Becoming dad: Exploring the neurobiology of the transition into fatherhood

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geboren te Amsterdam

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“If the human brain were so simple that we could understand it, we would be so simple that we couldn’t.”

- Emerson M. Pugh

Contents

Chapter 1

General introduction

In modern Western societies, paternal involvement has significantly increased in recent years; the time that fathers spend on child care (e.g., playing, educating, supervising) on a daily basis has shown a three- to six-fold increase from one generation in 1970 to the next generation of parents in 2010 (Bakermans-Kranenburg, Lotz, Alyousefi-van Dijk, and Van IJzendoorn, 2019). However, (clinical) family services, as well as parenting research, still predominantly focus on mothers (Cabrera, Volling, and Barr, 2018). Despite findings indicating that fathers are important for child development from the earliest stages of parenthood onward (see Fitzgerald, von Klitzing, Cabrera, de Mendonça, and Skjøthaug, 2020; Lamb, 2010, for reviews), relatively little is known about the development of parenting behaviours in men or about the underlying biological mechanisms. In this thesis, we therefore report on a series of experiments in first-time expectant and new fathers called 'Father Trials', in an attempt to investigate paternal behaviour during the transition into fatherhood, and to shed light on relevant neuroendocrine processes.

Traditionally, mothers and fathers are often examined quite differently in scientific research; where mothers have frequently been the subject of studies examining the quality of parent-child interactions through observation, paternal behaviour is often taken into account via maternal reporting, commonly focussing on negative parenting aspects such as abuse or absence. To illustrate this matter, we conducted a literature search using Web of Science on the published studies on parenting in *Child Development*, the flagship journal of the Society of Research in Child Development, focussing on periods between 1970 and 1980, and one generation later; between 2000 and 2010[1]. In the years 1970 until 1980, 155 empirical papers on parenting were published. Of these, 77% focused exclusively on mothers and a tiny 4% focused exclusively on fathers. Half of these papers focusing on fathers concerned the effects of father absence. Between 2000 and 2010, 433 empirical papers on parenting were published in Child Development. Half of these focused exclusively on mothers whereas merely 2% focused entirely on fathers. Out of the 7 papers with an exclusive focus on fathers, 6 papers concerned either fathers' absence, antisocial behaviour, or role in children's delinquency or psychopathology. The percentage of parenting papers reporting on both fathers and mothers increased from 19% in 1970-1980 to 40% in 2000-2010. However, when both parents are taken into account the mother is often used for parent-child observations and for reports on both the child and the father. Information on fathers' income, education, absence, or abuse as reported by the mother is then used only as a covariate. Consequently, a majority of the papers counted here as reporting on both fathers and mothers primarily looked at mothers

1 topic parent* or caregiver or mother* or father* or maternal or paternal, selecting empirical papers and excluding papers with subjects other than parenting

and merely included father data as a confounder. In an attempt to uncover the mechanisms of paternal care, we investigated fathers directly by means of self-report, observations, and neurobiological measurements.

In this thesis, we have focussed on a particularly important and understudied period: men's transition into parenthood. Recent findings indicate that an important precursor of paternal care is present even before the child is born (e.g., Cabrera, Fagan, and Farrie, 2008; Cook et al., 2005; Fagan, Bernd, and Whiteman, 2007; Lucassen et al., 2015; Witte, Bakermans-Kranenburg, Van IJzendoorn, Szepsenwol, and Shai, 2019). In mothers, mental representations of the unborn child, as well as the imagined current and future relationship with the child, are thought to be the foundation for early postnatal parenting quality (Siddiqui and Hägglöf, 2000). In fathers, prenatal sensitivity is predictive of parenting sensitivity at six weeks postnatally (Hechler, Beijers, Riksen-Walraven, & De Weerth, 2019). Sensitive parenting (i.e., accurately observing and interpreting the signals of a child, and reacting promptly and appropriately) by mothers, as well as fathers, is known to be important for optimal child development (Lucassen et al., 2011), and to play a particularly important role for attachment security (Ainsworth, Blehar, Waters, & Wall, 1978; Steele and Steele, 2017; Verhage et al., 2016). It has been documented that parenthood brings about biological changes (e.g., in hormonal levels and neural reactivity to infant cues) which are similar but not identical for mothers and fathers and are thought to facilitate adequate parental behaviour (see Fitzgerald, von Klitzing, Cabrera, de Mendonça, and Skjøthaug, 2020, for a review). However, how parental behaviour and its underlying mechanisms develop during the transition into parenthood, and how these mechanisms and behaviour relate to each other, remains largely unclear for fathers.

In this thesis we will discuss findings on early fatherhood on several levels; i.e., paternal behaviour, hormones, and brain (see Figure 1.1). Firstly, we will examine perinatal paternal behaviour. Appropriate parental reactions in response to infants' distress are particularly import for children's social-emotional development (e.g., Leerkes, Weaver, and O'Brien, 2012). Through evolution, infant survival and optimal development in the pre-verbal period has been facilitated by shaping infant crying to be a highly salient cue acting as a strong incentive for caregivers to provide effective care (Soltis, 2004). However, infant crying also holds the potential for triggering child abuse and neglect because it can elicit feelings of anxiety, aversion or anger in some parents (e.g., Out, Bakermans-Kranenburg, Van Pelt, & Van IJzendoorn, 2012; Reijneveld, van der Wal, Brugman, Sing, and Verloove-Vanhorick, 2004). In particular, fathers' who themselves received suboptimal parental care are at risk of struggling to provide appropriate care during stressful situations such as exposure to infant crying (e.g., Buisman et al., 2018). In the studies described here, we investigated prenatal

and early postnatal paternal sensitivity by observing fathers' interaction with an infant simulator or their own child (chapter 2 and 5, see Figure 1.1). Additionally, we report findings on fathers' ability to regulate behavioural responses (i.e., handgrip force) in response to infant crying, and paternal involvement with their (unborn) child (chapters 2, 3, 4, and 5, see Figure 1.1).

Secondly, we report findings of neural structure and activation patterns. Neural activation in response to infant crying which has previously been found to be associated with paternal behaviours (see Feldman, Braun, and Champagne, 2019 for a review). Neuroimaging studies suggest that both parents and non-parents show robust neural activations to infant cry sounds, but that parents (compared to non-parents) display enhanced neural processing of infant distress (see Witteman et al., 2019 for a meta-analysis). However, men are typically underrepresented in these studies and how the neural processes involved in parental behaviour develop during the transition into fatherhood remains largely unknown. Although fathers do not show the same structural neural changes that are found in women after the birth of the first child (Hoekzema et al., 2017), variations in neural structure might predispose fathers to display more or less optimal parenting behaviours, especially when under pressure in stressful situations such as exposure to infant crying. In particular, parents' own childhood experiences with abuse and neglect is known to be associated with atypical brain structure in connective tissues which in turn has been found to be related to functional outcomes such as emotional dysregulation (e.g., Riem et al., 2019). Therefore, we conducted experiments exploring neural activation in response to infant crying before and after the birth of fathers' first child (chapter 2, see Figure 1.1). Also, we tested whether fathers' own childhood experiences were related to behavioural responses to infant crying and whether this was mediated or moderated by brain structure (chapter 3, see Figure 1.1).

Thirdly, we included hormonal measures since the level of neural activations in response to infant cues, as well as paternal behaviour, are related to hormone levels (see Feldman, Braun, and Champagne, 2019 for a review). Testosterone levels are commonly thought to be low in fathers as compared to other men in order to facilitate nurturing rather than mating behaviours, but support for this theory is modest (Meijer, van IJzendoorn, & Bakermans-Kranenburg, 2019). Likewise, studies attempting to link testosterone levels to parenting behaviours in fathers show mixed findings (for a review see Kuo and Gettler, 2018). Importantly, longitudinal and multidimensional studies including fathers in the early stages of parenthood are missing (see Fitzgerald, von Klitzing, Cabrera, de Mendonça, and Skjøthaug, 2020, for a review). In this thesis we therefore report on our findings of testosterone levels before and after the birth of fathers' first child and how these levels relate to parenting behaviours and neural

activations in response to infant signals (chapter 2, see Figure 1.1). Additionally, arginine vasopressin (AVP), rather than oxytocin, may be particularly important for attuning the paternal brain to infant signals and may therefore play a role in shaping paternal behaviour (see Fitzgerald, von Klitzing, Cabrera, de Mendonça, and Skjøthaug, 2020, for a review). In chapter 4 we will therefore discuss our findings on the effects of paternal modulation of handgrip force in response to infant crying after administration of AVP (see Figure 1.1).

In addition to correlational research presented in chapters 2 and 3, and the hormone administration study discussed in chapter 4, we documented the development of a behaviourally focused parenting intervention for first-time fathers (chapter 5, see Figure 1.1). Importantly, we attempted to fill the gap for positive, father-focused, early parenting interventions. Previously, a meta-analysis found that brief and behaviourally focused parental interventions may be capable of improving parenting sensitivity as well as increasing the chances of secure child attachment (Bakermans-Kranenburg, Van IJzendoorn, and Juffer, 2003). In line with this finding, one study showed that a limited number of prenatal and postnatal visits aimed at providing maternal support and information led to more secure child attachment at 14 months (Leitch, 1999). In another study, as little as a single prenatal session focusing on infant communication was related to better postnatal sensitivity to infant cues (Jacobson and Frye, 1991). Moreover, a recent umbrella synthesis indicated that a single prenatal intervention session (O'Connor and Whaley, 2007) is among the most effective interventions in preventing child abuse (Van IJzendoorn, Bakermans-Kranenburg, Coughlan, and Reijman, 2019). Importantly, a study investigating a large sample of Dutch expectant fathers found that fathers' prenatal feelings of being connected to the foetus were interrelated with their representations of the unborn child (Vreeswijk, Maas, Rijk, and Van Bakel, 2014). Together, these findings indicate that a short, prenatal, and interaction-based parenting intervention could increase paternal sensitivity and potentially his involvement in parenting. Therefore, we report on the feasibility of a prenatal parenting intervention which has been embedded in a randomized controlled trial examining fathers' behaviour, hormones, and brain during the transition into fatherhood (chapter 5, see Figure 1.1).

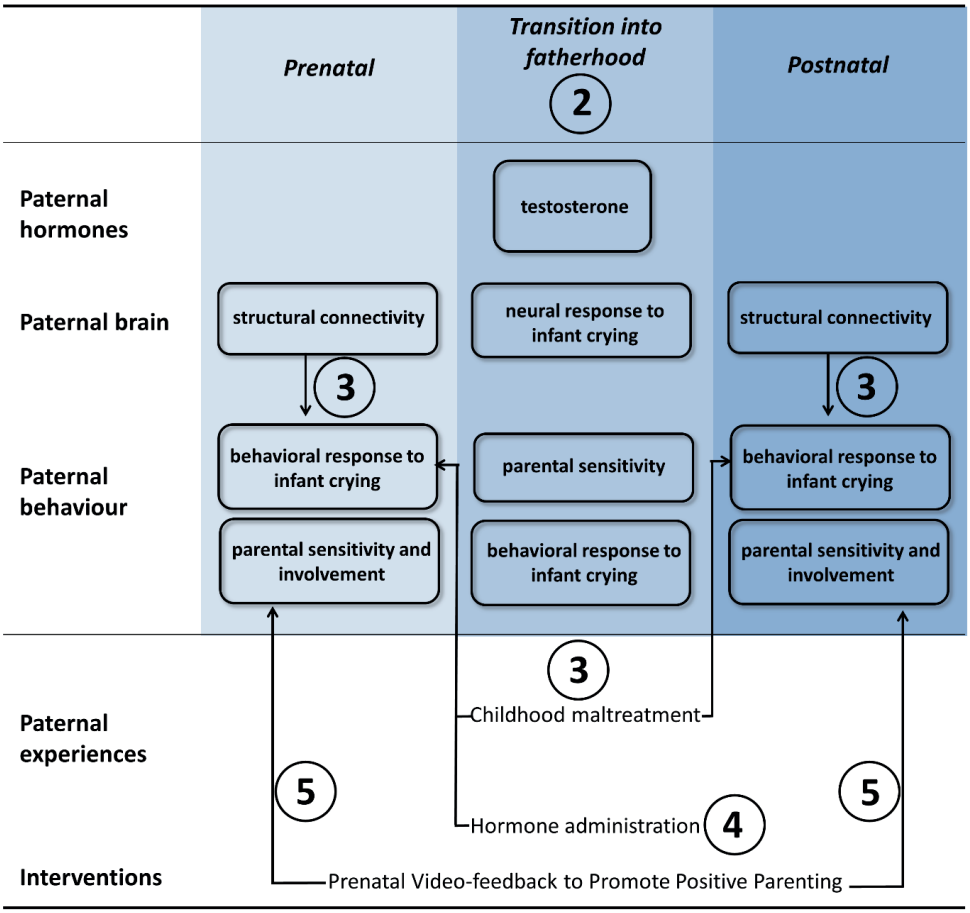

Figure 1.1. Visualization of the different modalities of early fatherhood (i.e., hormones, brain and behaviour), as well as paternal experiences and interventions, reported upon in this thesis. The numbers (i.e., 2-5) indicate the subjects of the corresponding chapters.

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Chapter 2

Exploring the transition into fatherhood: behavioral, hormonal, and neural underpinnings of responses to infant crying

Alyousefi-van Dijk, K., Thijssen, S., van 't Veer, A. E., Buisman, R. S. M., van IJzendoorn, M. H., & Bakermans-Kranenburg, M. J. (2020, July 7). Exploring the transition into fatherhood: behavioral, hormonal, and neural underpinnings of responses to infant crying. PsyArXiv. https:/doi.org/10.31234/osf.io/5bxk9

Abstract

In the present hypothesis generating study, behavioral and neural responses to infant crying, as well as paternal hormone levels, were measured in both the prenatal and early postnatal period. Using a longitudinal design, we investigated parental sensitivity, handgrip force, and neural activation in response to infant crying sounds, in addition to testosterone baseline levels, in 25 first-time fathers. We describe the extent to which these aspects of paternal care are related across the perinatal period. The current exploratory study adds to the understudied field of early paternal care by making recommendations, and proposing hypotheses for future studies.

Introduction

In a rapidly growing body of both human and animal literature, biological processes have been documented to be associated with parental behavior. Essential for the survival and wellbeing of offspring, infant crying has been shaped by evolution to be perceived as an aversive stimulus. Distressed infants' vocalizations therefore act as a strong incentive for caregivers to provide effective parental care and consequently stop the infant's distress. Robust effects of offspring vocalization on different modalities, such as hormones (e.g. Fleming et al., 2002; Van Anders et al., 2012) and neural processing (e.g. Rigo et al., 2019), are found in a wide variety of mammals regardless of parenting status. However, these processes show some disparities for males and females, as well as for parents and non-parents (e.g. Witteman et al., 2019). Importantly, hormonal and neural responses to infant crying have not only been found to correlate with each other (e.g. Bos et al., 2010), they also have been found to relate to behavioral outcomes such as parental involvement (Mascaro et al., 2014), as well as quality of caregiving (Kuo, Carp, Light, & Grewen, 2012; and Weisman, Zagoory-Sharon, and Feldman, 2014).

