might explain the lack of support for relations between fathering behavior and the endocrine system in the articles presented in this dissertation. For this reason, future research is encouraged to study the relation between paternal behavior and the endocrine system longitudinally, incorporating the first few years of fatherhood.

Third, the possible underlying neural system is complex as well. Although previous research suggests the existence of a "parental brain", it should be kept in mind that brain areas thought to be involved in parenting are associated with a lot of different cognitive processes and functions. Moreover, it has recently been demonstrated that fMRI tasks may have a low test-retest reliability (Elliott et al., 2020), suggesting that the interpretation of neural activation in the context of observed parenting behavior should be made carefully. Additionally, neuro-imaging studies mainly use paradigms with exposure to infant pictures, movies, or infant sounds (Feldman, 2015). This approach is most feasible due to the restricted instrumental set-up of fMRI studies, but may limit the ecological validity of the tasks. This limitation might make it difficult to directly measure underlying neural responses to real-life parenting behavior and must be kept in mind when interpreting fMRI results in the context of observed paternal behavior or the endocrine system.

Approaches to study dimensions of paternal behavior

Parenting behavior is very complex. It involves different behavioral dimensions, such as sensitivity, discipline, and infant protection (Bakermans-Kranenburg & Van IJzendoorn, 2017; Verhees et al., 2021), and their underlying behavioral components, such as the ability to notice and interpret infants' signals and environmental stimuli, and to respond adequately (Hahn-Holbrook et al., 2011; Ainsworth, Bell, & Stayton, 1974). In the chapters presented in the current dissertation, we aimed to provide a more thorough picture of the behavioral dimensions sensitivity and infant protection by combining various behavioral measurements. Expanding our knowledge of the development of parental sensitivity and infant protection during pregnancy, in the first year of the infant's life, and beyond, is of large interest as these are thought to be important for, amongst others, the promotion of secure infant attachment and positive child development (e.g., Bowbly, 1982; Lucassen et al., 2011; Rodrigues et al., 2021).

Fathers' sensitive behavior was assessed by 1) observing father-infant interactions during free play episodes (Chapter 4); and 2) coding parental thoughts and feelings about their child and about the relationship with their child measured via the FMSS (Chapter 3). As we did not examine these measurements in the same sample, we are not able to draw any conclusions about the relation between the two. However, previous research indicated that fathers' prenatal emotional overinvolvement (EOI), including excessive praise (Lambregtse-van den Berg et al., 2013), was related to higher levels of intrusiveness 4 years later (Lucassen et al., 2015). Thus, it could be hypothesized that fathers expressing more positive statements about their (unborn) infant will be more intrusive, and thus less sensitive, to their infants several months after birth.

Future research should address this hypothesis to gain more insights on the predictive power of prenatal parental thoughts and feelings about their infant for early postnatal sensitive parenting in fathers.

To further explore fathers' expressed thoughts and feelings about their infant, we addressed both traditional coder-rated Expressed Emotion and a computerized coding of the FMSS via automated analyses to measure the degree of positivity, negativity and subjectivity in the audio recording. Prenatally, we observed meaningful, although modest, associations between the two coding approaches in the prenatal placebo condition, suggesting that computerized coding may be a valuable addition when studying fathers' thoughts and feelings about their (unborn) infant.

To gain more insight in fathers' protective behavior, we assessed both observed and self-reported behavior with two newly developed instruments, respectively, the 'Auditory Startling Task' and the 'Paternal Protection Questionnaire'. As the two measures were not significantly related to each other, it may be concluded that the tasks assess different aspects of paternal protective behavior. More specifically, in the AST, an actual stressor is present calling for an immediate protective response, whereas the PPQ examines the behavior focusing on the prevention of possible harm to the infant. In addition, the non-significant relation supports the idea that the tasks focus on different response processes (Dang et al., 2020). In the AST, fathers' actual behavior is assessed in a controlled unknown laboratory setting, while with the PPQ, fathers' own and partners' perceptions of protective behavior in daily life situations are measured. By incorporating both the PPQ and the AST in future studies, we should be able to obtain a more complete picture of fathers' protective behavior to their infant.

Limitations

The following limitations should be discussed in context of the research designs. First, it should be mentioned that our recruitment approach resulted in rather homogenous study samples. For the two described study samples, we used an opt-in recruitment approach: participants received initial information about the studies via midwife practices, municipal records, infant welfare centers, and social media and had to contact us for further information and participation. This recruitment strategy may have resulted in including relatively involved and motivated fathers. In addition, all participants lived together with the mother of the infant and most participants reported to be highly educated. Although this approach may have resulted in a selection bias, the current samples were suitable for a proof of principle as behavioral, neural and hormonal data revealed sufficient inter-individual variation for further analyses. Future

research into the relation between parenting behavior and the neuroendocrine system is advised to include a more heterogeneous sample of participants that may provide a better demographic representation of fathers.

Second, the endocrine data described in the dissertation are all based on single measurements as this approach was most feasible in these already time-consuming research protocols. Although basal T and CORT are reported to have good stability coefficients (Liening et al., 2010), it might be questioned whether a single saliva sample provide a sufficiently reliable estimate of basal hormone levels. Notably, in addition to the lab samples, multiple morning and evening hormone samples were collected in the research project Father Trials. Future research may use these repeated measurements to provide a more robust indication about basal hormone levels, and the associations between hormones and behavior.

Last, the presented studies are likely to be underpowered to detect small effect sizes due to small to modest sample sizes. This was supported by the observed perfect fit in combination with non-significant parameter estimates (Muthen, 2013) in Chapter 4 and the non-significant equivalence tests (Lakens et al., 2018) in Chapter 5. We originally aimed to obtain a large sample size, however the recruitment of participants was more difficult than we expected. Notably, our sample sizes were similar or larger compared to previous paternal research focusing on the effect of hormone administration (range N: 17 to 35), the relation between paternal sensitivity and involvement and hormones (range N: 12 to 298), and paternal protection (range N: 15 – 55). Future studies may consider replications with larger sample sizes.

Conclusion and future implications

The overall aim of the current dissertation was to explore the psychobiology of fathering in the early phases of fatherhood. To replicate previous findings and further develop our insights in paternal caregiving behavior and its underlying biology, we studied both behavioral and hormonal aspects in several different ways. Paternal behavior was assessed via measurements in the context of sensitivity and infant protection, namely a 10-min observation of free play, the FMSS, the PPQ and the AST. The role of four hormones (OT, AVP, T and CORT) in relation to paternal behavior was studied via hormone administration, basal hormone levels and hormone reactivity. Moreover, we explored the possible underlying neural mechanism of protective parenting. Together, the results provided some insights in the associations between the neuroendocrine system and parenting behavior in fathers. However, to be able to draw firm conclusions about the psychobiological processes underlying paternal behavior, better understanding about the role of the neuroendocrine system in the development of both paternal protective behavior and paternal sensitivity is necessary. Future studies

are advised to elaborate on the possible causal relations between the neuroendocrine system and fathers' parenting behavior, for example, via manipulation of hormones or parenting behavior. Ultimately, when we unravel the psychobiological basis of paternal behavior, we may be able to better explain the observed inter-individual behavioral variation in fathers.