Human fathers, who find infant crying more aversive than mothers do (Zeifman, 2003), remain underrepresented in these studies. Although father involvement has significantly increased in modern western societies (see Bakermans-Kranenburg, Lotz, Alyousefi-van Dijk, & Van IJzendoorn, 2019), the mechanisms underlying the highly variable quality of paternal care are still poorly understood (Lucassen et al., 2011; Van IJzendoorn and De Wolff, 1997). Previous attempts at unravelling these mechanisms have sometimes been clouded by variety in parental phase of participants (i.e. varying number and age of children; Roellke et al., 2019; Weisman, Zagoory-Sharon, & Feldman, 2014; Fleming et al., 2002; Mascaro al., 2014; but not Storey, Walsh, Quinton, & Wynne-Edwards, 2000), and have been limited in the number of different modalities assessed within participants. We therefore conducted a hypothesis generating study, including elaborate behavioral, hormonal, and neural measures, during a particularly important period of parenting: the transition into fatherhood.

Providing prompt and appropriate parental responses to infant distress is a crucial component of parental sensitivity, which is paramount for optimal child development, in particular attachment (Ainsworth, Blehar, Waters, & Wall, 1978). This holds for mothers as well as for fathers (Lucassen et al., 2011; Verhage et al., 2016). To date, a small number of studies have examined early observed paternal sensitivity. Although one study has indicated that paternal sensitivity may be unstable between the child's first and third year of life (Brown, Mangelsdorf, & Neff, 2012), prenatal parental

sensitivity, measured during the third trimester using a life-like infant simulator, has been found to predict postnatal parental sensitivity six weeks after birth for both mothers and fathers (Hechler, Beijers, Riksen-Walraven, & De Weerth, 2019). Complementing the limited available literature on this important topic, we will examine differences and correlations between prenatal and postnatal observed paternal sensitivity (see solid red arrow in Figure 2.1).

In addition to observed parental sensitivity, the handgrip paradigm is used in the parenting literature to assess a more specific behavioral aspect of parental care. Designed to measure the degree to which someone can modulate handgrip force during cry exposure, the relevance of this paradigm lies in the fact that the use of excessive force during infant cry exposure has been associated with experienced childhood maltreatment (Buisman et al., 2018) as well as (risk of) perpetuating child maltreatment (Crouch, Skowronski, Milner, & Harris, 2008; Compier-de Block et al., 2015). Despite the known importance of fathers' quality of parenting for child development (e.g. Ramchandani et al., 2013), little is known about the differences and correlations in control over behavioral responses to infant crying between de prenatal and postnatal period in first-time (expectant) fathers. Therefore, we will examine differences and correlations between prenatal and postnatal paternal ability to modulate handgrip force during exposure to infant crying sounds (see the lower solid red arrow in Figure 2.1).

Several biological processes have been related to paternal behavior. For example, hormones have been shown to play an important role in both parental sensitivity (Naber, Poslawsky, Van IJzendoorn, Van Engeland, & Bakermans-Kranenburg, 2013) and handgrip force used in response to infant crying in nulliparous women and men (Bakermans-Kranenburg et al., 2012; Riem et al., 2016; Riem et al., 2017), as well as in first-time expectant fathers (Alyousefi-van Dijk et al., 2019). Specifically, low levels of testosterone have been found to relate to higher observed quality of parenting in expectant but not new fathers, and only in those with low levels of cortisol (Bos et al., 2018). Likewise, lower baseline testosterone levels have been found to relate to more affectionate touch, infant-father gaze, and positive vocalizations of fathers with 3-8 month old infants (Weisman, Zagoory-Sharon, and Feldman, 2014), and more interactive and social touch in fathers of 1-6 month old infants (Gordon et al., 2017). However, testosterone levels do not relate to father-child interaction quality in older children (i.e., 1 and 3-5 year old; Endendijk et al., 2016; Kuo et al., 2016). Also, lower levels of testosterone in fathers have been related to more parental investment (Alvergne, Faurie, and Raymond, 2009; Mascaro, Hackett, and Rilling, 2013) as well as to more sympathy towards, and tendency to respond to, infant cries (Fleming, Corter, Stallings, and Steiner, 2002). In this study, we will examine possible associations

between paternal behavior (i.e. paternal sensitivity and performance on a handgrip task) and baseline testosterone levels in both the prenatal and the early postnatal period (see dotted green lines in Figure 2.1).

The transition to fatherhood, and subsequent exposure to an infant, are commonly associated with decreasing levels of salivary testosterone (e.g. Gettler, McDade, Feranil, and Kuzawa, 2011; Gray et al., 2006; Kuzawa et al., 2009; Muller et al., 2009), which presumably allows for the display of paternal care while minimizing mating efforts and aggression (see Wynne-Edwards, 2001 for a review). However, not all studies find lower baseline levels of testosterone in fathers compared to non-fathers (e.g. Roellke, Raiss, King, Lytel-Sternberg, & Zeifman, 2019), and indeed, meta-analytic support for lower testosterone levels in fathers is modest (Meijer, Van IJzendoorn, & Bakermans-Kranenburg, 2019). Questions have been raised about the exact effects of relationship investment (Grebe, Sarafin, Strenth, & Zilioli, 2019) and parity (e.g. Fleming et al., 2002). Studies using more homogenous samples of first-time parents paint a more straightforward picture; levels of testosterone decrease during pregnancy (Edelstein et al., 2015), and importantly, this prenatal decrease of testosterone as well as baseline testosterone in the immediate postpartum, seems to predict paternal involvement early in the child's life (Edelstein et al., 2017; Kuo et al., 2018). In this study, we will examine differences and correlations between prenatal and postnatal testosterone baseline levels in first-time fathers (see solid red arrow in Figure 2.1).

The presence of robust neural activation in response to infant crying is another striking example of biological preparedness of parental responses. Recently, a meta-analysis showed marked neural activation in parents, non-parents, males, and females during exposure to infant cries in the auditory system (supporting auditory and semantic processing), the thalamocingulate circuit (supporting redirection of attention towards salient sensory input), the dorsal anterior insula (supporting empathy), and various sub-regions in the dorsomedial prefrontal cortex (supporting the evaluation of emotional information and motivated action initiation; Witteman et al., 2019). Specifically, parents showed more neural activation than non-parents while listening to infant cries in the bilateral auditory cortex, dorsal anterior and posterior insula (supporting emotional processing and integration of emotionally relevant auditory information with somatosensory and motor information respectively), pre- and postcentral gyrus (supporting motor simulation), and right putamen (supporting motor preparation; Witteman et al., 2019). However, this effect might be driven by an overrepresentation of mothers in the group of parents. Since the neural dimension of the biological preparedness for responses to infant crying has likely developed through different pathways in men and women (for a review see Feldman, Braun

and Champagne, 2019), fathers and mothers may show overlapping but not identical neural responses while listening to infant crying. As one of the few studies looking exclusively at fathers, Mascaro and colleagues (2014) showed that in fathers of 1-2 year olds the bilateral inferior frontal gyrus, bilateral globus pallidus, and bilateral auditory cortex showed increased activation during infant cry sounds compared to control sounds. In a similar group of participants, Li and colleagues (2017) showed that listening to infant cries induced activation in the right auditory cortex, and deactivation in the supplementary motor cortex, somatosensory cortex, insula, and visual cortex. Paternal neural responses to infant signals had previously been shown to change with increasing parental experience (e.g. Abraham et al., 2014), in that infant cry sounds become more salient than infant laughter with changing parental status (Seifritz et al., 2003).

Indeed, widespread changes in neural responses to infant cry perception can be found between the first and fourth month postpartum (Kim et al., 2014). Likewise, our lab recently found that before the birth of their first child, fathers-to-be activate fewer brain areas than reported in studies with large variety in parental status and experience; prenatally fathers activate the bilateral auditory cortex and bilateral posterior cingulate cortex during exposure to infant crying (PCC, Thijssen et al., 2018). The sudden onset of neural changes seen in response to infant signals shortly after birth of the first child was further highlighted by Li et al. (2018), showing widespread neural activation in response to infant crying in first-time fathers of 2-month-olds, including (but not limited to) the medial prefrontal cortex, bilateral anterior insula and inferior frontal gyrus, bilateral striatum, bilateral thalamus, bilateral auditory cortex, bilateral posterior cingulate, and bilateral midbrain including the ventral tegmental area, and substantia nigra. In the current study, we will report on the early postnatal, rather than prenatal, neural activations in response to infant crying of the same fathers reported by Thijssen et al., 2018. In case similar areas are found to be active during both time points, prenatal-postnatal differences and correlations will be examined (see solid red arrow in Figure 2.1). Any differences in the brain areas that activate in response to infant crying in the prenatal versus postnatal period will be described in the discussion.

Examinations of associations between behavioral, hormonal, and neural aspects of paternal care are scarce. Mascaro and colleagues (2014) showed a non-linear relation between activation in the anterior insula during infant cry exposure and paternal participation in childcare as reported by mothers, indicating that fathers with the highest levels of involvement showed intermediate levels of neural activation. Also, testosterone administration has been found to increase thalamocingulate activation in response to infant cries in women (Bos et al., 2010), but an association between

baseline testosterone and neural activations during infant cry exposure has not been found in fathers (Mascaro et al., 2014). Additionally, neural activations in reaction to infant cry perception were found not to be related to performance on a handgrip task in women (Riem et al., 2012), but have not yet been investigated in fathers. Consequently, hormonal underpinnings of neural responses to infant crying, as well as behavioral effects of these neural activations in fathers, remain elusive. Therefore, we will examine possible associations between neural activations in response to infant crying and paternal behavior (i.e. paternal sensitivity and performance on a handgrip task) in both the prenatal and early postnatal period, see dotted green lines in Figure 2.1. Also, we will examine possible associations between lower level prenatal measures (e.g., testosterone levels) and higher level postnatal measures (e.g., paternal sensitivity), see dashed blue arrows in Figure 2.1.

To our knowledge, the current exploratory study is the first to examine behavioral, hormonal, and neural aspects of paternal responses to infant crying in the perinatal period, in first-time (expectant) fathers. Using a longitudinal design we will firstly describe differences and correlations between prenatal and postnatal aspects of paternal care. More specifically, we will address the question whether testosterone baseline levels decrease from the prenatal to the postnatal period in first-time expectant fathers. Likewise, we will explore if prenatal and postnatal measurements of paternal behavior (i.e., parental sensitivity and handgrip force) are related, and explore if fathers show more widespread neural activation in response to infant crying in the postnatal versus the prenatal period. Secondly, we will investigate concurrent correlations between the different modalities (i.e., behavioral, hormonal, and neural measures) in both the prenatal and postnatal period. Thirdly, we examine correlations between prenatal neurobiological measures (e.g. hormones) and postnatal behavioral measures (e.g. parental sensitivity). See Figure 2.1 for a design overview. Our study is a hypothesis generating study on a topic that is currently still within the context of discovery, thus no specific directed hypotheses were formulated. Consequently, our results can be used as guidance for future (confirmatory) studies on this topic.

Material and methods

Participants

First-time expectant fathers were recruited through midwives and advertisements on Leiden University affiliated webpages. Participants were required to cohabitate with their pregnant partners, speak Dutch, and were screened and excluded for claustrophobia, metal parts in the body, self-reported neurological, neuroendocrine and psychiatric disorders, alcohol and substance abuse, recreational drug use within

6 months prior to participation, and use of steroidal or other medications interfering with hormonal or neural measures. After these inclusion and exclusion criteria, a total of 25 participants, as was determined by our ethics proposal for a pilot study, took part in this study before the birth of their first child. Of these initial 25 participants, 20 returned for a postnatal visit upon our further request.

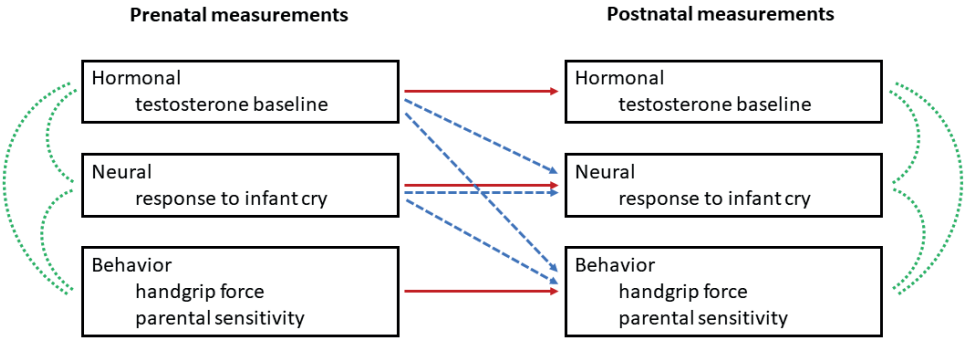

Figure 2.1. Graphical overview of study variables. We examined (i) prenatal-postnatal differences and correlations of hormonal, neural, and behavioral measures (solid red arrows), (ii) concurrent associations between hormonal, neural, and behavioral measures at prenatal and postnatal time points (dotted green lines), and (iii) associations between prenatal lower level measures (e.g. hormonal) and postnatal higher level measures (neural and behavioral, see dashed blue arrows). Note that brain areas significantly activated during infant cry perception both at the prenatal and postnatal assessment can be tested for prenatal-postnatal differences and correlations (solid red arrow), while areas activated only prenatally can be tested for prenatal to postnatal correlations with other areas postnatally (horizontal dashed blue arrow).

At the time of inclusion, the mean age of the expectant fathers was 31.92 years (*SD* = 4.30, range = 24-43) and the mean gestational age of the child was 27.02 weeks (*SD* = 4.91, range = 20-36). All participants enjoyed either secondary (20%) or higher education (80%), and 23 of the 25 participants were right handed. During the postnatal follow-up infants were between 12.71 and 20.71 weeks old (*M* = 15.66, *SD* = 2.36, range = 12-20). Fourteen out of these 20 infants were male, all infants were born with normal birth weights (M_{grams} = 3586.30, SD_{grams} = 439.39, range = 2780-4360 grams), and mothers reported the overall health of their infants as excellent (45%), very good (45%), good (5%), or moderate (5%). Approval for this study was obtained from the Ethics Committees of the Institute for Education and Child Studies at Leiden University and the Leiden University Medical Centre, as well as the Dutch Central Committee on Research Involving Human Subjects. All participants gave informed consent.

Due to technical problems with the sound system, fMRI data of one participant in the postnatal visit was missing resulting in fMRI data for 25 participants prenatally and 19 postnatally.

Procedure

Participants were instructed to abstain from alcohol and excessive physical activity during the 24h before the start of each visit and from caffeine on the day of the visit. Prenatal and postnatal laboratory visits took place at similar times of day and had identical procedures, starting with instructions about the visit. Hereafter participants rinsed their mouth with water, and saliva was collected for a baseline hormone measurement. Participants collected approximately 1.5 ml saliva using a passive drool method in which participants drool (rather than spit) saliva either directly into a 2 ml cryogenic vial or indirectly by using a straw. Next, participants self-administered a placebo nasal spray, and underwent a brief training of the functional magnetic resonance imaging (fMRI) tasks on a laptop, which familiarized them with the tasks. A resting-state scan and working memory fMRI paradigm (also using cry stimuli), as well as a fMRI task with video vignettes preceded the fMRI cry paradigm described here. The neural measures were followed by the handgrip cry paradigm. Next, participants took care of an infant stimulator for 10 min for the observation of their parenting behavior, during which the doll was programmed to cry uncontrollably for five min. In between prenatal visits, as well as after the postnatal visit, participants completed online questionnaires. See figure 2.2 for a design overview of the study.

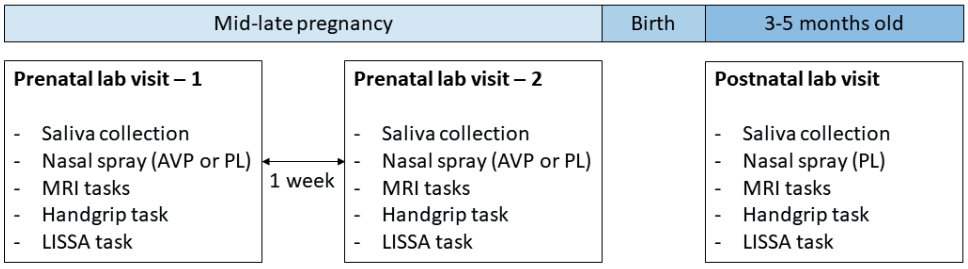

Figure 2.2. Graphical overview of the study design. Participants were seen twice prenatally with one intervening week. As part of a randomized, double blind, placebo-controlled, within subject trial they self-administered a placebo (=PL) or vasopressin (=AVP) during the prenatal visits. A placebo was self-administered during all postnatal visits. The prenatal AVP visit is not reported here, which corresponded to the first prenatal visit for 52% of participants. Testosterone baselines levels were assessed through saliva at the start of each session. Brain activation and a behavioral response in reaction to infant crying was assessed during one of the MRI tasks and the handgrip task respectively. Finally, parental sensitivity was observed using a LISSA task.

Measures

Hormonal assessment

Testosterone. Most prenatal visits took place in the late afternoon or early evening (range = 17:10-19:14), except for four participants who were seen in the morning (range = 9:00-11:01), and four participants who were seen in the early afternoon (range = 13:02-14:02). Importantly, participants were scheduled for the postnatal visit around the same time their prenatal visit took place. However, one participant was seen during the late afternoon prenatally and in the early morning postnatally. For this participant, an extra saliva sample was collected at home during the late afternoon of the same day as the postnatal visit, which was used as the baseline hormonal measurement. This resulted in an overall mean difference between time points (prenatal placebo visit and postnatal visit) of 51 min (range = 0:02–2:28 hours). Saliva samples were stored at -20°C until they were shipped on dry ice 0-5.5 months later for analysis by Dresden LabService GmbH. The concentration of salivary testosterone in each sample was determined using high performance Liquid Chromatography-tandem Mass Spectrometry in combination with on-line solid phase extraction. Intra- and inter-assay coefficients of variances of this method were between 4.3% and 10.8% (Gao et al, 2015). Since two prenatal samples (collected one week apart but during similar time points within participants) were available for all participants, and the measurements correlated substantially (r = .60), a mean testosterone baseline level was calculated for the prenatal measurements. A check revealed that the use of a mean prenatal testosterone baseline level (resulting from averaging the baseline measurement of the two prenatal visits), instead of using only baseline levels measured in the placebo visit, did not affect concurrent associations with other measures.

Neural assessment

fMRI cry paradigm. The neural data described here stems from a fMRI paradigm previously described in detail for the same sample in Thijssen et al., (2018). Although Thijssen et al. (2018) described only the prenatal visits, the paradigm, parameters, preprocessing, and statistical analysis for the postnatal visit added here were identical. In summary, the fMRI task contained 48 trials of auditory exposure of either an infant cry sound or a control sound (10s duration). In a group-level analysis, we then tested the difference between cry sounds and control sounds to assess the regions involved in the processing of infant crying in both the prenatal and postnatal visit. Only significant results of the F-test are reported. See supplemental materials for a more detailed description the of fMRI methods.

Behavioral assessments

Handgrip cry paradigm. The handgrip data described here stems from a paradigm previously described in detail for the same sample in Alyousefi-van Dijk et al. (2019). Although Alyousefi-van Dijk et al., (2019) described only the prenatal visits, the paradigm, preprocessing, and statistical analysis for the postnatal visit added here were identical. In summary, the handgrip task contained 30 trials of auditory exposure of either an infant cry sound or a control sound (12s duration) while participants were asked to squeeze a handgrip dynamometer with alternating full or half strength. Grip strength modulation was then calculated by dividing half-strength squeeze intensity by the preceding full-strength squeeze intensity, meaning that scores of over .50 indicated excessive force on the half-strength squeeze attempt. In a group-level analysis, we then tested the difference between cry sounds and control sounds to assess a behavioral response to infant crying in both the prenatal and postnatal visit. See supplemental materials for a more detailed description the of fMRI methods.

Observed parental sensitivity. The infant simulator (RealCare Baby II-Plus; Realityworks, Eau Claire, WI, USA) is a life-like doll resembling a 0-3 months old infant in appearance, size, and weight (2.95 kg). Use of the infant stimulator has previously been shown to provide a reliable way of assessing parental sensitivity (Bakermans-Kranenburg, Alink, Biro, Voorthuis, & Van IJzendoorn, 2015; Voorthuis et al., 2013), also suitable for populations without children of their own. In this study, participants were asked to take place in a room with a table and chair, and a laptop or PC with internet access as a potentially attractive competing activity. The experimenter explained to the participants that they would be asked to take care of a doll that acts like a real infant. Participants were instructed to take care of the doll as if it were their own child, including careful handling such as offering appropriate neck support. They were told that the doll could cry just like a real infant. Participants were shown different objects they could use to soothe the child (i.e. a blanket, toys, a bottle, a second diaper, and a second set of clothes). Also, they were given permission to use the laptop or PC if they wanted to check their e-mails or do something else online.

Next, the experimenter would re-enter the room with the simulator in a baby seat. The simulator was then handed to the (expectant) father and introduced as “baby Robin” (a gender-neutral name). For the purpose of this study, the simulator was programmed to be quiet for approximately 3 min, then cry for approximately 5 min, followed by being quiet for approximately 2 more min (see Voorthuis, Bakermans-Kranenburg, & Van IJzendoorn, 2017, for a similar protocol). The cry sounds consisted of pre-set recordings of a real infant and built up in intensity during the 5 min cry episode. Unbeknownst to the participants, they were not able to effectively soothe the infant. When asked about whether or not their actions could prevent or stop the doll from crying, the

experimenter would reply that the simulator reacts just as a real infant would. Prenatal and postnatal videos of 10 min interactions with the infant simulator were coded by independent coders for parental sensitivity with scores ranging from 1 (insensitive) to 9 (sensitive) using the Ainsworth Sensitivity scale (Ainsworth et al., 1974). After intensive training, all coders were found to be reliable with expert coders (ICC = .73-.92). A consensus score of two coders was used in case of any atypical recordings (i.e. 2 videos) that made coding more difficult. Due to technical problems the video for one participant was missing in the postnatal visit. This sensitivity score was then imputed by means of a regression analysis using the postnatal sensitivity scores as a dependent and the prenatal sensitivity scores as the predictor, see Supplemental Materials Table 2.2 for the minimal effect of this imputation on the correlations with other measures.

Statistical analyses

Although our sample is small, we report descriptive statistics as well as relevant assumption checks for our correlational analyses in order to facilitate the reader in assessing the effect sizes and potential patterns in the data, see supplemental materials for a detailed description as well as more information on all variables in Supplemental Materials Table 2.1.

Prenatal-postnatal differences and correlations. Paired sample t-tests were performed on prenatal and postnatal measurements for testosterone baselines, handgrip strength (only in response to infant crying), and parental sensitivity, and accompanying effect sizes are reported. In addition, bivariate linear correlations were calculated within measures (e.g. prenatal and postnatal parental sensitivity).

Concurrent associations. Bivariate linear correlations were computed between modalities at the prenatal as well as the postnatal assessment (e.g. correlation between prenatal neural response to infant crying and prenatal parental sensitivity).

Prenatal to postnatal correlations. Bivariate linear correlations were computed between lower level prenatal measures (e.g. testosterone baseline) and higher level postnatal measures (e.g. parental sensitivity).

Given our small sample size in combination with a high number of correlational tests, and consequent increased risk of false positives, we decided to focus our in-text discussion on large effect sizes (i.e. $r \geq .50$) and present the full range of effect sizes in Tables 2.1-2.4.

Results

Descriptive results

Results on differences and correlations between prenatal and postnatal mean-levels are reported in Table 2.1, and concurrent associations are shown in Table 2.2 and 2.3. Correlations between lower prenatal measures and higher level postnatal measures can be found in Table 2.4. All correlations of $r \geq .50$ are depicted in Figure 2.3.

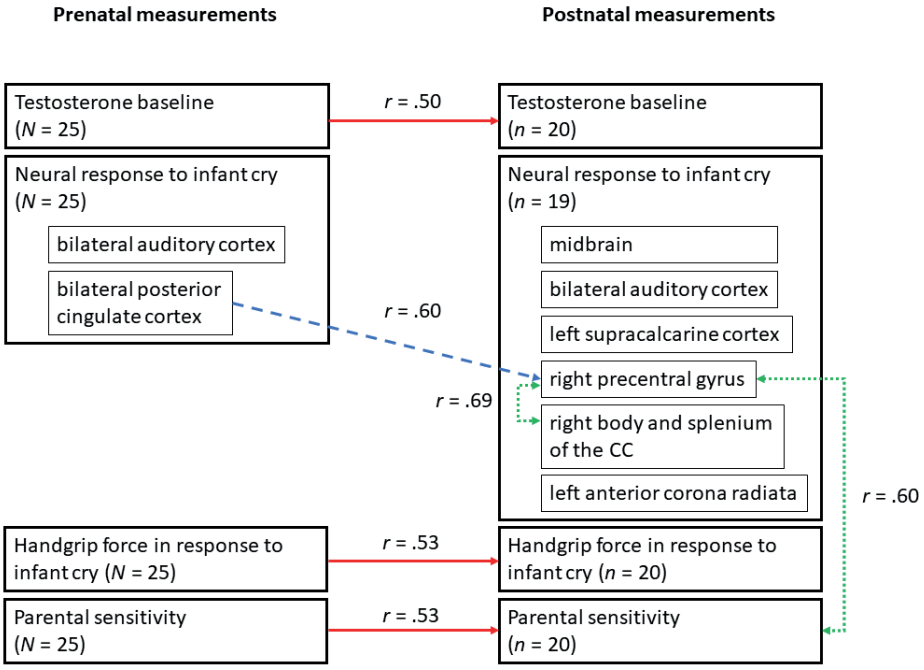

Figure 2.3. Bivariate correlations of $r \geq .50$ are depicted. Solid red arrows indicate correlations of measurements between prenatal and postnatal time points. Dotted green lines indicate concurrent relations. The dashed blue arrow indicate a prenatal to postnatal correlation. PCC = posterior cingulate cortex, CC = corpus callosum

Prenatal-postnatal differences and correlations

Testosterone levels. The difference between prenatal and postnatal testosterone baseline levels was small ($t = 0.99$, $d_z = 0.22$), and they correlated positively ($r = .50$), indicating that baseline testosterone levels do not change much from late pregnancy to early postpartum and that higher prenatal testosterone baseline levels might be related to higher postnatal testosterone baseline levels, see Table 2.1.

Table 2.1. Results for prenatal-postnatal differences and correlations for all measurements.

	N	*M(SD)*	Min	Max	Differences pre-post (Cohen's d_z)	Correlations pre-post (Pearson's *r*)
Testosterone baseline						
Pre (pg/ml)	25	54.11 (21.90)	25.35	112.00	0.22	.50
Post (pg/ml)	20	47.95 (10.78)	34.20	76.90		
Neural activation in bi auditory cortex						
Pre (mean Z)	25	1.33 (0.93)	-0.14	3.06	0.58	.05
Post (mean Z)	19	.75 (.60)	-.11	1.60		
Handgrip force						
Pre (ratio)	25	.64 (.12)	.37	.86	-0.00	.53
Post (ratio)	20	.63 (.09)	.44	.81		
Parental sensitivity						
Pre (score 1-10)	25	5.40 (1.67)	2	8.5	-0.18	.53
Post (score 1-10)	20	5.88 (1.60)	3	8.5		

Note. Pre = prenatal, Post = postnatal, bi = bilateral

fMRI response to infant cry sounds. The prenatal comparison between cry sounds and control sounds resulted in three significant clusters showing significant activation (cry sound > control sound): the left and right auditory cortex, and the bilateral PCC (Thijssen et al., 2018). Because of the high correlation between activation in the right and left auditory cortex in the prenatal measurements (r = .82), we averaged the mean left and right scores in the analyses reported here. The same was done for the significant activations found in the postnatal left and right auditory cortex (r = .96).

The postnatal assessment showed seven significant clusters for the comparison between cry sounds and control sounds, see Supplemental Materials Table 2.3. The first cluster (p < 0.001) spans several (presumably functionally) distinct brain regions, including, but not limited to, the midbrain (containing the highest levels of activation), bilateral anterior cingulate cortex, left accumbens, bilateral caudate nucleus, bilateral insular cortex, bilateral amygdala, bilateral thalamus, bilateral hippocampus, left precentral gyrus, and bilateral superior cerebellar peduncle. The second cluster (p < 0.001) corresponds to the left auditory cortex (including the parietal operculum cortex, supramarginal gyrus, and planum polare). The third cluster (p < 0.001) corresponds to the left supracalcarine cortex bordering on the cuneal and precuneous cortex. The fourth cluster (p <0.001) corresponds to the right auditory cortex (including the central opercular cortex, planum temporale, and Heschl's gyrus). The fifth cluster (p = .002) corresponds to the right precentral gyrus extending slightly

into the right postcentral gyrus as well as ventrally into the right superior longitudinal fasciculus and corticospinal tract. The sixth cluster (p = .004) corresponds to the right body and splenium of the corpus callosum (CC) extending into the right posterior corona radiata and retrolenticular part of internal capsule. The seventh cluster (p = .016) corresponds to the left anterior corona radiate descending into the left frontal operculum cortex. See Supplemental Materials Figures 2.1-2.7 for the corresponding anatomical images.

The difference between prenatal and postnatal mean Z-values in response to the cry sound in the bilateral auditory cortex was substantial (t = 2.52, d_z = 0.58), and these ratios did not correlate (r = .01), indicating that stronger neural activation in this region prenatally might not be related to stronger neural activation in this region postnatally, see Table 2.1.

Table 2.2. Prenatal concurrent associations between the measurements (Pearson's *r*).

	1	2a	2b	3	4
T baseline					
Neural activation					
bi auditory cortex	-.05				
bi PCC	.21	.23			
Handgrip force	-.01	.09	.26		
Parental sensitivity	.32	.05	.23	.10	

Note. T = testosterone, bi = bilateral, PCC = posterior cingulate cortex

Table 2.3. Postnatal concurrent associations between the measurements (Pearson's *r*).

	1	2a	2b	2c	2d	2e	2f	3	4
T baseline									
Neural activation									
midbrain	-.26								
bi auditory cortex	.05	.49							
l supraCal cortex	.00	.23	.29						
r precentral gyrus	-.24	.14	-.48	-.26					
r body and splenium of CC	-.15	.46	-.06	-.11	.69				
l ant CorRad	-.30	.02	-.17	-.27	.01	-.05			
Handgrip force	-.21	-.27	-.12	-.28	-.15	-.49	.18		
Parental sensitivity	-.13	.05	-.36	-.45	.60	.36	.25	.09	

Note. T = testosterone, bi = bilateral, l = left, r = right, antCorRad = anterior corona radiata, CC = corpus callosum, supraCal cortex = supracalcarine cortex.