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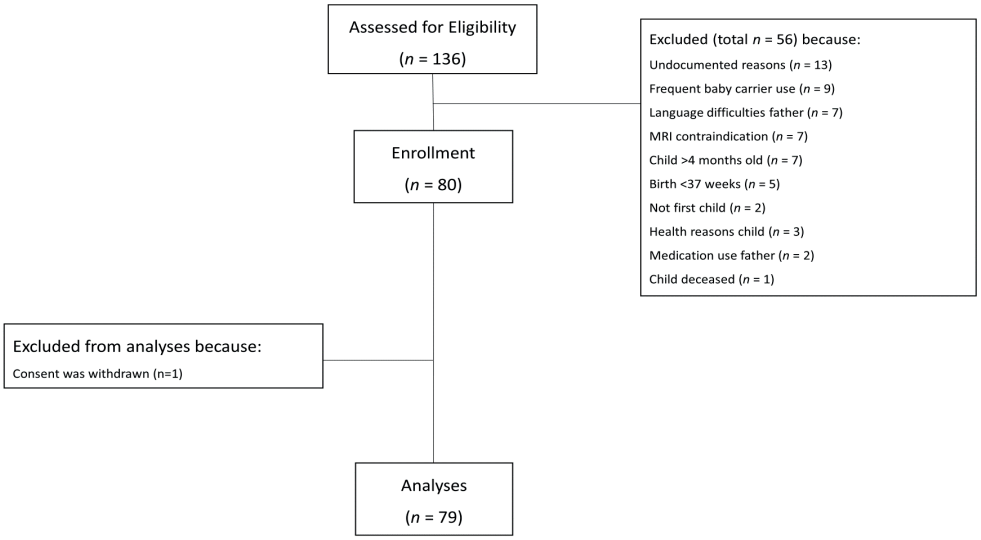
Supplemental Materials

Chapter 4.

Lotz, A.M., Buisman, R.S.M., Alyousefi-van Dijk, K., Witte, A.M., Bakermans-Kranenburg, M.J., & Verhees, M.W.F.T. Exploring the role of endocrine factors in paternal sensitive parenting. *Submitted for publication*



Supplementary Material Figure 4.1

Flow chart of participant inclusion

Note. The data reported in the current paper was collected either in the Leiden University Medical Centre (LUMC, *n* = 65) or at the participant's home (*n* = 14)

Supplementary material Table 4.1a

Multiple linear regression with baseline hormone levels as predictors of sensitive paternal behavior.

Variables	β	SE	t	*p*
Baseline OT	-0.15	0.25	-1.18	.24
Baseline AVP	0.15	0.23	1.24	.22
Baseline T	0.12	0.34	0.81	.42
Baseline CORT	0.08	0.31	0.56	.58

$R^2 = 0.09$, $F(6,65) = 1.03$, $p = .42$

Note. Baseline T and CORT levels were log transformed. Predictors are controlled for infant age and saliva collection time

Supplementary material Table 4.1b

Multiple linear regression with sensitive paternal behavior as predictor of hormonal reactivity

Variables	B	SE	t	*p*
OT reactivity	0.19	0.12	1.49	0.14
AVP reactivity	-0.01	0.13	-0.09	0.93
T reactivity	-0.13	0.13	-1.07	0.30
CORT reactivity	-0.20	0.13	-1.51	0.14

Note. Hormonal reactivity was calculated with a residualized change score, i.e., post-interaction samples were residualized by corresponding baseline samples. Baseline and post-interaction samples of T and CORT levels were log transformed. Outliers for T reactivity and OT reactivity were winsorized ($n = 2$). Sensitive paternal behavior is an average score of the standardized scores of observed sensitivity and observed cooperation.

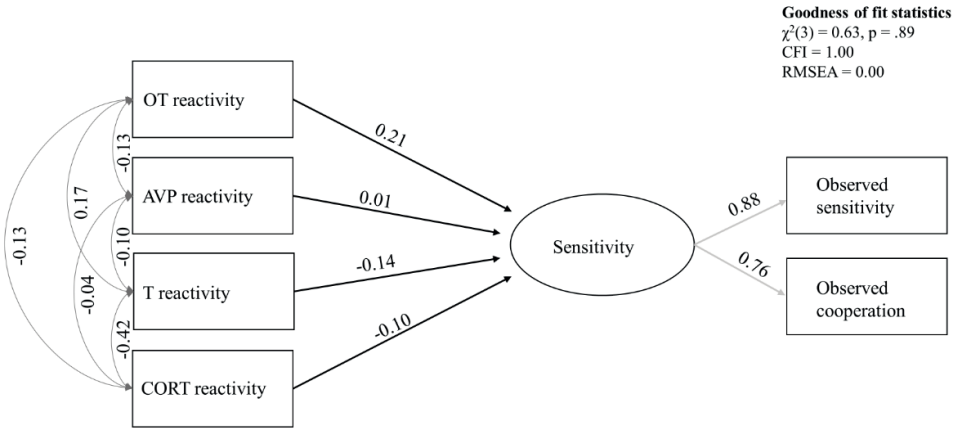
Supplementary material Table 4.1c

Multiple linear regression with hormonal reactivity as predictors of sensitive paternal behavior

Variable	β	SE	t	*p*
OT reactivity	0.18	0.12	1.47	.15
AVP reactivity	-0.00	0.11	-0.02	.99
T reactivity	-0.11	0.13	-0.84	.40
CORT reactivity	-0.11	0.12	-0.79	.43

$R^2 = 0.06$, $F(4,69) = 1.17$, $p = .33$

Note. Hormonal reactivity was calculated with a residualized change score, i.e., post-interaction samples were residualized by corresponding baseline samples. Baseline and post-interaction samples of T and CORT levels were log transformed. Outliers for T reactivity and OT reactivity were winsorized ($n = 2$). Sensitive paternal behavior is an average score of the standardized scores of observed sensitivity and observed cooperation.