Handgrip force. Prenatal mean handgrip force ratios showed that fathers had some difficulty modulating their force to both the control and the infant cry sound (see also Supplemental Materials Table 2.1). The difference between prenatal and postnatal mean handgrip force ratios in response to the cry sound was negligible (t = -0.01, d_z = -0.00), and these ratios correlate positively (r = .53), indicating that more prenatal handgrip force might be related to more postnatal handgrip force, see Table 2.1.

Parental sensitivity. Since parental sensitivity scores did not depend strongly on whether the placebo session was the first or the second prenatal visit (t = 1.81, d_z = 0.36), the scores were not corrected for the order of the visits. The difference between prenatal and postnatal parental sensitivity scores was small and negative (t = -0.80, d_z = -0.18). The prenatal and postnatal measures of parental sensitivity correlated positively (r = .53), indicating that higher prenatal parental sensitivity might be related to higher postnatal parental sensitivity, see Table 2.1.

Concurrent relations

Bivariate correlations between prenatal measures were found to be low and are reported in Table 2.2. Postnatal measures indicated noteworthy positive correlations between neural activation in the right precentral gyrus and the right body and splenium of the CC (r = .69), as well as between neural activation in the right precentral gyrus and parental sensitivity (r = .60), indicating that more activation in this area during exposure to infant crying after the birth of their first baby might be related to fathers' higher observed parenting sensitivity, see Table 2.3.

Prenatal to postnatal correlations

Prenatal neural activation in the bilateral PCC was found to correlate positively with postnatal neural activation in the right precentral gyrus (r = .60), suggesting that more activation prenatally in the bilateral PCC might be related to more activation postnatally in the right precentral gyrus, see Table 2.4.

Discussion

The present study examined behavioral, hormonal, and neural aspects of paternal responses to infant crying in the prenatal and early postnatal period, in first-time fathers. In aid of generating hypotheses for this understudied area of research, we firstly examined prenatal-postnatal differences and correlations of various parenting modalities. We found little differences, and high correlations, over the transition to fatherhood for baseline paternal sensitivity, handgrip force in response to infant crying, and testosterone levels, suggesting that these variables might be stable over

Table 2.4. Prenatal to postnatal correlations (Pearson's *r*).

	Post midbrain	Post bi auditory cortex	Post l supraCal cortex	Post in r precentral gyrus	Post r body and splenium of CC	Post l antCorRad	Post handgrip force	Post sensitivity
Pre T baseline	-.25	.01	.11	.10	-.17	-.12	.02	.15
Pre bi PCC	-.10	-.28	-.02	.60	.45	.14	-.35	.43
Pre bi auditory cortex	.02	.05	.44	.04	-.08	.09	-.46	-.23

Note. Pre = prenatal, Post = postnatal, T = testosterone, bi = bilateral, l = left, r = right, PCC = posterior cingulate cortex, antCorRad = anterior corona radiata, CC = corpus callosum, supraCal cortex = supracalcarine cortex.

time in the perinatal period. However, the neural response to infant crying changed remarkedly from the prenatal to the postnatal period, indicating that some neural processes (e.g., those involved in visual imagery) might emerge in new fathers. Secondly, we examined concurrent correlations between the measures at both the prenatal and postnatal assessment. Whereas prenatal behavioral, hormonal, and neural measures were not highly correlated, we found that postnatal neural activation in the right precentral gyrus and the right body and splenium of the CC during infant cry perception were correlated, indicating that neural processes that emerge in new fathers might be functionally interrelated. Additionally, we found that postnatal neural activation in the right precentral gyrus during infant cry perception was strongly related to observed postnatal parenting sensitivity, possibly indicating an important role for neural reactivity in response to infant signals in the constitution of parenting quality. Lastly, we examined prenatal to postnatal correlations between different measures. We found that prenatal neural activation in the bilateral PCC was strongly related to postnatal neural activation in the right precentral gyrus while listening to infant cry sounds, possibly pointing towards a prenatal neural predictor for early postnatal parenting quality in new fathers.

For the remainder of this paper, we will discuss these findings, as well as how they can guide future studies, with a focus on the patterns in the data with large effect sizes. It should be noted, however, that large effect sizes have to be interpreted with care, as the effect size is often overestimated in underpowered studies (Curran-Everett, 2017). Therefore, the interested reader will find all findings reported in Tables 2.1-2.4. We also haste to note that some of our conjectures are unproven and speculative, as this will aid future work in establishing new areas for research where ultimately certainty about the (non) existence of these associations can be accumulated.

In addition to the findings on neural activations in response to infant crying in the prenatal period (Thijssen et al., 2018), we examined postnatal activations during infant cry exposure in the same participants. Contrary to prenatal findings, early postnatal neural activations were found to be widespread throughout the brain, similar to others' findings in new fathers in the early postnatal period (Li et al., 2018). The discrepancy between prenatal and postnatal findings supports the notion that neural activation during exposure to infant crying is dependent on parental status and/or exposure to an infant. Indeed, we found one particular brain region, the precentral gyrus, that showed activation in our sample while listening to infant crying in the postnatal assessment, and this region has previously been shown to activate more in parents than in non-parents (Witteman et al., 2019). Finding activation in the precentral gyrus in the postnatal period is in line with research in women, and may point to motion preparedness while listening to infants' distress (e.g. Bornstein et al.,

2017; Messina et al., 2016). It thus suggests a potential functional relation between neural activation and parenting behavior. In line with these studies, postnatal neural activation in the right precentral gyrus in the present study was shown to relate to early postnatal parenting sensitivity. Speculatively, this relation hints towards biological preparedness to respond appropriately to an infant's distress. Future sufficiently powered studies examining new fathers' neural and behavioral responses towards infant signals can add more insight into this process. Additionally, we found a high correlation between prenatal neural activation in the PCC and postnatal neural activation in the precentral gyrus during infant cry exposure. Future studies could investigate a potential predictive role of neural activation in the PCC prenatally for neural activation in the precentral gyrus (and behavioral sensitivity) postnatally.

Furthermore, during our postnatal measurements, but not prior to the birth of fathers' first child, we also found significant neural activation during exposure to infant crying in the calcarine cortex which has been implicated in connecting auditory and visual cortex (Beer, Plank, and Greenlee, 2011; Eckert et al., 2008), as well as supporting visual imagery (Klein, Paradis, Poline, Kosslyn, and Le Bihan, 2000). In addition, activation in this area, as well as in the midbrain, has been found to be involved in early detection of, and saccades towards, stimuli (Astafiev, Stanley, Shulman, and Corbetta, 2004) and specifically infant vocalizations (see Young et al., 2017 for a review). Likewise, another two areas anatomically supporting primary sensory processing and interhemispheric transmission thereof (i.e. anterior corona radiate and corpus callosum, respectively), were found to be activated during infant cry perception in the early postpartum in the first-time fathers in the current study. Taken together, we suggest that it would be valuable to direct future efforts towards testing the hypothesis that after the birth of their first child, new fathers use visual imagery while listening to infant crying and are more likely than expectant fathers to activate brain regions involved in involuntary motor actions such as saccades towards this salient stimulus.

Only the bilateral auditory cortex was found to be activated significantly during infant cry exposure (versus control sounds) in both prenatal and postnatal periods. Not surprisingly, this area is known to respond to cry sounds regardless of parenting status, but shows stronger activation in parents than in non-parents during cry perception (Witteman et al., 2019). We found that neural activation in the bilateral auditory cortex while listening to infant crying was not correlated between the prenatal and postnatal period, indicating that higher activation in this region to infant cry exposure prenatally might not relate to higher activation in the same anatomical structure postnatally. Noteworthy, the neural masks used for calculating the mean activation levels were based on significant activations at that particular time

point and were therefore not identical across prenatal and postnatal measurements. Therefore, it might be that the exact (sub)regions involved in the processing of infant cry sound might have changed slightly after the birth of fathers' first child. Also, this findings potentially fits recent literature indicating that reliability of fMRI measures across time is limited (see Elliott et al., 2019).

In the current study, baseline testosterone levels were not found to change from (late) prenatal to early postnatal time points in first-time fathers, although the variation between fathers seems to diminish substantially after the birth of their first child. Furthermore, testosterone levels did not show strong linear correlations with neural or behavioral measures. Although some studies investigating the behavioral effects of testosterone in fathers found an association between baseline testosterone and quality of parenting (Weisman, Zagoory-Sharon, and Feldman, 2014), others did not (Endendijk et al., 2016; Gray, Kahlenberg, Barrett, Lipson, and Ellison, 2002), or identified factors that moderate the relation between testosterone and parenting behavior (Van der Pol et al., 2019). Importantly, several studies indicating involvement of testosterone in paternal behavior and even in neural activation have emphasized the importance of testosterone reactivity rather than baseline levels (e.g. Kuo, Carp, Light, and Grewen, 2012; Van Anders, Goldey, and Kuo, 2011) as an important additional variable.

As an explorative study, our focus here lies in providing hypotheses for future neurobiological studies in (new) fathers. With regard to hormonal assessments, we would propose to add measurements of hormone reactivity after infant exposure, especially when investigating relationships with neural processes or behavior. Importantly, studies investigating relations between hormones and parental behavior have to be sufficiently powered in order to avoid the winner's curse that has plagued findings on this topic (Meijer, Van IJzendoorn, and Bakermans-Kranenburg, 2019). We may expect to see different effects on behavior or neural responses when looking at hormonal reactivity as compared to baseline levels.

Importantly, although not examined within the current sample, we would expect that not all associations between hormones and neural or behavioral measures are linear. Even though some studies have found support for the existence of non-linear relationships between various parenting-related measures (e.g. Mascaro et al., 2014), this is rarely investigated. This would be particularly interesting when examining variables such as testosterone, where both 'too much' and 'too little' could be problematic in terms of behavioral outcomes just as is the case with neural activations

(e.g. see Rilling and Young, 2014), as well as tasks such as the handgrip paradigm where both a relative minor reaction as well as an overreaction are potentially detrimental for parenting quality (Buisman et al., 2018).

Regarding neural assessments in response to infant crying, we propose that the effect of parental status should not be underestimated since we found large seemingly different patterns in neural responses to infant crying in the same participants on two different measurements with little time in between. Interestingly, while the various modalities (behavioral, hormonal, and neural) of parenting showed little correlation within the late prenatal period, concurrent relations seem to emerge after the birth of the child. In a similar vein, expectant fathers have shown adapted behavioral responses to hormone administration in comparison to childless control men, whereas they do not show differences in baseline levels of the same hormone (Cohen-Bendahan, Beijers, van Doornen, & de Weerth, 2015). This might represent a prenatal mechanisms preparing expecting men for paternal behavior while the full effect of these mechanisms does not become apparent until after birth. Additionally, we hypothesize that brain areas activated by infant distress prenatally might relate to neural activation postnatally, which in turn are related to complex social behaviors such as parenting sensitivity. Lastly, we would propose to experiment with other measures of parenting behavior, in an effort to 'break down' complex constructs such as sensitivity (e.g. irritation versus apathy towards infant crying) when examining underlying mechanisms.

This study has been conducted in a small yet unique sample, and we had the chance to explore many different associations, thus ensuring a low chance of missing interesting findings. Even so, several limitations have to be mentioned. Firstly, as we did not know what effect sizes to expect or predict and we did not rely on p-values as this study was not confirmatory (i.e., we did not pre-specify hypotheses for null hypothesis testing), we did not perform a power analysis. Importantly, due to our relatively small sample size, estimates may be overestimated. Ideally, future studies can use the patterns observed in this study to guide their hypotheses. Secondly, our prenatal measurements were implemented in the late prenatal stage. This timing of the prenatal visits might have created a representation of the prenatal situation and mental state that is more similar to the postnatal situation than to earlier prenatal time points. Future studies on the neurobiology of parenting may include appropriate controls such as pre-pregnancy couples (such as in Hoekzema et al., 2017) since the differences found here between the prenatal and postnatal stage could be related to multiple measurements rather than the birth of a child. Thirdly, confirmatory and well-powered studies will be in the position to apply high standards to the inclusion of participants, e.g., eliminate left handed participants from MRI analyses. Also,

future studies should look critically at the possible effect of repeated exposure to infant signals during data collection as was the case in this study. Lastly, the study was correlational in design and there is great need for intervention studies in (early) parenting research in order to draw conclusions on causality.

To summarize, we described data suggesting that paternal behavioral responses to infant crying, as well as baseline testosterone, are relative stable constructs, largely unaffected by the birth of the first child, and we propose that future studies test this hypothesis. Neural responses to infant signals, on the contrary, seem highly dependent on parental status and might relate to complex behavioral responses to infants in some, but not all, phases of parenthood. Also, future endeavors could test the possibility that concurrent associations between behavioral, hormonal, and neural aspects of parenting arise in the early postpartum and might change over the course of parenting.

Conclusion

In an exploratory study we found that paternal testosterone baseline levels and behavioral responses to infant crying might be stable over time in the perinatal period, but that neural response to infant crying might change remarkedly after the birth of the first child, indicating that some neural processes (e.g., those involved in visual imagery) might emerge in new fathers. Additionally, various dimensions of paternal care might become functionally related in the early postnatal period. Taken together, this first attempt at a longitudinal study in first-time fathers assessing behavioral, hormonal, and neural aspects of paternal care provides fruitful avenues for further research on this important and understudied topic.

CRediT author statement

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Chapter 3

White matter integrity moderates the relation between experienced childhood maltreatment and fathers' behavioural response to infant crying

Alyousefi-van Dijk, K., van der Knaap, N., Buisman, R.S.M., Horstman, L.I., Lotz, A.M., Riem, M.M.W., 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. https:/doi.org/10.1002/dev.22058

Abstract

The ability to provide appropriate responses to infant distress is vital to paternal care, but may be affected by fathers' experiences of childhood maltreatment. Detrimental effects of childhood maltreatment have been found in the adult brain's white matter fibers, accompanied with impaired emotional and cognitive functioning. In the current study (N = 121), we examined new and expectant fathers' childhood maltreatment experiences (i.e., emotional and physical abuse and neglect), current behavioral responses (i.e., handgrip force) to infant cry sounds, and white matter integrity using diffusion tensor imaging. Firstly, more exposure to childhood maltreatment was associated with more use of excessive handgrip force in response to infant crying by fathers. Secondly, the association between experienced childhood maltreatment and white matter integrity was not significant in whole-brain analyses. Lastly, we found that the association between maltreatment exposure and excessive handgrip force during infant crying was absent in fathers with high tract integrity in the bilateral uncinate fasciculus. These findings possibly point to insufficient behavioral inhibition or emotional dysregulation in fathers who experienced childhood maltreatment, but buffering for this effect in those with larger integrity in brain fibers connecting the amygdala and prefrontal cortex.

Introduction

Paternal care greatly impacts the development of children; higher quality of care has been found to positively affect children's social, cognitive, and linguistic development (see Lamb, 2010, for reviews). Several neural factors such as brain structure and function have been shown to play an important role for the quality of paternal care (see Feldman, Braun, and Champagne, 2019; Rogers and Bales, 2019 for reviews). In females, experiences of childhood maltreatment have been found to affect both later parenting (see Norman et al., 2012; Van IJzendoorn, Bakermans-Kranenburg, Coughlan, and Reijman, 2019) and brain structure (e.g., see Teicher, Samson, Anderson, and Ohashi, 2016 for a review).