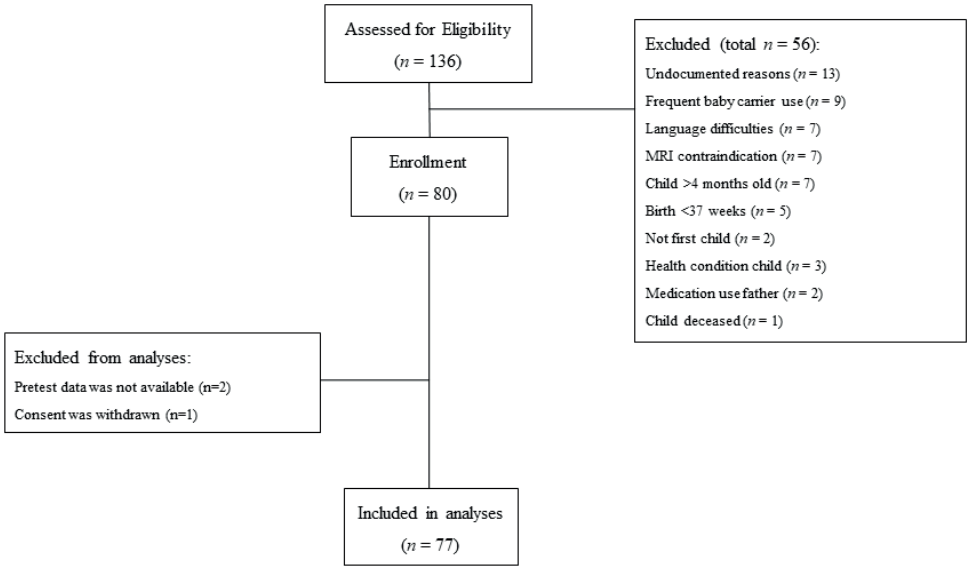
Supplementary Material Figure 4.3

SEM model with hormone reactivity levels as predictors of Sensitivity

Note. Path coefficients are standardized parameter estimates. Black arrows indicate non-significant standardized β's. Dark grey arrows indicate correlation coefficients between the predictors. Light grey arrows indicate standardized factor loadings for latent construct Sensitivity. Outliers (n = 2) for T reactivity and OT reactivity were winsorized.

Chapter 5.

Lotz, A.M., Verhees, M.W.F.T., Horstman, L.I., Riem, M.M.E., van IJzendoorn, M.H., Bakermans-Kranenburg, M.J., Buisman, R.S.M. (2020). Exploring the hormonal and neural correlates of paternal protective behavior to their infants. *Developmental Psychobiology*, 00,1–12. https://doi.org/10.1002/dev.22055



Supplementary Material Figure 5.1

Flow-chart participant inclusion

Note. Data reported in the current article were collected during visits either in the Leiden University Medical Centre (LUMC, $n = 68$) or at the participant's home ($n = 9$).

Coding scheme Auditory Startling Task (AST)

The coding system was developed for the current study. Two authors (MBK & AL) watched 10 AST videos and listed the observed protective responses and added other possible protective behaviors in reaction to the auditory stimuli. Subsequently, 10 members of the research team, including MBK and AL, rated these behaviors (1= least protective; 8= most protective). All $r > .80$, indicating agreement on rating order. The final coding scheme consists of a 10-point scale, with higher scores reflecting more protective behavior (Supplementary Material Table S5.1).

Supplementary Material Table 5.1

Overview of the coding scheme for parental protective behavior.

	Parental protective response (1 = least protective; 10 = most protective)
1.	Parent covers own ears, no attention to baby
2.	Parent looks at child and does not do anything
3.	Parent looks at sound box but does not do anything
4.	Parent looks at sound box, looks at baby, switches regularly
5.	Parent looks at child and tries to distract child (e.g., with toys, talking to child, or hand on belly; distraction actions have to start during the noise)
6.	Parent makes an attempt to stop sound on sound box (e.g. stands up, moves towards sound box)
7.	Parent picks up baby or holds baby more closely (increased bodily contact) after more than 5 seconds of noise start
8.	Parent protects baby by covering baby's ears after more than 5 seconds of noise start
9.	Parent picks up baby or holds baby more closely (increased bodily contact) within 5 seconds of noise start but does not cover ears of the baby
10	Parent protects baby by covering baby's ears within 5 seconds of noise start

Supplementary Material Table 5.2

Scenario description of the threatening and matched neutral videos presented in the threat task

Threatening videos	Matched neutral videos
Hot tea is accidentally spilled on a baby	Tea is placed on a table next to the baby
A baby stroller accidentally rolls into a river	A baby stroller does not roll into the river
An adult loses grip of a baby stroller that rolls off a bridge and crashes into a cyclist	An adult on top of a bridge safely puts baby stroller on the brakes
A car seat with a baby is accidently pushed down the stairs	A car seat with a baby is not placed close to the stairs and not pushed down the stairs
A baby accidentally falls off a changing table while being changed	A baby lies on the changing table while being changed
A car is parked backwards and hits a baby in a car seat which was placed on the parking lot	A car parks backwards at a safe distance from a baby in a car seat placed on sidewalk
A baby seat falls from a bench when adult stands up and hits the bench	A baby seat is placed on the ground next to the bench
A baby stroller accidentally falls sidewise due to bags on the left handle	The weight of the bags is divided over both handles, keeping the stroller in balance
Car door closes accidentally and hits a baby in the car seat	Baby in baby seat is not located between the car door and car
Baby stroller with a baby falls down the escalator	Baby stroller is safely placed on the escalator
A football is kicked at a baby	A football is kicked in another direction than the baby
Cable of a vacuum cleaner causes a vase to drop on a baby	Cable of vacuum cleaner is not placed close to the vase

fMRI preprocessing using fMRIPrep

Anatomical data preprocessing. T1-weighted (T1w) images were corrected for intensity non-uniformity (INU) with N4BiasFieldCorrection (Tustison et al., 2010) distributed with ANTs 2.2.0 (Avants et al. ,2008, RRID:SCR_004757). The T1w-reference was then skull-stripped with *Nipype* implementation of the antsBrainExtraction.sh workflow (from ANTs), using OASIS30ANTs as target template. Brain tissue segmentation of cerebrospinal fluid (CSF), white-matter (WM) and gray-matter (GM) was performed on the brain-extracted T1w using fast (FSL 5.0.9, RRID:SCR_002823, Zhang, Brady, and Smith, 2001). A T1w-reference map was computed after registration of T1w images (after INU-correction) using mri_robust_template (FreeSurfer 6.0.1, Reuter, Rosas, and Fischl, 2010). Brain surfaces were reconstructed using recon-all (FreeSurfer 6.0.1, RRID:SCR_001847, Dale, Fischl, and Sereno, 1999), and the brain mask estimated previously was refined with a custom variation of the method to reconcile ANTs-derived and FreeSurfer-derived segmentations of the cortical gray-matter of Mindboggle (RRID:SCR_002438, Klein et al., 2017). Volume-based spatial normalization to two standard spaces (MNI152NLin2009cAsym, MNI152NLin6Asym) was performed through nonlinear registration with antsRegistration (ANTs 2.2.0), using brain-extracted versions of both T1w reference and the T1w template. The following templates were selected for spatial normalization: *ICBM 152 Nonlinear Asymmetrical template version 2009c* [Fonov et al., (2009), RRID:SCR_008796; TemplateFlow ID: MNI152NLin2009cAsym], *FSL's MNI ICBM 152 non-linear 6th Generation Asymmetric Average Brain Stereotaxic Registration Model* [Evans et al., (2012), RRID:SCR_002823; TemplateFlow ID: MNI152NLin6Asym].

Functional data preprocessing. For each BOLD run, the following preprocessing was performed. First, a reference volume and its skull-stripped version were generated using a custom methodology of *fMRIPrep*. A deformation field to correct for susceptibility distortions was estimated based on *fMRIPrep*'s *fieldmap-less* approach. The deformation field is that resulting from co-registering the BOLD reference to the same-subject T1w-reference with its intensity inverted (Wang et al., 2017; Huntenburg, 2014). Registration is performed with antsRegistration (ANTs 2.2.0), and the process regularized by constraining deformation to be nonzero only along the phase-encoding direction, and modulated with an average fieldmap template (Treiber et al., 2016). Based on the estimated susceptibility distortion, an unwarped BOLD reference was calculated for a more accurate co-registration with the anatomical reference. The BOLD reference was then co-registered to the T1w reference using bbregister (FreeSurfer) which implements boundary-based registration (Greve and Fischl, 2009). Co-registration was configured with six degrees of freedom. Head-motion parameters with respect to the BOLD reference (transformation matrices, and six corresponding rotation and translation parameters) are estimated before any spatiotemporal filtering

using mcflirt (FSL 5.0.9, Jenkinson et al., 2002). BOLD runs were slice-time corrected using 3dTshift from AFNI 20160207 (Cox and Hyde, 1997, RRID:SCR_005927). The BOLD time-series, were resampled to surfaces on the following spaces: *fsaverage6*. The BOLD time-series (including slice-timing correction when applied) were resampled onto their original, native space by applying a single, composite transform to correct for head-motion and susceptibility distortions. These resampled BOLD time-series will be referred to as *preprocessed BOLD in original space*, or just *preprocessed BOLD*. The BOLD time-series were resampled into several standard spaces, correspondingly generating the following *spatially-normalized, preprocessed BOLD runs*: MNI152NLin2009cAsym, MNI152NLin6Asym. First, a reference volume and its skull-stripped version were generated using a custom methodology of *fMRIPrep*. Automatic removal of motion artifacts using independent component analysis (ICA-AROMA, Pruim et al., 2015) was performed on the *preprocessed BOLD on MNI space* time-series after removal of non-steady state volumes and spatial smoothing with an isotropic, Gaussian kernel of 6mm FWHM (full-width half-maximum). Corresponding "non-aggresively" denoised runs were produced after such smoothing. Additionally, the "aggressive" noise-regressors were collected and placed in the corresponding confounds file. Several confounding time-series were calculated based on the *preprocessed BOLD*: framewise displacement (FD), DVARS and three region-wise global signals. FD and DVARS are calculated for each functional run, both using their implementations in *Nipype* (following the definitions by Power et al., 2014). The three global signals are extracted within the CSF, the WM, and the whole-brain masks. Additionally, a set of physiological regressors were extracted to allow for component-based noise correction (*CompCor*, Behzadi et al., 2007). Principal components are estimated after high-pass filtering the *preprocessed BOLD* time-series (using a discrete cosine filter with 128s cut-off) for the two *CompCor* variants: temporal (tCompCor) and anatomical (aCompCor). tCompCor components are then calculated from the top 5% variable voxels within a mask covering the subcortical regions. This subcortical mask is obtained by heavily eroding the brain mask, which ensures it does not include cortical GM regions. For aCompCor, components are calculated within the intersection of the aforementioned mask and the union of CSF and WM masks calculated in T1w space, after their projection to the native space of each functional run (using the inverse BOLD-to-T1w transformation). Components are also calculated separately within the WM and CSF masks. For each CompCor decomposition, the *k* components with the largest singular values are retained, such that the retained components' time series are sufficient to explain 50 percent of variance across the nuisance mask (CSF, WM, combined, or temporal). The remaining components are dropped from consideration. The head-motion estimates calculated in the correction step were also placed within the corresponding confounds file. The confound time series derived from head motion estimates and global signals were expanded with the inclusion of temporal derivatives and quadratic terms for each (Satterthwaite et

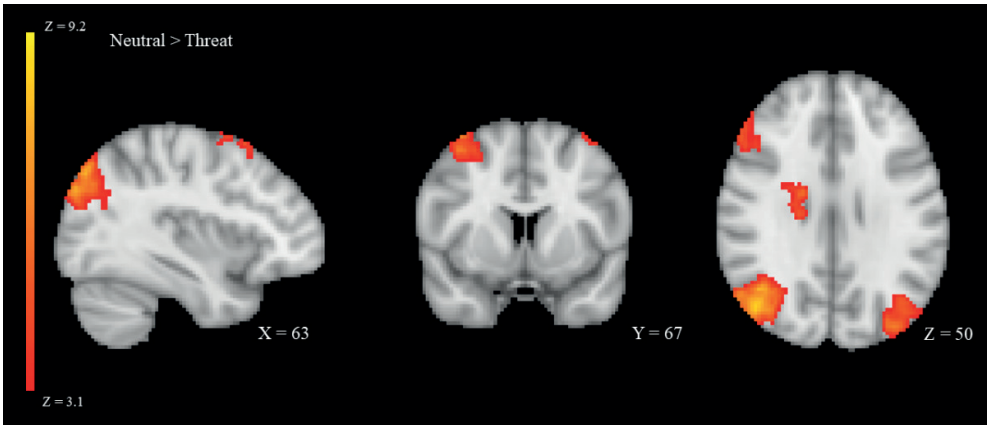
al. 2013). Frames that exceeded a threshold of 0.5 mm FD or 1.5 standardised DVARS were annotated as motion outliers. All resamplings can be performed with *a single interpolation step* by composing all the pertinent transformations (i.e. head-motion transform matrices, susceptibility distortion correction when available, and co-registrations to anatomical and output spaces). Gridded (volumetric) resamplings were performed using antsApplyTransforms (ANTs), configured with Lanczos interpolation to minimize the smoothing effects of other kernels (Lanczos, 1964). Non-gridded (surface) resamplings were performed using mri_vol2surf (FreeSurfer).