To date, studies investigating the influence of experiences of childhood maltreatment on *paternal* brain and behavior are rare, even though their participation in childcare has substantially grown in modern western societies (Bakermans, Lotz, Alyousefi-van Dijk, and Van IJzendoorn, 2019). Moreover, parenting researchers have recently been calling for a shift in attention towards biobehavioral models of fatherhood as the underlying mechanisms of paternal care remain relatively unknown and likely developed along different evolutionary pathways than those of mothers (Bakermans-Kranenburg et al., 2019; Saxbe, 2017). In particular, studies examining responses to infant crying by fathers with varying degrees of experienced childhood maltreatment are needed because responses to infant signals are a crucial component of the parent-child relationship (Leerkes, Parade, and Gudmundson, 2011). Also, child maltreatment is still prevalent worldwide (Stoltenborgh, Bakermans-Kranenburg, Alink, and Van IJzendoorn, 2015) with emotional maltreatment being particularly prevalent in many countries (Gilbert et al., 2009; Stoltenborgh, Bakermans-Kranenburg, Alink, and Van IJzendoorn, 2012).

In the current study, we therefore examined the relation between fathers' childhood maltreatment experiences (i.e., emotional and physical abuse and neglect) and their current behavioral responses to infant cry sounds (i.e., handgrip force). Additionally, we explore if this association is mediated or moderated by fathers' brain structure (i.e., white matter integrity). Our focus lies on a particularly important but understudied area of parenting; the perinatal period, a period in which the foundation for postnatal parenting is build (e.g., Cabrera, Fagan, and Farrie, 2008; Hechler, Beijers, Riksen-Walraven, and De Weerth, 2019; Lucassen et al., 2015; Witte, Bakermans-Kranenburg, Van IJzendoorn, Szepsenwol, and Shai, 2019).

Infant crying is a highly salient stimulus aimed at motivating a caregiver to provide appropriate parental care and consequently stop the infant's distress (Soltis, 2004). However, infant crying also holds the potential for triggering child abuse and neglect because it can onset feelings of anxiety, aversion or anger in parents (e.g., Out, Bakermans-Kranenburg, Van Pelt, & Van IJzendoorn, 2012; Reijneveld et al., 2004, Soltis, 2004). Having endured childhood maltreatment in one's past has been documented to be associated with emotional dysregulation throughout later life (e.g., Dvir, Ford, Hill, and Frazier, 2014; Pears & Capaldi, 2001). In turn, emotional dysregulation is thought to be detrimental for effectively managing emotional and distressing situations (e.g., see Mikulincer and Shaver, 2008; Reijman et al., 2016 for reviews), such as soothing a crying infant. Adults who experienced more childhood maltreatment show more negative behavioral responses to child signals and respond with harsher reactions when exposed to infant crying (Buisman et al., 2018; Buisman et al., 2019).

Commonly found deficits in inhibitory and affective control in maltreated individuals (e.g., see Cowell et al., 2015; Dvir, Ford, Hill, and Frazier, 2015 for reviews) might cause these individuals to interpret infant signals as relatively negative and call upon time and energy consuming cognitive strategies to provide appropriate responses. This cognitive control may break down in cases of unconscious decision making or when under time pressure, such as is the case in responding to infant crying. Although all adults experience some level of physiological arousal when exposed to infant crying (e.g., Groh & Roisman, 2009; Out, Pieper, Bakermans-Kranenburg, and Van IJzendoorn, 2010), men tend to find infant crying particularly aversive (Zeifman, 2003). Fathers have however been included in very few studies examining possible biological mechanisms underlying the relation between childhood maltreatment and responses to infant signals (but see Buisman et al., 2018; for a meta-analytic comparisons of male versus female brain reactivity to infant crying see Witteman et al., 2019). As men now participate more in childcare and an increasing number of studies confirm their influence on child development (e.g., see Lamb, 2010), a better understanding of (biological) factors contributing to their ability to provide appropriate care is needed.

The handgrip dynamometer paradigm is used in parenting research as a behavioral marker of the ability to modulate a behavioral response (i.e., handgrip force) while being exposed to infant crying. Typically, females with insecure attachment representations (often resulting from experiencing suboptimal parenting) as well as parents at risk for perpetrating child abuse experience more hostile feelings and irritation while listening to infant crying and use more excessive handgrip force than females with secure attachment representations and parents at low-risk for perpetrating child abuse (Crouch, Skowronski, Milner, & Harris, 2008; Riem et al., 2012). Similarly, maltreating

mothers used more excessive handgrip force than non-maltreating mothers while listening to both infant crying and laughter (Compier-de Block et al., 2015). Notably, males and females with experiences of childhood maltreatment (i.e., parental neglect) were found to have more difficulty modulating handgrip force when exposed to infant crying even though they did not rate the sound more negatively (Buisman et al., 2018). Combined, these studies call for a closer look at how fathers' experiences of childhood maltreatment relate to maladaptive responses to infant signals. In particular, fathers' functioning in the peripartum is of interest as this is a formative time that poses high demands on parents' mental and physical health but is also crucial for successful adjustment to parenthood (e.g., see Saxbe, Rossin-Slater, and Goldenberg, 2018). Moreover, exposure to infant crying, and the incidence of shaken baby syndrome, is especially frequent in the early postpartum (e.g., see Barr, Trent, and Cross, 2006).

Connective white matter fibers are sensitive to adverse experiences throughout childhood and have, therefore, been a focal point in investigating the biological effects of childhood maltreatment (e.g., see Teicher et al., 2016 for a review). Since Teicher and colleagues concluded in 2016 that childhood maltreatment likely affects white matter tracts of the dorsolateral prefrontal and orbitofrontal cortex, anterior cingulate, hippocampus and corpus callosum (CC), several studies have added findings on the relation between childhood maltreatment exposure and white matter structure in young healthy individuals in particular. These studies confirmed the existence of a relation between childhood maltreatment and fibers connecting prefrontal and occipital areas in general (Ohashi et al., 2017), in the fronto-occipital fasciculi (FOF; Lim et al., 2019; McCarthy-Jones et al., 2018; Meinert et al., 2019), and in the longitudinal fasciculi specifically (LF; Lim et al., 2019; Meinert et al., 2019; Tendolkar, Mårtensson, Kühn, Klumpers, and Fernández, 2018). Findings of atypical structure in fibers connecting the orbitofrontal cortex and temporal regions (e.g., the uncinate fasciculus (UF)) were also confirmed in several studies (Ohashi et al., 2017; McCarthy-Jones et al., 2018; Meinert et al., 2019). Four recent studies confirmed structural changes in the cingulum or in fibers connecting the cingulum with other brain regions (Kim et al., 2019b; McCarthy-Jones et al., 2018; Meinert et al., 2019; Tendolkar et al., 2018), and in the CC (Jensen et al., 2018; Lim et al., 2019; McCarthy-Jones et al., 2018; Meinert et al., 2019). Only one study so far confirmed a relation between childhood maltreatment and hippocampal projections (McCarthy-Jones et al., 2018). An overview of samples, maltreatment measures, imaging parameters, tract delineation, and performed analyses in these studies has been presented in Table 3.1. In summary, consensus seems to be emerging on which white matter tracts are affected by exposure to childhood maltreatment in healthy adults. However, no studies so far have looked at possible functional outcomes related to these changes in white matter integrity that might be relevant for parenting behaviors.

Table 3.1. Overview of recent studies on associations between experienced maltreatment and white matter integrity in healthy youth and adults.

	Sample	DWI acquisition	Tract delineation	Maltreatment	Analysis
Ohashi et al., 2017[1]	262 healthy young adults	3T; 72 directions; b = 1000 s/mm^2; TE = 81 ms; TR = 6000 ms; voxel size = 1.8 mm x 1.8 mm x 3.5 mm	Tractography	Categorical analysis of Maltreatment and Abuse: Chronology of Exposure scale[2]	Graph Theory Analysis (e.g., number of fiber streams between groups)
Jensen et al., 2018[1]	393 healthy young men	3T; 30 directions; b = 1200 s/mm^2; TE = 87 ms; TR = cardiac gated; voxel size = 2.4 mm isotropic	Tractography	Continuous analysis of prenatal and early life stress via maternal report, and adolescent stressful life events via self-report	Correlational analysis between maltreatment and FA, MD, MTR and MWF in the genu and splenium, and in global (lobar) WM
Tendolkar et al., 2018	120 healthy young men	1.5T; 34 directions; b = 1000 s/mm^2; TE = 98 ms; TR = 8000 ms; voxel size = 2.5 mm isotropic	TBSS	Continuous analysis of Childhood Trauma Questionnaire[3]	Whole brain correlational analysis between maltreatment and FA and MD
McCarthy-Jones et al., 2018[1]	147 healthy middle aged adults	1.5T; 64 directions, b = 1000 s/mm^2; TE = 88 ms; TR = 8400 ms; voxel size = 2.4 mm isotropic	TBSS	Continuous and categorical analysis of Childhood Adversity Questionnaire[4]	Correlational analysis between maltreatment and FA, FAT, and FW in ROIs
Lim et al., 2019	18 maltreated youth, 18 psychiatric control youth, and 25 healthy control youth	3T; 32 directions; b = 1300 s/mm^2; TE = 104.5 ms; TR = cardic gated; voxel size = 2.4 mm isotropic	Tractography and TBSS	Continuous and categorical analysis of Childhood Trauma Questionnaire[3]	ANCOVA including streamline count, tract volume, FA, MD and RD; and whole brain correlational analysis

Meinert et al., 2019	MNC cohort: 186 depressed adults and 210 healthy control adults MACS cohort: 397 (previously) depressed adults and 462 healthy control adults	MNC cohort: 3T; 20 directions; b = 1000 s/mm^2; TE = 95 ms; TR = 9473 ms; voxel size = 1.8 mm x 1.8 mm x 3.6 mm MACS cohort: 3T; 2 x 30 directions; b = 1000 s/mm^2; TE = 90 ms; TR = 7300 ms; voxel size = 2.5 mm isotropic	TBSS	Continuous analysis of Childhood Trauma Questionnaire[3]	Whole brain correlational analysis between maltreatment and FA, MD, RD, and AD
Kim et al., 2019b	46 healthy young adults	3T; 30 directions for each b-value; b = 1000, 1500, 2000; TE = 94.2 ms; TR = 5520 ms; voxel size = 2 mm isotropic	Tractography	Continuous analysis of Verbal abuse questionnaire[5]	Partial least square regression including maltreatment and connectivity likelihood maps based on ROIs

Note. Studies listed here appeared in a systematic literature search performed on Web of Science on January 17th, 2020 using the search terms (TS=(white matter* OR DTI OR DWI OR fractional anisotropy OR diffusion tensor* OR structural integrity) AND TS=(maltreat* OR abus* OR neglect* OR early life stress) NOT TS=(visual neglect OR substance abuse)) AND LANGUAGE: (English) Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI Timespan=from 2012.

[1] These studies did not appear in the literature search but were added after a manual search of the literature.

[2] Teicher, M.H., Parigger, A., 2015. The "Maltreatment and Abuse Chronology of Exposure" (MACE) scale for the retrospective assessment of abuse and neglect during development. PLoS ONE 10, e0117423. http://dx.doi.org/10.1371/journal.pone.0117423.

[3] Teicher, M.H., Samson, J.A., Rosenman, S., & Rodgers, B. (2004). Childhood adversity in an Australian population. Social Psychiatry and Psychiatric Epidemiology, 39, 695–702. https://doi.org/10.1007/s00127-004-0802-0

[4] Bernstein DP, Fink L. *Childhood Trauma Questionnaire: a retrospective selfreport manual.* San Antonio (TX): The Psychological Corporation; 1998.

[5] Teicher, M. H., Samson, J. A., Polcari, A., and McGreenery, C. E. (2006). Sticks, stones, and hurtful words: relative effects of various forms of childhood maltreatment. Am. J. Psychiatry 163, 993–1000.

T = tesla; TE = echo time; TR = repetition time; TBSS = tract-based spatial statistics; ROI = region of interest; WM = white matter; FA = fractional anisotropy; MD = mean diffusivity; MTR = magnetization transfer ratio; MWF = myelin water fraction; RD = radial diffusivity; AD = axial diffusivity; FAT = free-water corrected fractional anisotropy; FW = free-water

A growing body of literature suggests that atypical neural structure and function resulting from received parental care underlie parenting-related responses in mothers (e.g., Kim et al., 2010; Mielke et al., 2016). This is not surprising since atypical white matter structure has been found to play an important role in cognitive and emotional difficulties as well as psychopathology among maltreatment survivors (e.g., Riem et al., 2019). Although fathers have not yet been investigated directly, atypical brain structure associated with childhood maltreatment has been found to mediate detrimental functional outcomes such as psychopathology and vulnerability to later life stress in both young males and females (Gorka, Hanson, Radtke, and Hariri, 2014; Hanson et al., 2016). Speculatively, the documented risk of intergenerational transmission of child maltreatment (e.g., see Buisman et al., 2020; Van IJzendoorn, et al., 2019) may therefore rest in part on the neurobiological consequences of child maltreatment and the cognitive and emotional dysfunction resulting from these changes in brain structure and function, potentially interfering with nurturing, timely and appropriate parental responses.

Based on the available literature, we suggest that the association between experienced maltreatment and fathers' ability to modulate handgrip force in reaction to infant crying might be mediated by the brain's white matter structure in regions commonly associated with childhood maltreatment. Alternatively, brain structure might play a moderating role leaving individuals more or less susceptible to cognitive and emotional dysfunction after experiencing maltreatment depending on their biological make-up (e.g., see McCrory, De Brito, and Viding, 2010 for a review on the moderating role of genetics on the effects of maltreatment). Moreover, in infants white matter structure has been found to moderate environmental influences on their negative emotional reactivity (Nolvi et al., 2020). Since few studies are available on a possible moderating role of white matter on behavioral outcomes relevant for parenting, we will merely explore (i.e., test without specific hypotheses) this moderation model.

Primarily, we hypothesize that higher levels of exposure to childhood maltreatment (i.e., emotional and physical abuse and neglect) is associated with more use of excessive handgrip force in response to infant crying in new and expectant fathers. Secondly, we hypothesize that white matter integrity in structures potentially affected by childhood maltreatment (the FOF, LF, UF, cingulum projections, and CC) mediates this relation. Lastly, we will explore the alternative model that white matter integrity in these structures moderates the relation between experienced childhood maltreatment and handgrip force in response to infant crying.