Supplementary Material Table 5.3

Correlations between neural, behavioral and hormonal measurements based on full-cases data

	1.	2.	3.	4.	5.	6.	7.	8.
1. testosterone	.							
2. vasopressin	-.05	.						
3. AST	-.11	-.22†	.					
4. PPQ	-.05	-.07	.19	.				
5. fMRI cluster 1	.19	.01	-.00	.08	.			
6. fMRI cluster 2	.23†	.08	-.02	.09	.87**	.		
7. fMRI cluster 3	.17	-.07	-.02	.03	.75**	.72**	.	
8. fMRI cluster 4	.19	.00	-.08	-.00	.82**	.78**	.91**	.

Note. Bivariate Pearson correlations are calculated based on complete cases data. AST: protective behavior observed during the Auditory Startling task.
PPQ: self-reported protective behavior measured with the Paternal Protection Questionnaire, reflective log transformed data is used for Pearson correlations. fMRI cluster 1 – 4 are individual mean *z*-values based on the contrast threat > neutral. Cluster 1: left cuneal cortex, left lateral occipital cortex and left occipital pole. Cluster 2: right cuneal cortex, right lateral occipital cortex and right occipital pole. Cluster 3: left supramarginal gyrus, planum temporale, lateral occipital cortex, central opercular cortex, middle temporal cortex, parietal operculum cortex. Cluster 4: insular cortex, frontal orbital cortex, temporal pole, superior frontal gyrus, frontal operculum cortex, central operculum cortex, thalamus, putamen, precentral gyrus, right planum temporale, right supramarginal gyrus, right middle temporal gyrus, right inferior temporal cortex, right superior temporal gyrus, anterior cingulate gyrus, amygdala. Testosterone values were log transformed and corrected for time of collection for Pearson correlations. Spearman correlations did not differ significantly from Pearson correlations shown above.
** $p < .01$, † $p < .1$



Supplementary Material Figure 5.2

Neural activation for the contrast neutral > threat

Note: Activation is thresholded at Z > 3.2, $p < .05$

Supplementary Material Table 5.4

Brain coordinates of the peak average z-value for the contrast neutral > threat.

Cluster index	voxels	region	x	y	z	Peak z	*p*
14	2551	R Lateral occipital cortex	40	-74	40	7.42	7.39e-20
13	2080	R Middle frontal gyrus	34	16	60	6.21	3.00e-17
12	1201	L Lateral occipital cortex	-38	-78	42	6.25	9.18e-12
11	703	R Frontal pole	48	52	-8	5.00	5.96e-08
10	607	R Precuneus cortex	16	-58	14	5.31	2.98e-07
9	501	R Precuneus cortex	8	-68	40	5.96	2.80e-06
8	497	L Occipital pole	-30	-96	-10	5.34	3.04e-06
7	425	R Inferior temporal cortex	56	-44	-22	5.90	1.45e-05
6	352	R Occipital pole	28	-100	-8	5.46	7.87e-05
5	222	R Caudate nucleus	18	-4	26	4.96	.00
4	189	R Frontal pole	26	46	-6	4.16	.01
3	147	L Middle frontal gyrus	-32	16	58	4.40	.02
2	144	L Frontal pole	-46	54	-10	4.80	.02
1	124	L Middle temporal gyrus	-64	-14	-6	4.69	.04

Note. L = left, R = right. Cluster 14 also contains the left Lateral occipital cortex (superior division) and the left angular gyrus. Cluster 10 also contains the right Lingual gyrus.

Supplementary Material Table 5.5

Correlations between reversed contrast fMRI clusters, behavioral and hormonal measurements

	Mean (*SD*)	AST	PPQ	AVP	T
fMRI cluster 2	-0.72 (1.07)	- .09	-.27	-.02	-.10
fMRI cluster 3	-0.58 (0.84)	- .04	-.07	.01	-.12
fMRI cluster 4	-0.58 (0.75)	.13	.04	-.01	-.02
fMRI cluster 5	-0.59 (0.83)	-.32	.07	.11	.20
fMRI cluster 6	-0.69 (0.98)	-.04	.18	.04	.08
fMRI cluster 7	-0.73 (0.90)	.19	.13	-.03	.16
fMRI cluster 8	-0.68 (0.95)	-.06	.21	-.00	.09
fMRI cluster 9	-0.62 (0.85)	-.05	-.05	.06	.00
fMRI cluster 10	-0.58 (0.73)	-.07	.16	.00	.02
fMRI cluster 11	-0.72 (0.87)	.15	-.12	-.01	.04
fMRI cluster 12	-0.68 (0.74)	-.14	.11	.19	-.02
fMRI cluster 13	-0.66 (0.71)	.02	-.06	.02	.04
fMRI cluster 14	-0.85 (0.73)	.08	.05	.03	-.01

Note. Bivariate Pearson correlations were calculated on full case dataset and Benjamini – Hochberg corrections were performed. Individual mean *z*-values of the fMRI clusters are based on the contrast neutral vs threat. fMRI cluster 1 was too small to calculate individual mean z-values. Cluster 2: left frontal pole. Cluster 3: left middle frontal gyrus. Cluster 4: right frontal pole. Cluster 5: right caudate nucleus. Cluster 6: right occipital pole. Cluster 7: right inferior temporal cortex. Cluster 8: left occipital pole. Cluster 9: right precuneus cortex. Cluster 10: right precuneus cortex, right lingual gyrus. Cluster 11: right frontal pole. Cluster 12: left lateral occipital cortex. Cluster 13: right middle frontal gyrus. Cluster 14: right lateral occipital cortex, left lateral occipital cortex (superior division), left angular gyrus. AST: protective behavior observed during the Auditory Startling task. PPQ: reflective log transformed self-reported protective behavior measured with the Paternal Protection Questionnaire. Testosterone values were log transformed and corrected for time of collection.

Supplementary Material Table 5.6

Sensitivity correlations between neural, behavioral and hormonal measurements based on multiple imputed data

	1.	2	3.	4.
1. testosterone	.			
2. vasopressin	-.04	.		
3. AST	-.05	-.28	.	
4. PPQ	-.10	-.07	.16	.
5. fMRI cluster 1	.22	.06	.04	.15
6. fMRI cluster 2	.26	.17	-.01	.13
7. fMRI cluster 3	.17	-.01	.02	.07
8. fMRI cluster 4	.19	.07	-.03	.05

Note. Bivariate Pearson correlations are calculated based on pooled multiply imputed data without 9 participants who did not met a priori stated inclusion criteria. Benjamini – Hochberg corrections were performed. AST: protective behavior observed during the Auditory Startling task.
PPQ: reflective log transformed self-reported protective behavior measured with the Paternal Protection Questionnaire. fMRI cluster 1 – 4 are individual mean z-values based on the contrast threat > neutral. Cluster 1: left cuneal cortex, left lateral occipital cortex and left occipital pole. Cluster 2: right cuneal cortex, right lateral occipital cortex and right occipital pole. Cluster 3: left supramarginal gyrus, planum temporale, lateral occipital cortex, central opercular cortex, middle temporal cortex, parietal operculum cortex. Cluster 4: insular cortex, frontal orbital cortex, temporal pole, superior frontal gyrus, frontal operculum cortex, central operculum cortex, thalamus, putamen, precentral gyrus, right planum temporale, right supramarginal gyrus, right middle temporal gyrus, right inferior temporal cortex, right superior temporal gyrus, anterior cingulate gyrus, amygdala. Testosterone values are log transformed and corrected for time of collection. Spearman correlations did not differ significantly from Pearson correlations shown above.