Methods

Participants

First-time expectant (N = 117) and new fathers (N = 136) were assessed for eligibility after reacting positively to recruitment invitations distributed via midwives, municipal records, infant welfare centers, and (online) advertisements. Fathers had to cohabitate with their partners who also did not have any previous children, speak Dutch, and were screened and excluded for MRI contraindications (e.g., metallic foreign objects, claustrophobia). Also, fathers were screened and excluded for current endocrine, psychiatric, or neurological disease, current or past serious head injury, use of soft drugs (e.g., cannabis) on a regular basis or hard drugs (e.g., cocaine, heroin) more than once within 3 months prior to participation, current heavy smoking or drinking, and use of (psychotropic) medication potentially interfering with neural measurements. Additionally, expectant fathers had to meet several other requirements due to an intervention taking place after the measurements reported here. Partners had to have an uncomplicated pregnancy of a singleton with a pregnancy duration of 18-31 weeks at the time of inclusion. Expectant fathers were excluded when their partners used alcohol, tobacco, or illicit drugs during the pregnancy or had a BMI over 30 before pregnancy. Additionally, participants were excluded when abnormalities were found during the medical 20-week ultrasound examination, or in case of known birth defects in the families of either parent that caused excessive worry for the current pregnancy. For new fathers, the infants had to be full-term (i.e., born after 37 week gestation), healthy, and around two to four months of age at time of inclusion. Additionally, new fathers were excluded if they used a baby carrier more than 5 hours a week due to an intervention taking place after the measurements reported here. One infant was born at 36 weeks and 6 days, but was considered healthy and therefore included. One father was not the biological father of the infant, but he had been cohabitating with the mother since mid-pregnancy. Three participants reported a past diagnosis of depression, and one participant reported a diagnosis of a past anxiety disorder. All diagnoses occurred between 2 and 10 years before inclusion into the study. They did not have a current psychiatric diagnosis and did not currently use psychotropic medications and were therefore included in the analyses here.

As a result, 121 first-time fathers with diffusion tensor imaging (DTI) data available were included into the analyses reported here, see Supplementary Materials Figure 3.1 for a flow chart. Of these 121 participants, handgrip data were missing for three participants due to time constraints during the lab session or technical difficulties, and information based on questionnaires was missing for five participants. Independent t-tests indicated that new and expectant fathers did not differ in age, but there was a difference in the years of education following primary education;

new fathers studied fewer years (M = 8.29, SD = 1.90) than expectant fathers (M = 8.98, SD = 1.30; t(108.27) = 2.37, p = .02). Kolmogorov-Smirnov test indicated that the education scores were not normally distributed (p = .00) and the distribution was skewed (i.e., skewness = 5.81). A chi-square test indicated that country of birth (i.e., the Netherlands or other) did not differ between new and expectant fathers. See Table 3.2 for more sample characteristics.

Participants received financial compensation for each lab visit; €25 (plus travel allowance) for the visit described here. Participants received an extra €10 after the completion of the study if they completed at least 80% of the questionnaires. 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 informed consent.

Table 3.2. Demographic information of the sample.

		M(SD)/N(%)	**Range**
Participant age (years, N = 121)		33.03(4.09)	25-50
Education (years past primary education, n = 120)		8.62(1.67)	3-10
Country of birth (n = 120)			
	The Netherlands	114(95%)	
	Other	6(5%)	
Handedness (N = 121)			
	Right	107(88%)	
	Left	12(10%)	
	Ambidexter	2(2%)	
Infant or fetal age (weeks)			
	Gestational age (n = 57)	24.99(2.77)	20-31
	Infant age (n = 64)	11.24(3.03)	7-21
Fetal sex(n = 57)			
	Male	18(32%)	
	Female	28(49%)	
	Unknown	11(19%)	
Infant sex(n = 64)			
	Male	35(55%)	
	Female	29(45%)	

Note. Information on education and country of birth is missing for one participant as he dropped out of study between the lab session and filling out online questionnaires.

Procedure

Participation in the study started with the visit to the lab described here. Participants were instructed to abstain from alcohol and excessive physical activity during the 24h before the visit, and from caffeine on the day of the visit. The visit started with instructions about the visit, after which saliva collection (for hormone measurements) took place. Next, participants took care of an infant simulator or their own infant for 10 min for the observation of their parenting behavior, during which the doll was programmed to cry uncontrollably for five min. This was followed by another saliva sample collection, after which participants underwent a brief training of the upcoming functional magnetic resonance imaging (fMRI) tasks on a laptop, which familiarized them with the tasks. A resting-state scan, and a fMRI paradigm (using cry stimuli), as well as a fMRI task using video vignettes preceded the DTI scan described here. The neural measurements were followed by the handgrip cry paradigm. In the week following the visits, participants completed an online questionnaire. This questionnaire included basic demographics, the Love Withdrawal subscale of the Children's Report of Parental Behavior Inventory (CRPBI, Schludermann and Schludermann, 1983; Beyers and Goossens, 2003), the Conflict Tactics Scale – Parent Child (CTS; Strauss et al., 1998), and the Edinburgh Postnatal Depression Scale (EPDS; Cox, Holden & Sagovsky, 1987).

Measures

Neural assessment – DTI

Data acquisition. DTI data were collected on a Philips 3.0 T Achieva MRI scanner (Philips Medical Systems, Best, The Netherlands) using a multi-band single-shot echo-planar imaging sequence and an eight-channel SENSE (Sensitivity Encoding) head coil. The following scan parameters were used: repetition time = 2777 ms, echo time = 98 ms, flip angle = 90°, b-value = 2000 s/mm2, voxel dimensions = 2 mm isotropic, number of slices = 57, and no slice gap. DTI data were acquired along 80 directions, together with nine images having no diffusion weighting (b=0), scanned in posterior-anterior direction. One additional reversed b=0 scan was made in anterior-posterior direction. The total scanning time was 4.47 min.

Data preprocessing. The Oxford Centre for Functional MRI of the Brain software library (FMRIB's Software Library version 6.0; Smith et al., 2004) was used to preprocess and analyze DTI data. First, *topup* was run because data were collected with reversed phase-encode blips, resulting in pairs of images with distortions going in opposite directions. From these pairs the susceptibility-induced off-resonance field was estimated using a method similar to that described in Andersson, Skare, and Ashburner (2003). In order to run *topup*, the number of slices was reduced to 56 by removing the most inferior slice. Next, *topup* combined two images (i.e., the first b=0

volume from the DWI dataset and the reversed b=0 scan) into a single file which was used to estimate the susceptibility field. Then, all non-brain material was extracted using *BET* (Brain Extraction Tool, Smith, 2002). Second, diffusion data were corrected for eddy current-induced distortions and subject movements using *eddy* (Andersson and Sotiropoulos, 2016). Outliers were replaced within eddy using the *repol* option (Andersson, Graham, Zsoldos, and Sotiropoulos, 2016). We visually examined corrected diffusion images, and also obtained quantitative metrics relating to image quality using FSL's *QUAD* (QUality).

Assessment for DMRI) and *SQUAD* (Study-wise QUality Assessment for DMRI) tools (Bastiani et al., 2019). Third, fractional anisotropy (FA) images were created by fitting a tensor model to the raw diffusion data using *dtifit* from the FMRIB's Diffusion Toolbox. From these maps, FA was calculated. Fourth, to reduce partial volume effects and registration misalignments, *TBSS* (Tract-Based Spatial Statistics; Smith et al., 2006) was used. All subjects' FA data were aligned into a 1x1x1 mm standard space (i.e., FMRIB58_ FA template) using the nonlinear registration tool *FNIRT* (Andersson, Jenkinson, and Smith, 2007; Smith et al., 2004), which uses a b-spline representation of the registration warp field (Rueckert et al., 1999). Next, the mean FA images were created and thinned to create a mean FA skeleton which represents the centers of all tracts common to the group. After visual inspection of our data, we set a threshold of 0.3 for the average of all aligned FA images in order to reduce inter-subject variability when creating a white matter skeleton. Each subject's aligned FA data were then projected onto this skeleton and the resulting data fed into voxelwise cross-subject statistics. Additionally, mean diffusivity (MD) images were also created and fed into TBSS.

DTI data analysis. To test for statistically significant associations between maltreatment scores and FA or MD values, we employed nonparametric permutation testing using maltreatment scores as a covariate. Voxelwise permutation based analyses (Winkler, Ridgway, Webster, Smith, and Nichols, 2014) were performed using *randomise* with 5,000 permutations. Images were corrected for multiple comparisons using *TFCE* (Threshold-Free Cluster Enhancement; Smith and Nichols, 2009), and significance was determined by using the 95th percentile of the null distribution of permutated input data of the maximum *TFCE* scores, allowing to correct estimated cluster sizes for family-wise error. For the mediation analysis, individual FA and MD values for any significant clusters were extracted using *cluster* and *fslmaths* functions. For the moderation analysis, anatomical skeletonized masked were created using *fslmaths* and the JHU White-Matter Tractography Atlas (Hua et al., 2008; Mori, Wakana, Van Zijl, and Nagae-Poetscher, 2005; Wakana et al., 2007) for the CC (including the genu, body, and splenium; label numbers 3-5), bilateral cingulum (including both the gyrus and hippocampal projections, label numbers 35-38), bilateral sagittal stratum (including

the inferior LF and inferior FOF, label numbers 31-32), bilateral superior FOF (label numbers 43-44), bilateral superior LF (label numbers 41-42), and bilateral UF (label numbers 45-46). Individual FA values were then extracted using *fslmeants* and used in further analyses. Visual inspection indicated that all ROIs contained voxels that survived the FA threshold. All extracted variables were normally distributed.

Behavioral assessment – handgrip paradigm

Procedure. Participants were exposed to infant crying and images representing either their own or an unknown infant while they were asked to squeeze a handgrip dynamometer. During the task, participants were seated in front of a computer screen wearing headphones while holding a dynamometer in their dominant hand. During an initial training period without cry sounds or images, participants were asked to alternate between squeezing the handgrip dynamometer at full and half strength while they received visual feedback from a monitor indicating the strength they used. Once participants could accurately alternate between full and half strength (half strength being 50% of the strength used at full strength), the monitor was turned away and the actual task began without feedback on performance.

Task images. In order to create suitable own infant images for this task, new fathers either provided a full-color digital photo of their infant's face with a neutral expression prior to the visit, or a picture was taken at the beginning of the visit. New fathers' own infant images were overlain with a black face contour mask using Adobe Photoshop CS removing all background features and resized to 640 × 480 pixels. Expectant fathers either provided a full-color digital photograph of themselves prior to the first visit, or a picture was taken at the beginning of the visit. The expectant participant's picture met the following criteria: it showed their face, en face, with a neutral expression, a light and neutral background, without piercings, make-up, or glasses. Expectant fathers' photographs were edited using Adobe Photoshop CS in order to remove unwanted facial features (e.g., facial hair). Subsequently, morphed images representing participant's own infant were created by combining 75% of an average infant image (created by the authors of Hahn, DeBruine, Fischer, & Jones, 2015, from 10 female and 10 male infant faces) and 25% of participant's own picture, using Fantamorph 5 Deluxe (www.fantamorph.com). These morphed images based on their own picture were overlain with a black face contour mask removing all background features and resized to 640 × 480 pixels. Participants were familiarized with their edited own infant image (i.e., picture of their own infant for new fathers and morphed images based on their own picture for expectant fathers) before onset of the task. Additionally, expectant fathers were told that a future infant of theirs might look similar to this image. In order to create suitable 'unknown infant' images the same protocol was used. This resulted in a masked and resized picture of a real but

unknown infant used for new fathers, and a masked and resized morphed image of an infant for expectant fathers (i.e., 75% of the average infant image morphed with 25% of a male unknown to the participants). The decision to include images of 'own' and 'unknown' infants was based on the idea in evolutionary psychology that perceived genetic relationships influence paternal behavior, with closer genetic relationships supposedly enhancing paternal investment. This is considered particularly relevant in assessing the effects of threat to infant (see Van 't Veer et al., 2019) and the effects of vasopressin on handgrip force (see Alyousefi-van Dijk et al., 2019). The distinction between own and unknown infants was expected to be nonrelevant for the analyses reported here.

Task sounds. In order to create suitable sounds for this task, a total of six cry sounds were recorded from 6 infants (3 males, 3 females), using a TasCam DR-05 solid state recorder with at a 44.1 kHz sampling rate and 16 bit. All sounds were recorded between 2 days and 5,5 months postnatally. All cry sounds were scaled, the intensity is normalized to the same mean intensity (74 Db) and sounds are edited to last for 10 seconds using PRAAT software (version 6.0.37; Boersma and Weenink, 2017). For each cry sound, a neutral auditory control stimulus was created by calculating the average spectral density over the entire duration of the original sound. A continuous sound of equal duration was re-synthesized from the average spectral density and amplitude modulated by the amplitude envelope, extracted from the original sound. After this procedure, all auditory stimuli and control stimuli were intensity matched. The neutral auditory control stimuli were identical to the original auditory stimuli in terms of duration, intensity, spectral content, and amplitude envelope.

Task design. The procedure used here was identical to that used in a similar (but not the same) sample (Alyousefi-van Dijk et al., 2019; see also Alyousefi et al., 2020). The task was administered using E-Prime software (version 2.0; Psychology Software Tools, Inc., PA, USA). Squeeze intensities (in kg) were transferred directly from the dynamometer to AcqKnowledge software (version 4.3.1; Biopac Systems, 2004). First, a baseline measure of three maximum strength trials, each followed by half strength trials, was administered. Then, four conditions of three max-half trials were presented in semi-random order; 1) viewing an image of own infant while hearing control (scrambled) sounds (Own Neutral); 2) viewing an image of own infant while hearing cry sounds (Own Cry); 3) viewing an image of an unknown infant while hearing control (scrambled) sounds (Other Neutral); 4) viewing an image of an unknown infant while hearing cry sounds (Other Cry). Sounds and images were presented throughout each trial lasting 12 seconds. Eight seconds after the beginning of each trial, participants were prompted to squeeze maximally (instructions displayed for 1s). After an interval of 2s, participants were prompted to squeeze at half strength (instructions were displayed for 1s). A fixation cross was shown for 3s between each trial.

Scoring. Similar to previous studies (e.g., Alyousefi-van Dijk et al., 2019; Bakermans-Kranenburg et al., 2012; Compier-de Block et al., 2015; Riem et al., 2012), grip strength modulation was calculated by dividing half-strength squeeze intensity by the preceding full-strength squeeze intensity, meaning that scores of over .50 indicated excessive force on the half-strength squeeze attempt. MATLAB (version 8.0.0.783; Mathworks, MA, USA) was used to identify peak intensities for each squeeze. Trials believed to represent measurement errors (i.e., ratios <0 or >2) were disregarded. Handgrip force measures were found to be reliable for the four conditions (α_{range} = .75-.83). Therefore, the three trials per condition were averaged as indicators of handgrip force in each condition. Since the distinction between own and unknown infants was not relevant for the analyses described here, and the conditions with own or unknown images showed high correlations (r = .72 for neutral sounds and r = .79 for cry sounds), the own and unknown infant trials were taken together. Mean handgrip force ratios (n = 118) were roughly around the intended .5 for both the control (M = .59, SD = .14, range .22-.95) and the infant cry sounds (M = .58, SD = .14, range .23-.96). In order to create one value representing the cry-control sound contrast, a residualized score was calculated by residualizing the squeeze during cry trials for the squeeze during control trials (identical to Alyousefi-van Dijk et al, 2020). Residualized scores were created in order to avoid issues associated with difference scores (MacKinnon, 2012).

One outlier (i.e., Z score > 3.29) was detected in the residualized scores, and this value was winsorized by adding the difference between the second and third largest values to the second largest value, and replacing the outlier with this new value. Residualized scores were found to be distributed normally, and did not differ between new and expectant fathers ($t(116) = 1.31$, p = .19).