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Summary

In the past decades an increase of fathers' participation in infant caregiving has been observed (Bakermans-Kranenburg et al., 2019; Cabrera et al., 2000; Cowan & Cowan, 2019). This change is beneficial, as fathers' involvement and sensitive parenting behavior are associated with positive child development, attachment security, and well-being of the child (Barker et al., 2017; Brown et al., 2012; Cabrera et al., 2000; Deans, 2020; Lucassen et al., 2011; Pleck, 2012; Rodrigues et al., 2021). Interestingly, only little research focused on the onset of these parental behaviors and its possible underlying biological mechanism in men becoming a father. Several studies points towards potential roles of the endocrine system and neural system as changes in these systems are observed in men in transition to fatherhood (Bos, 2017; Bos et al., 2018; Edelstein et al., 2015, 2017; Gettler et al., 2011; Storey et al., 2000). However, how these endocrine, neural and behavioral factors are related is still largely unknown. The overall aim of the current dissertation was to further explore the psychobiology of fatherhood and to test the associations between the neural and hormonal components and parenting behavior in fathers.

In Chapter 2, we reviewed previous literature on fatherhood and proposed a biobehavioral model of the emergence of fatherhood incorporating social-cultural, behavioral, hormonal, and neural aspects in the context of the prenatal, perinatal and postnatal phases of fatherhood. For each of these three phases, bidirectional relations between paternal behaviors, hormonal and neural components are described. Moreover, the model illustrates how sociocultural aspects may influence these behaviors and biological components. Lastly, unidirectional relations are proposed for each of the four levels throughout the different phases of fatherhood.

In Chapter 3, we focused on the influence of vasopressin (AVP) administration and infant's birth on fathers' thoughts and feelings about their infant and the desired relationship measured via the Five Minute Speech Sample (FMSS, Lambregtse-van den Berg et al., 2013; Magaña et al., 1986; Weston et al., 2017). Previous research indicates that Expressed Emotion, the overall outcome of the assessment, might be associated with parenting style, the quality of the parent–child relationship and the wellbeing of the child (Sher-Censor, 2015; Weston et al., 2017). Analyses did not reveal a significant effect of AVP administration on FMSS-based expressed emotion, emotional content, and emotional prosody in the current study. These results suggest that fathers' thoughts and feelings about their unborn child might be independent of AVP. In the context of infant's birth, analyses showed that, on average, the fathers stated more positive comments about their infant after birth compared to when they were expecting. Moreover, a decrease in emotional prosody parameters was observed.

Based on these results, it might be speculated that infant's birth is more influential with regard to fathers' expressed thoughts and feelings than AVP administration in the late prenatal phase of fatherhood.

In Chapter 4, we studied the separate and combined associations between oxytocin (OT), AVP, testosterone (T) and cortisol (CORT), and fathers' sensitive parenting behavior in the early postnatal phase of fatherhood. Structural Equation Models did not reveal any significant associations between paternal sensitivity and basal hormone levels or hormone reactivity. Exploration of interaction effects of basal hormones on sensitivity indicated that the interaction T * CORT best predicted paternal sensitive parenting behavior. Post-hoc analyses indicated a stronger positive association between T and sensitivity for fathers with lower CORT levels compared to fathers with higher CORT levels. These results suggest that observed variation in paternal sensitivity might be better explained by interactions between hormones than by single hormone levels.

In Chapter 5, we explored fathers' protective parenting behavior and its possible hormonal and neural correlates. In order to study paternal protection, we introduced three new paradigms, that is, a newly developed questionnaire 'Paternal Protection Questionnaire', a new behavioral paradigm 'the Auditory Startling Task', and an adapted version of an fMRI threat task (Van 't Veer et al., 2019). Furthermore, both basal T and AVP levels were incorporated as these hormones are hypothesized to be important in the context of protective parenting behavior (Van Anders et al., 2011). Analyses revealed that the new paradigms for self-reported and observed protective behavior obtained good reliability. However, there was little overlap between observed and self-reported protective behavior. FMRI analyses revealed that we replicated and validated the role of several brain networks in the processing of infant-threatening situations previously observed by van 't Veer and colleagues (2019). Lastly, bivariate correlations revealed no associations between basal T and AVP, neural responses and paternal protective behavior. Based on these findings, it may be concluded that both T and AVP baseline levels and neural responses to infant threatening situations may not be suitable correlates of paternal protective behavior in the early phase of fatherhood.

In sum, based on the empirical results presented in this dissertation, we cannot conclude that basal hormone levels and hormone reactivity are related to fathers' sensitive and protective behavior in the late prenatal and early postnatal phase of fatherhood. Moreover, our results do not support our hypothesis that neural responses to infant threatening stimuli are related to behavioral components of infant protection in fathers. Interestingly, exploratory analyses indicated that the interaction effects of basal hormones may be promising for future research to explain observed variations

in paternal behavior. This finding is in line with the idea that hormones act in concert, rather than in isolation (Feldman & Bakermans-Kranenburg, 2017; Rajhans et al., 2019). Further examination of the psychobiology of paternal behavior is necessary to better understand the role of the neuroendocrine system in the development of both paternal protective behavior and paternal sensitivity. Future studies are advised to elaborate on the possible causal relations between the neuroendocrine system and fathers' parenting behavior, for example, via manipulation of hormones or parenting behavior. Ultimately, when we unravel the psychobiological basis of paternal behavior, we may be able to explain the observed inter-individual behavioral variation in fathers.