Self-reported child maltreatment

Identical to the procedure in a similar (but not the same) sample (Thijssen et al., 2018), participants completed seven items from the Withdrawal of Relations subscale of the Children's Report of Parental Behavior Inventory (CRPBI, Beyers and Goossens, 2003; Schludermann and Schludermann, 1983) of which two items were slightly adapted for a smoother translation. To obtain a more comprehensive measurement of parental love-withdrawal and emotional maltreatment, the questionnaire was complemented with four items from the Parental Discipline Questionnaire (Patrick and Gibbs, 2007, see Huffmeijer et al., 2011 for the resulting scale). The resulting scale contained 11 items such as "My mother/father is a person who, when I disappoint her/him, tells me how sad I make her/him". Participants rated how well each of the statements described their mother's and father's behavior separately on a 5-point scale ranging from 1 = 'not at all' to 5 = 'very well'. Two participants reported that one parent had not been present throughout their childhood and scores for this particular parent

where therefore not taken into account. A mean parental love-withdrawal score was computed by averaging the highest scores per item, being either that reported about the participant's father or mother. Scores per item were roughly 50% of the times highest for father and for mother, except for item 7 (i.e., "When I disappointed my parent he/she told me how sad I made him/her"), where the score for mother was more often the highest. Additionally, participants completed the Conflict Tactics Scale – Parent Child (CTS, Straus et al., 1998). We used items from the subscales Psychological aggression, Minor physical assault, Severe physical assault, and Neglect, resulting in a total of 18 items. Items were answered on a 7-point scale (0 ='never', 1 = 'once', 2 = 'twice', 3 = '3–5 times', 4 = '6–10 times', 5 = '11–20 times', 6 = 'more than 20 times'). Averaging scores on the minor and severe physical assault scales resulted in a Physical assault score, which combined with the scores on Psychological aggression formed an Abuse score. An overall CTS score was computed by averaging the Abuse and Neglect scales. Both maltreatment questionnaires were found to be reliable (α = .85 for CTS and α = .90 for CRPBI). Average maltreatment scores (n = 116) were 0.75 (SD = 0.75) for the CTS and 2.02 (SD = 0.78) for the CRPBI, $range_{CTS}$ = 0-3.48 and $range_{CRPBI}$ = 1-4.18. Additionally, we found good reliability for the combined CTS and CRPBI item scores (α = .89), and therefore combined the standardized total scores of both questionnaires into one average maltreatment score, which was used in all further analyses.

A Kolmogorov-Smirnov test indicated that the combined standardized maltreatment average was somewhat skewed (i.e., skewness = 5.47). Data were not transformed as maltreatment scores were the predictor in our model. Average maltreatment scores did not differ between new and expectant fathers ($t(114) = .51$, $p = .61$).

Self-reported perinatal depression

Participants filled out all 10 items of the Postnatal Depression Scale (EPDS; Cox, Holden & Sagovsky, 1987), where a total score represents the sum of all symptoms present. The EPDS is a self-report screening tool, devised to detect mild perinatal depression in the community. Previously, the EPDS has been shown to be suitable for the assessment of depression in the prenatal period (e.g., see Cox, Holden, and Henshaw, 2014) and in fathers (e.g., Edmondson, Psychogiou, Vlachos, Netsi, and Ramchandani, 2010). The clinically relevant cut-off for EPDS scores in fathers is currently under debate, but it is believed to be lower than that for mothers, typically between 7 and 10 (e.g., Edmonson et al., 2010) but possibly even lower (Matthey, Barnett, Kavanagh, and Howie, 2001). The EPDS questionnaire was found to be reliable in the sample described here (α = .74).

A Kolmogorov-Smirnov test indicated that the total EPDS score was somewhat skewed (skewness = 4.68). Data were not transformed as perinatal depression scores were a covariate in our model. Average EPDS scores (n = 116) were low (M = 4.55, SD = 0.28, range 1-14). Perinatal depression scores did not differ between new and expectant fathers ($t(114) = 1.32$, $p = .19$).

Imputation

After obtaining descriptive results for all variables, multiple imputation was applied. The majority of missing values were the results of participants not filling out the questionnaires, resulting in 4% of cases missing for experienced maltreatment and perinatal depression scores. Additionally, handgrip data was missing for three participants (3%). Educational score was missing for one participant (1%). Age, and FA and MD values in all ROIs were available for all participants. Missing values were imputed using multiple imputation where these values were estimated several times, resulting in several complete datasets. Missing values were imputed using the package *mice* (Van Buuren & Groothuis-Oudshoorn, 2011) in R (R Development Core Team, 2008). Specifically, *mice* imputes multivariate data by means of chained equations. In all further statistical analyses, all imputed datasets (i.e., 50) are analyzed, and the results are then combined using specific combination procedures based upon variability in the standard errors and p-values of the imputed datasets. Predictive mean matching (Little, 1988) was used to guarantee that imputed values do not fall outside the range of the variable or outside the observed values of the variable. One hundred iterations were run. Autocorrelation function plots (Azur, Stuart, Frangakis & Leaf, 2011) were visually inspected and indicated that all imputations converged. Little's MCAR test was not significant ($X^2(26) = 19.09$, $p = .83$), indicating that data was missing completely at random. Importantly, bivariate correlations between all variables were approximately the same in the imputed dataset (see Table 3.3) and in the non-imputed dataset (see Supplementary Material Table 3.1). Further analyses were conducted in SPSS version 25.

Statistical analyses

A mediation analysis was run on the imputed dataset in order to test individual FA or MD values in any significant clusters (i.e., clusters significantly associated with experienced maltreatment scores in whole brain analyses) as mediators for an association between experienced maltreatment scores and handgrip force during infant crying. Next, an exploratory moderation analysis was run on the imputed dataset in order to test moderation by individual FA values for the anatomical structures mentioned in the hypotheses on an association between experienced maltreatment and handgrip force. Perinatal depression, age, and education levels were used as covariates.

Table 3.3. Correlations of the pooled observed variables in the imputed dataset (N = 121). Pearson's correlations (r) are reported.

	Age	Edu	EPDS	Maltr	HG	CC	Bi cingulum	Bi inf FOF LF	Bi sup FOF	Bi sup LF	Bi UF
Age		-0.04	-0.07	0.08	-0.05	-0.08	0.02	-0.06	-0.14	-0.19*	0.01
Edu			0.02	-0.17	0.16	-0.04	0.01	-0.02	0.00	-0.09	-0.07
EPDS				0.15	0.00	0.09	0.08	0.05	0.02	0.07	-0.12
Maltr					0.22*	0.04	0.00	0.12	-0.04	-0.10	0.01
HG						-0.05	0.02	-0.01	-0.07	0.08	0.00
CC							0.64**	0.57**	0.48**	0.57**	0.43**
Bi cingulum								0.52**	0.38**	0.49**	0.40**
Bi inf FOF LF									0.41**	0.45**	0.36**
Bi sup FOF										0.43**	0.26**
Bi sup LF											0.38**
Bi UF											

Note. Edu = educational level, EPDS = Edinburgh Postnatal Depression Scale, Maltr = experienced childhood maltreatment, HG = residualized handgrip force ratio, CC = corpus callosum, Bi = bilateral, inf = inferior, FOF = fronto-occipital fasciculus, LF = longitudinal fasciculus, sup = superior UF = uncinate fasciculus, * = p<0.05 (2-tailed), ** = p<0.01 (2-tailed)

Results

Association between childhood maltreatment and handgrip force

Childhood maltreatment scores showed a significant positive correlation with handgrip force in response to infant crying (i.e., r (119) = .22, p = .02; see Table 3.3), indicating that higher levels of maltreatment were related to more use of excessive force during infant crying in new and expectant fathers.

Association between childhood maltreatment and white matter integrity

No white matter clusters were found to relate significantly to childhood maltreatment scores in whole brain analyses (i.e., p > .05 corrected) for either FA or MD, thus no mediation analysis was run. Likewise, there were no significant correlations between extracted FA values in the regions of interest (ROI) and experienced maltreatment, see Table 3.3.

Moderation effects of white matter integrity

Individual mean skeletonized FA values structurally defined by the JHU White-Matter Tractography Atlas were extracted (N = 121) for the CC (M = .65, SD = .00), bilateral cingulum (including both the gyrus and hippocampal projections; M = .50, SD = .00),

bilateral sagittal stratum (including the inferior LF and inferior FOF; *M* = .51, *SD* = .00), bilateral superior FOF (*M* = .47, *SD* = .00), bilateral superior LF (*M* = .51, *SD* = .00), and bilateral UF (*M* = .46, *SD* = .00). The association between maltreatment and handgrip force was moderated by FA values in the bilateral UF, *B* = -8.11, *SE* = 3.02, 95% confidence interval = [-14.02, -2.19], *t*(114) = -2.69, *p* = .01. A closer look at this interaction effect revealed that participants with low FA values in the bilateral UF (based on a median split at 0.0009) showed a significant positive association between experienced child maltreatment and handgrip force (*B* = .52, *SE* = .15, 95% CI [.22, .82], *t*(56) = 3.41, *p* < .01), whereas no significant association was found between experienced child maltreatment and handgrip force for participants with high FA values in this structure (*B* = .09, *SE* = .16, 95% CI [-.22, .40], *t*(55) = 0.57, *p* = .57.), see Figure 3.1.

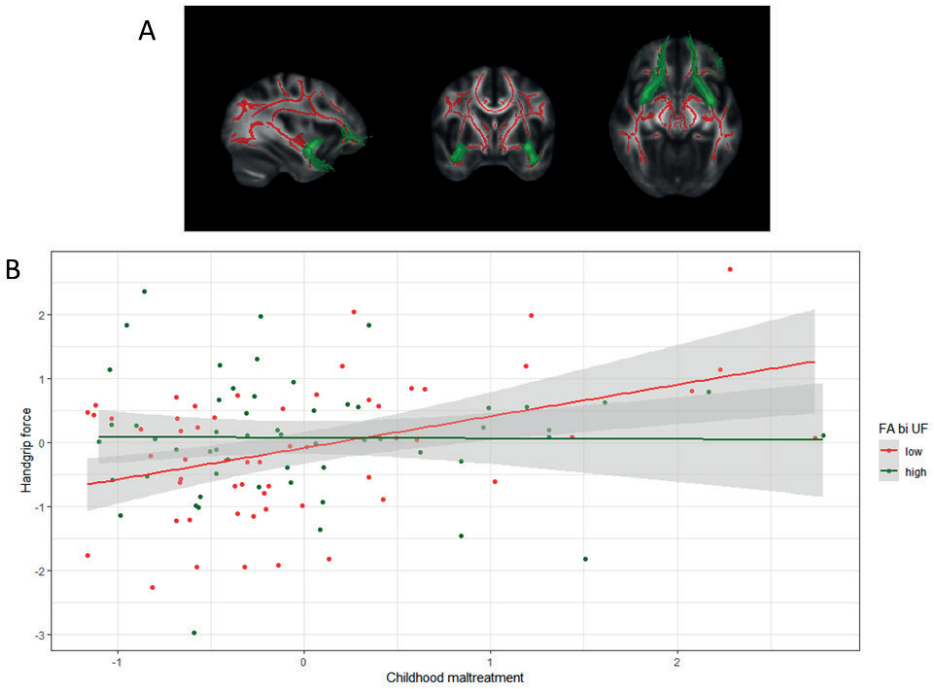

Figure 3.1. Mean skeletonized FA in the bilateral uncinate fasciculus (bi UF) moderates the association between experienced childhood maltreatment and handgrip force ratios in response to infant crying. A) Skeletonized FA values are depicted in red, with an anatomical mask (JHU White-Matter Tractography Atlas) for the bilateral UF depicted in green. B) A significant two-way interaction was observed such that the mean FA value in the bilateral UF moderated the association of experienced childhood maltreatment and handgrip force in response to infant crying. The significant predictive value of maltreatment on handgrip force was only present for those individuals with low (*N* = 58; depicted in red) rather than high (*N* = 56; depicted in green) FA levels in the UF. Visualization is based on the complete cases.

No significant moderation effects were found for the CC, bilateral cingulum, bilateral sagittal stratum, bilateral superior FOF, or bilateral superior LF. Findings of the moderation analyses were comparable with and without multiple imputation (see Supplemental Materials Table 3.2). Also, results were comparable in new and expectant fathers (i.e., confidence intervals in both groups overlapped with the overall results), see Supplemental Materials Tables 3.3 and 3.4.

Discussion

In this study, we investigated the relation between childhood maltreatment experiences, handgrip force in reaction to infant crying, and white matter tract integrity in new and expectant fathers. As expected, we found that childhood maltreatment experiences were related to paternal behavioral responses; fathers with higher levels of experienced maltreatment used more excessive handgrip force while listening to infant crying. No significant relation was found between reported maltreatment and white matter integrity in the whole brain analysis. Therefore, white matter integrity did not mediate the relation between maltreatment and handgrip force. However, this relation was moderated by white matter integrity in the bilateral UF, such that childhood maltreatment experiences were only predictive of handgrip force during infant cry exposure in fathers with low levels of white matter integrity in the bilateral UF.

In line with earlier findings in mothers and fathers (Buisman et al., 2018), we found that fathers' experiences of childhood maltreatment were predictive of using more handgrip force during infant cry exposure. Speculatively, this finding might indicate that maltreated fathers experience more aversion and anxiety when presented with negative infant signals (e.g., Out, Pieper, Bakermans-Kranenburg, Zeskind, and Van IJzendoorn, 2010), and are therefore more likely to respond harshly. Emotional dysregulation or deficient inhibitory control may underlie this phenomenon. Indeed, childhood maltreatment is known to be related to an attentional bias towards negative or threatening stimuli in both childhood and adulthood, possible serving as an adaptive mechanism preparing the individual for frequent exposure to threatening situations (e.g., Gibb, Schofield, and Coles, 2009). Also, neural hyperactivation in regions involved in threat-detection in response to various emotional facial expressions (e.g., Van Harmelen et al., 2013) points to a mechanism of interpreting emotional expressions as highly salient and potentially dangerous in maltreated individuals (see also Oosterman, Schuengel, Forrer, and De Moor, 2019; Pollak, Cicchetti, Hornung, and Reed, 2000).

Parenting research supports this idea as mothers exposed to childhood sexual and/or physical abuse have been found to provide lower quality of care with their own child, and this parental quality has been found to relate to the anatomy of brain structures known to underlie cognitive (and not emotional) empathy (e.g., Mielke et al., 2016). Specifically, when given the instruction to inhibit prepotent motor responses, maltreated individuals show larger reaction times despite increased brain activation in areas responsible for inhibitory and response control, as compared to individuals who were not exposed to early life adversity (Mueller et al., 2010; Navalta et al., 2006). Childhood maltreatment has been found to impact on the effective connectivity of the neural inhibitory control network during a task in which prepotent motor responses had to be inhibited (Elton et al., 2014). Taken together, it is plausible that fathers with higher levels of experienced childhood maltreatment in our sample struggled to modulate handgrip force in response to infant crying because the stimulus was processed as particularly aversive and inhibitory control over their behavioral response was inadequate.