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Summary

Nederlandse samenvatting

De afgelopen decennia is de deelname van vaders in de zorg voor hun kind(eren) toegenomen (Bakermans-Kranenburg et al., 2019; Cabrera et al., 2000; Cowan & Cowan, 2019). Dit is een gunstige ontwikkeling omdat de betrokkenheid van vaders en sensitief ouderschap samenhangt met positieve ontwikkelingen van het kind zoals een veilige gehechtheid en het welzijn van het kind (Barker et al., 2017; Brown et al., 2012; Cabrera et al., 2000; Deans, 2020; Lucassen et al., 2011; Pleck, 2012). Desondanks heeft weinig onderzoek zich nog gericht op de ontwikkeling van vaderlijke gedrag en het mogelijk biologische mechanisme dat aan dit gedrag ten grondslag ligt. Het onderzoek dat hierover is gepubliceerd geeft aan dat het neuro-endocrine systeem mogelijk betrokken is bij deze ontwikkeling aangezien veranderingen in hormoonwaardes en hersenen zijn waargenomen bij mannen in de transitie naar het vaderschap (Bos, 2017; Bos et al., 2018; Edelstein et al., 2015, 2017; Gettler et al., 2011; Storey et al., 2000). Het is echter nog niet bekend hoe deze endocriene, neurale en gedragsaspecten aan elkaar gerelateerd zijn. Het doel van de huidige dissertatie was om de psychobiologie van vaderschap verder te bestuderen en de relaties tussen de neurale en hormonale componenten en ouderlijk gedrag in vaders te onderzoeken.

De onderzoeksbevindingen

In hoofdstuk 2 bespreken we eerdere literatuur over vaderschap. Op basis van deze eerdere bevindingen stellen we een model voor dat mogelijk ten grondslag ligt aan het vaderschap in eerste 1000 dagen na de bevruchting. Het model omvat de sociaal-culturele, hormonale, neurale en gedragsaspecten in de prenatale, perinatale en postnatale periodes. Voor elk van deze drie periodes beschrijft het model de verbanden tussen de hormonale, neurale en gedragscomponenten in vaders. Daarnaast stellen we voor hoe socioculturele aspecten deze componenten in iedere fase kunnen beïnvloeden. Tenslotte laat het model zien hoe componenten uit eerdere fases mogelijk dezelfde componenten in een latere fase in het vaderschap zouden kunnen beïnvloeden.

In hoofdstuk 3 onderzochten we wat de invloeden van het hormoon vasopressine en de geboorte van het eerste kind zijn op de gedachten en gevoelens die vaders hebben over hun (ongeboren) kind. Deze gedachten en gevoelens werden gemeten met de Five Minute Speech Sample (FMSS, Lambregtse-van den Berg et al., 2013; Magaña et al., 1986; Weston et al., 2017). Eerder onderzoek laat zien dat de geuite emoties, de belangrijkste uitkomstmaat van de FMSS, mogelijk samenhangt met de manier van opvoeden, de kwaliteit van ouder-kind relatie en het welzijn van het kind (Sher-Censor, 2015; Weston et al., 2017). Hierdoor zou de FMSS een indicatie kunnen geven over de sensitiviteit van de geïnterviewde ouder. De analyses lieten geen significant effect van vasopressine toediening zien op de FMSS variabelen bij aanstaande vaders.

Er was echter wel een invloed van de geboorte. Zo uitten de vaders meer positieve opmerkingen over hun kind na de geboorte dan voor de geboorte en veranderden de akoestische parameters van hun stem. Op basis van deze resultaten veronderstellen we dat de gedachten en gevoelens van vaders over hun (ongeboren) kind mogelijk meer afhankelijk is van de geboorte van hun kindje dan van een verhoging van het hormoon vasopressine in de late prenatale fase van het vaderschap.

In hoofdstuk 4 bekeken we of vaders hormonen (oxytocine, vasopressine, testosteron en cortisol) individueel en gecombineerd samenhingen met vaders sensitiviteit in de vroege postnatale fase van het vaderschap. Sensitiviteit omvat het vermogen van de ouder om de signalen van het kind waar te nemen, goed te interpreteren en accuraat en snel te reageren (Ainsworth, Bell, & Stayton, 1974), en werd door ons gemeten via de observatie van vader en kind terwijl ze samen aan het spelen waren. Analyses lieten geen significante associatie zien tussen vaders sensitiviteit en basale hormoonwaardes of hormoonveranderingen in reactie op het samen spelen. Exploratie van mogelijke interactie-effecten tussen basale hormoonwaardes op sensitiviteit liet zien dat de interactie tussen testosteron en cortisol het beste het sensitief gedrag voorspelde. Verdere analyses lieten zien dat er bij vaders met lagere cortisolwaardes, een sterkere positieve associatie tussen testosteron en sensitiviteit was dan bij vaders met hogere cortisol waardes. Deze resultaten suggereren dat geobserveerde variatie in sensitiviteit in vaders mogelijk beter verklaard kan worden door het samenspel tussen hormonen dan door individuele hormonen.

In hoofdstuk 5 onderzochten we protectief gedrag van vaders en de mogelijke hormonale en neurale correlaten hiervan in de vroege postnatale periode. Protectief gedrag richt zich op het beschermen van het kind tegen ziektes, ongelukken en geweld door onbekenden, en deze gedragingen zijn van vitaal belang voor de overleving van de baby tijdens de zwangerschap en na de geboorte (Bakermans-Kranenburg & Van IJzendoorn, 2017; Hahn-Holbrook et al., 2011). Hoewel protectief gedrag dus een belangrijk aspect binnen het ouderlijk gedrag is, is het nauwelijks bestudeerd in mensen. Om protectief gedrag te bestuderen introduceerden we drie nieuwe testparadigma's: de vragenlijst 'Paternal Protection Questionnaire' waarin vaders rapporteerden over hun eigen gedrag, het gedragsparadigma 'the Auditory Startling Task' waarin vaders reactie op een hard onverwachts geluid, terwijl vader en kind samen aan het spelen waren, werd getest in het lab, en een aangepaste versie van een fMRI taak waarin vaders keken naar video's waarin een baby in gevaar is (Van 't Veer et al., 2019). Ook bekeken we de basale waardes van testosteron en vasopressine aangezien deze twee hormonen mogelijk gerelateerd zijn aan protectief ouderlijk gedrag (Van Anders et al., 2011). Analyses toonden aan dat de metingen van de nieuwe vragenlijst en de observatie in het lab voldoende betrouwbaar waren, maar dat er weinig overlap

was tussen deze twee maten. FMRI-analyses bevestigden eerdere bevindingen van Van 't Veer en collega's (2019) aangezien we activatie zagen in dezelfde neurale netwerken bij het zien en verwerken van video's van baby's in gevaarlijke situaties. Tenslotte lieten analyses geen significante associaties zien tussen basale testosteron en vasopressine waardes, neurale responsen en vaders protectief gedrag. Op basis van deze bevindingen kunnen we concluderen dat zowel de basale hormoonwaardes van testosteron en vasopressine als de neurale responsen in reactie op het zien van een kind in een gevaarlijke situatie geen correlaten zijn van protectief gedrag van vaders enkele maanden na de geboorte van hun kind.

Conclusie

Het doel van de studies beschreven in deze dissertatie was om de psychobiologie van vaderlijke gedragingen in de vroege fase van het vaderschap te exploreren. De focus lag hierbij op de relaties tussen sensitief en protectief gedrag, hormonen en neurale activiteit. Op basis van de resultaten kunnen we niet concluderen dat basale hormoonwaardes of hormoonreactiviteit gerelateerd zijn aan sensitief of protectief gedrag in vaders in de late prenatale of vroege postnatale periode van het vaderschap. Daarnaast ondersteunden onze resultaten niet de hypothese dat neurale activiteit gemeten in reactie op videobeelden van baby's in gevaarlijke situaties gerelateerd is aan geobserveerd of gerapporteerd protectief gedrag in vaders. Exploratieve analyses lieten zien dat de interacties tussen hormonen mogelijk interessant is voor toekomstig onderzoek naar variatie in vaderlijk gedrag. Deze bevinding komt overeen met het idee dat hormonen gezamenlijk werken, in plaats van apart (Feldman & Bakermans-Kranenburg, 2017; Rajhans et al., 2019).

Samengevat geven de resultaten beschreven in deze dissertatie enkele aanvullende inzichten in de relaties tussen het neuroendocrine systeem en ouderlijk gedrag in vaders. Er is echter nog meer onderzoek nodig om beter inzicht te krijgen in de mogelijke rol van het neuro-endocrine system in de ontwikkeling van sensitiviteit en protectief gedrag in vader. Toekomstige studies zouden zich verder kunnen richten op het onderzoeken van mogelijke causale relaties tussen deze verschillende aspecten, bijvoorbeeld door hormonen of ouderlijk gedrag te manipuleren. Die verkregen kennis zou ons kunnen helpen om meer inzicht krijgen in de mogelijke verklaring van geobserveerde verschillen in het ouderlijke gedrag van vaders.

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Academic journal publications

Lotz, A.M., Rijlaarsdam, J., Witteman, J., Meijer, W., van Dijk, K., van IJzendoorn, M. H., & Bakermans-Kranenburg, M. J. (2020). Vasopressin and parental expressed emotion in the transition to fatherhood. *Attachment and Human Development*, 23, 1–17. https://doi.org/10.1080/14616734.2020.1719427

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Bakermans-Kranenburg, M. J., **Lotz, A.**, Alyousefi-van Dijk, K., & van IJzendoorn, M. (2019). Birth of a Father: Fathering in the First 1,000 Days. *Child Development Perspectives*, 13, 247-253. https://doi.org/10.1111/cdep.12347

Riem, M.M.E., **Lotz, A.M.**, Horstman, L.I., Cima, M., Verhees, M.W.F.T., Alyousefi-van Dijk, K., van IJzendoorn, M.H., Bakermans-Kranenburg, M.J. (in press). A soft baby carrier intervention enhances amygdala responses to infant crying in fathers: A randomized controlled trial. *Psychoneuroendocrinology*.

Alyousefi-van Dijk K., van 't Veer A.E., Meijer W.M., **Lotz A.M.**, Rijlaarsdam J., Witteman J. and Bakermans-Kranenburg M.J. (2019) Vasopressin Differentially Affects Handgrip Force of Expectant Fathers in Reaction to Own and Unknown Infant Faces. *Frontiers Behavioral Neuroscience*, 13, 1-10. https://doi.org/10.3389/fnbeh.2019.00105

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Verhees, M.W.F.T., van IJzendoorn, M.H., Alyousefi-van Dijk, K., **Lotz, A.M.**, de Waal, N., & Bakermans-Kranenburg (in press). Child maltreatment affects fathers' response to infant crying, not mediated by cortisol or testosterone. *Comprehensive Psychoneuroendocrinology*.

Alyousefi – van Dijk, K., van der Knaap, N., Buisman, R.S.M., Horstman, L.I., **Lotz, A.M.**, Riem, M.M.E., Schuengel, C., van IJzendoorn, M.H., Bakermans-Kranenburg, M.J. (2020). White matter integrity moderates the relation between experienced childhood maltreatment and fathers' behavioral response to infant crying. *Developmental Psychobiology*, 1-16. http://dx.doi.org/10.1002/dev.22058

Under review

Lotz, A.M., Buisman, R.S.M., Alyousefi-van Dijk, K., Witte, A.M., Bakermans-Kranenburg, M.J.,& Verhees, M.W.F.T. (under review). Exploring the role of endocrine factors in paternal sensitive parenting.

Verhees, M.W.F.T., **Lotz, A.M.**, de Moor, M.H.M., van IJzendoorn, M.H., Fidder, A.E.J., Buisman, R.S.M., & Bakermans-Kranenburg, M.J. (under review). Effects of a soft baby carrier on fathers' behavior and hormones: A randomized controlled trial.

de Waal, N., Buisman, R.S.M., Verhees, M.W.F.T., Alyousefi-van Dijk, K., **Lotz, A.M**., Witte, A.M., Kesarlal, A.R., Fidder, A.E.J.F., Bakermans-Kranenburg, M. J. (under review). Mind-mindedness, parenting sensitivity, and involvement in first-time expectant and new fathers.

Curriculum Vitae

Anna M. Lotz was born on September 13th 1993 in Wageningen, the Netherlands. In 2011, Anna graduated from high school (RSG Pantarijn, Wageningen) and started to study Psychobiology at the University of Amsterdam. She wrote her Bachelor's thesis entitled "Click- Evoked otoacoustic emissions (CEOAE's) and second to fourth digit ratio (2D:4D) in CAIS women" under supervision of Dr. Van Hemmen. In 2014, she obtained her Bachelor of Science degree and was admitted into the Research Master 'Brain and Cognitive Sciences' at the University of Amsterdam. During her Master's program, she completed two theses. For her first thesis project, Anna joined the research of Dr. Sarabdjitsingh at the Department of Translational Neuroscience/ Joëls group, UMC Utrecht, focusing on the effects of early life stress and heterozygous mineralocorticoid receptor knock-out on the development of social behavior in mice. Her second thesis was entitled "Size matters: reducing neuronal network in size affects SCN functionality", and was written under supervision of Dr. Michel at the Department MCB neurophysiology/Neurophysiology of the circadian system, LUMC Leiden. In July 2016, Anna followed the selective CAJAL Advanced Neuroscience Training course on Neuronal Cell Biology – Cytoskeleton and Trafficking at the University of Bordeaux.

After completing her studies, Anna started her PhD program at Leiden University and Vrije Universiteit Amsterdam, under supervision of Prof. Dr. Marian Bakermans-Kranenburg. During her PhD, Anna focused on the behavioral, hormonal and neural aspects of fatherhood in the prenatal and early postnatal phases of fatherhood. Anna is currently working as a teacher at the Institute of Education and Child Studies, Leiden University.