Contrary to our expectations, we did not find a direct relation between fathers' childhood maltreatment experiences and white matter integrity in a whole-brain approach. Previously, several studies examining continuous measures of maltreatment exposure (i.e. graduation of severity) in similar populations of healthy young adults have reported wide-spread associations between maltreatment and white matter integrity (e.g., Hanson et al., 2015; Jensen et al., 2018; Kim et al., 2019b; McCarthy-Jones et al., 2018; Ohashi et al., 2017; Tendolkar et al., 2018) and several of these studies looked at similar types and levels of abuse and neglect as in the study reported here (e.g., Hanson et al., 2015; McCarthy-Jones et al., 2018; Tendolkar et al., 2018). However, most of these studies only reported associations between maltreatment and specific ROIs. Notably, we also did not find correlations between self-reported childhood maltreatment and commonly reported ROIs, indicating that the absence of findings in our whole brain analysis is probably not merely due to stringent corrections for multiple testing in this analysis. Only one other study reported whole-brain white matter integrity in a similar sample size of healthy young men (N = 114), and no significant clusters were found when testing for an association with overall maltreatment severity (Tendolkar et al., 2018), although a significant reduction in white matter integrity for several areas (including the UF) was found when looking at physical neglect rather than a combined maltreatment score. Additionally, a recent large study examining whole-brain white matter integrity in adult participants with or without major depressive disorder (N = 396) found several clusters to be significantly associated with maltreatment scores (i.e., emotional and physical neglect and abuse, as well as sexual abuse), irrespective of psychiatric diagnosis (Meinert et al., 2019). These authors concluded that the exact type of abuse is probably irrelevant

and that an 'overall contribution of early negative life events' seems to underlie these effects. Taken together, these findings raise an important question. Why do sufficiently powered studies such as Tendolkar et al., 2018 and the current study find no significant association between DTI measures and overall maltreatment scores in whole-brain analyses such as in Meinert et al., 2019? Considering our sample size of $N = 116$, we were sufficiently powered (power .97) to detect the effect size reported by Meinert and colleagues (i.e., $\beta = -0.343$, CI -.428, -.252). More studies using unbiased whole-brain approaches investigating an association between maltreatment severity and white matter integrity are warranted as the current consensus in literature seems to be based upon ROI studies while outcomes have not yet been reproduced within whole brain studies (see also Hart and Rubia, 2012 for a review). Possibly, a robust effect of aberrant white matter integrity associated with maltreatment exposure in whole-brain analyses can only be found when comparing maltreated and non-maltreated groups (see Lim, Howells, Radua, and Rubia, in press for a meta-analysis).

Exploratively, we found that white matter integrity of the UF moderated the association between experienced maltreatment and fathers' modulation of handgrip force during infant cry exposure, where the association between maltreatment and handgrip force was absent in fathers with higher tract integrity in the UF. Interestingly, the UF is known to support adequate inhibitory regulation of emotional reactivity or motor responses that depend on effective communication between the frontal and temporal structures (i.e., prefrontal cortex and amygdala; Depue, Orr, Smolker, Naaz, and Banich, 2016; Versace et al., 2015). As such, the UF plays an important role in 'valence-based biasing of decisions' and in the incorporation of reward and punishment history into memory dependent processes (Von der Heide et al., 2013). Likewise, higher structural integrity of the UF has previously been shown to protect against the well-documented relation between childhood maltreatment and later anxiety and stress resilience (Kim et al., 2019a). Additionally, activity and connectivity of the prefrontal cortex has recently been found to be an important differential susceptibility marker for the effects of environmental influences on child development (Crone et al., 2020). Although further studies are needed to replicate and elaborate on this finding, we speculate that part of the dysfunctional effect of maltreatment on later parenting is dependent on structural integrity of the UF which is needed to effectively downregulate emotional hyperreactivity as well as support adequate inhibitory control over behavioral responses, particularly in reaction to negative stimuli. Hypothetically, maltreated fathers with high tract integrity in the UF might be protected against effects of childhood maltreatment on emotional hyperreactivity and impaired behavioral inhibition. If so, tract integrity in the uncinate fasciculus might be one of the underlying factors contributing to resilience in the intergenerational transmission of maltreatment.

Several limitations of the current study should be noted. First, the field of neurobiological aspects of paternal care is relatively unexplored territory and replication studies and meta-analyses will be highly valuable in approximating valid conclusions. Although the current study was relatively well-powered, more studies are needed to uncover the mechanisms and contributing elements of paternal care. Specifically, the moderation effect reported here was part of an exploratory analysis and therefore not corrected for multiple testing. Future studies could use these findings as hypotheses. Also, as our design was cross-sectional, any conclusion about the origins of the relation between maltreatment history and later parenting remain speculative. Although there is a large body of literature supporting the mechanism proposed here, it should be noted that other explanations for our findings (e.g., genetic factors contributing to both maltreatment and excessive force in the handgrip task) cannot be not ruled out. Secondly, there is little agreement between prospective and retrospective reports of maltreatment (Baldwin, Reuben, Newbury, and Danese, 2019). However, prospective measures (e.g., official CPS reports) are assumed to capture only the top of the proverbial iceberg, whereas retrospective measures (i.e., self-reported child maltreatment) have been suggested to capture a broader range of maltreatment experiences (e.g., Baldwin et al., 2019; Smith, Ireland, Thornberry, and Elwyn, 2008). Additionally, some (e.g., Buisman et al., 2019), but not others (e.g., Meinert et al., 2019), have found that a distinction between maltreatment subtypes is important for the neurobehavioral sequelae. Shedding more light on this issue was outside the scope of this study, and the measures used were not equipped to provide reliable subscales of common maltreatment types. However, the potentially differential effects of various types of maltreatment in fathers should be explored in future studies. Thirdly, in our moderation analyses we used averaged values of the most commonly used indicator of white matter integrity (i.e., FA). Previous studies have provided indications that various white matter indicators relate differently to maltreatment history (e.g., Jensen et al., 2018; McCarthy-Jones et al., 2018) and this should be studied further. Also, averaging skeletonized FA values within a (relatively) large ROI may have increased the chance of missing associations, leading to false negatives. Future studies looking into these associations could explore different methods, for example using small volume correction. Forth, our sample of relatively highly educated and low-risk fathers is not representative of the general population. Socioeconomic status may be related to maltreatment history and parenting, or may moderate associations between maltreatment history and parenting. Studies including more diverse samples could investigate this. Fifth, we did not include real-life parenting measures such as parenting sensitivity or involvement. Therefore, our speculations about the impact of the maltreatment-related effects on handgrip force on paternal care are not tested directly in the same sample, even though the handgrip paradigm is a highly standardized and well controlled measure of reactions to infant

signals. Ideally, future studies combine lower level mechanistic measures (e.g., brain structure and function, hormonal levels and reactivity, physiological responses) with parent-child observations, or include other measures more closely related to parenting quality and the effects thereof on children.

In conclusion, our results indicate that negative childhood caregiving experiences are associated with new and expectant fathers' difficulties to modulate behavioral response to infant crying. Speculatively, infant crying was processed as particularly aversive by maltreated fathers and inhibitory control over their behavioral response was inadequate. Moreover, this effect was only present in fathers with low structural connectivity between the prefrontal cortex and the amygdala, i.e., bilateral UF, a brain structure that supports effective downregulation of emotional hyperreactivity as well as adequate inhibitory control over behavioral responses to negative stimuli. Importantly, our findings indicate that the detrimental effects of child maltreatment history on parenting during exposure to infant distress are measurable in men shortly before and after the birth of their first child, a period in which exposure to infant crying is (about to be) common. As the perinatal period is particularly formative for new parents, our findings provide more insight into which fathers might be at risk of developing suboptimal behavioral reactions to infant distress signals. Future research could indicate how these findings relate to more direct measures of parenting (e.g., parenting sensitivity). In hopes of finding effective early intervening where needed, a more thorough understanding of fathers' abilities to provide adequate care for their children, and all contributing factors, is needed.

CREediT author statement

KA-vD: Methodology, Formal analysis, Investigation, Data Curation, Writing - Original Draft, Visualization, Project administration; NvdK: Software, Formal analysis, Investigation, Data Curation, Writing - Review & Editing; RSMB: Methodology, Software, Formal analysis, Data Curation, Writing - Review & Editing, Visualization; LIH: Software, Formal analysis, Investigation, Data Curation, Writing - Review & Editing; AML: Investigation, Data Curation, Writing - Review & Editing, Project administration; MMER: Methodology, Formal analysis, Writing - Review & Editing; CS: Methodology, Writing - Review & Editing, Supervision; MHvIJ; Conceptualization, Methodology, Writing - Review & Editing, Supervision, Funding acquisition; MJB-K: Conceptualization, Methodology, Writing - Review & Editing, Supervision, Funding acquisition

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Chapter 4

Vasopressin differentially affects handgrip force of expectant fathers in reaction to own and unknown infant faces

Alyousefi-van Dijk, K., van 't Veer, A. E., Meijer, W. M., Lotz, A. M., Rijlaarsdam, J., Witteman, J., & Bakermans-Kranenburg, M. J. (2019). Vasopressin differentially affects handgrip force of expectant fathers in reaction to own and unknown infant faces. Frontiers in behavioral neuroscience, 13. https:/doi.org/10.3389/fnbeh.2019.00105

Abstract

The underlying mechanisms of paternal responses to infant signals are poorly understood. Vasopressin has previously been proposed to affect these responses. Using a double-blind, placebo-controlled, within-subject design (N = 25 expectant fathers), we examined the effect of vasopressin administration on the use of excessive handgrip force during exposure to infant crying versus matched control sounds, while participants saw morphed images representing their own infant versus an unknown infant. We found that, compared to placebo, AVP administration elicited more excessive force while viewing an unknown infant image compared to viewing the image representing one's own infant, while the reverse was true under placebo. The results are discussed in light of vasopressin's role in parenting and parental protection among human fathers.

Introduction

Infant crying can evoke parental proximity and care (Bowlby, 1969/1982; Groh and Roisman, 2009), yet it is also an aversive stimulus (Murray, 1985; Fujiwara et al., 2011; Leerkes et al., 2011) with the potential to trigger child abuse, neglect and infanticide (e.g., Soltis, 2004; Out et al., 2012). Infant crying is a highly salient cue that results in physiological arousal in both females and males (Frodi and Lamb, 1978; Groh and Roisman, 2009) and is particularly potent in activating the parental caregiving system (George and Solomon, 2008). Individual variation in the physiological response to infant crying has previously been proposed to play a role in the behavioral response to these infant signals (e.g., Murray, 1985; Reijman et al., 2016). Although several researchers have studied the physiological response to infant crying in females, both with and without children of their own (e.g., Bugental et al., 1999; Bakermans-Kranenburg et al., 2012; Riem et al., 2012, 2016; Compier-de Block et al., 2015), the mechanisms involved in the reactions of males to infant crying remain largely unknown. At the same time, males represent about 50% of all parents, and they actively participate in parenting at increases rates, making insight into the mechanisms involved in reactions of males to infant crying urgent. In particular, the need to examine the role of hormones, especially vasopressin (AVP), in paternal behavior has recently been stressed (Rilling and Mascaro, 2017). The current study investigates whether AVP affects the use of handgrip force in reaction to infant crying while exposed to images representing one's own as well as an unknown infant in expectant fathers.

The handgrip dynamometer paradigm has previously been used as a behavioral measure to study responses to infant crying. This paradigm measures the degree to which someone does not have control over handgrip force, and excessive handgrip force is used as an indicator of physiological hyperactivity and/or a lack of control over autonomic responses. For example, parents at risk for child abuse—compared to low risk parents—are found to not only rate videos of crying infants more negatively and report higher levels of hostile feelings, they also use more excessive handgrip force after hostile priming than their low risk counterparts (Crouch et al., 2008). Likewise, in response to crying as well as laughter, maltreating mothers use more excessive handgrip force than non-maltreating mothers (Compier-de Block et al., 2015). Several factors have been shown to relate to the use of excessive handgrip force in pseudo-parenting contexts. For example, compared to other women, mothers with low perceived parental control have been found to show heightened autonomic arousal and more use of excessive force in operating the dynamometer while providing negative feedback to children who show ambiguous behavior (Bugental et al., 1999). Additionally, females with insecure attachment representations have been found to experience more irritation during infant crying and use more excessive handgrip force than females with secure attachment representations (Riem et al., 2012). Due to the association with maladaptive parenting, studying the processes underlying excessive handgrip force may help find physiological markers of parenting style in general.

Throughout evolution, human fathers have been faced with paternity uncertainty (Buss, 1999; Larsen and Buss, 2009) and have used cues of genetic relatedness, such as facial resemblance, in allocating offspring investment (e.g., Apicella and Marlowe, 2004; Alvergne et al., 2009; DeBruine et al., 2009; Yu et al., 2017, 2019). This strategy maximizes reproductive benefits as limited resources are preferentially assigned to offspring passing down fathers' genes to next generations (Kaplan and Gangestad, 2005; Griskevicius et al., 2011). When paternal care is provided, offspring has a higher chance of survival and a better quality of life (e.g., Hurtado and Hill, 1992; Flouri and Buchanan, 2003, 2004; Sear and Mace, 2008), even in modern societies (Vågerö et al., 1998). Likewise, men, rather than women, have been found to base a hypothetical adoption choice primarily on cues of kinship (Volk and Quinsey, 2002) and the self-reported quality of fathers' relationship with their children is predicted by the level of resemblance (Apicella and Marlowe, 2004). Naturally, human behavior is not exclusively shaped by evolutionary processes but also by social and cultural contexts (Shan et al., 2012; Bertamini and Lyons, 2015; Yu et al., 2017), as is evident by the findings of Abraham et al. (2014) indicating there are no differences in the neural processing of viewing one's own infant by either biological or adoptive fathers. Nonetheless, with the exception of adoptive fathers (Van IJzendoorn et al., 2009), parents tend to invest less in biologically unrelated versus related children (e.g.,

Alvergne et al., 2009). Moreover, Daly and Wilson (1984) found that males who had committed infanticide commonly report an absence of resemblance with the child in question [but see Temrin et al. (2000) and Daly and Wilson (2008) for a debate on the effects of these evolutionary processes in modern society]. Although not previously investigated, handgrip force (or a lack of control thereof) during exposure to resembling and non-resembling infant images could potentially highlight the evolutionary beneficial distinction commonly found in males since resources (e.g., time and energy spend on suppressing the aversiveness of infant crying in order to provide adequate parental care) are preferentially allocated to the own infant at the expense of unrelated infants. Combining the discussed findings on abuse with the fact that infant crying is a common trigger for child abuse and infanticide (see Zeifman and St James-Roberts, 2017 for a review), it is likely that there are differential physiological mechanisms at play when an aversive and highly salient stimulus such a as crying is coupled with the image of an infant that is likely versus unlikely related to the observing male, particularly in periods of changing hormone levels and reactivity.

Recent studies suggest that handgrip force in reaction to infant signals is influenced by hormones: administration of oxytocin (OT) reduces the use of excessive force in insecurely attached females (Riem et al., 2016), and in females without a history of harsh discipline (Bakermans-Kranenburg et al., 2012). Furthermore, Riem et al. (2017) showed that in males, an experimental increase in endogenous OT release through mechanically delivered massage is related to reduced handgrip force during exposure to infant sounds. These results suggest that hormones play an important role in the physiological response to infant crying in both females and males. Next to OT, AVP is also considered to be functionally significant in parental behavior (Wang et al., 2000; Ahern and Young, 2009; Ahern et al., 2010; Gouin et al., 2010; Snowdon et al., 2010; Apter-Levi et al., 2014). Specifically, AVP is suggested to be more strongly related to paternal parenting than to maternal parenting (Wang et al., 2000; Wynne-Edwards, 2001; Storm and Tecott, 2005; Carter et al., 2007; Taylor et al., 2010). Additionally, when it comes to pair bonding, AVP has been proposed to fulfill a similar role in males as OT in females (Taylor et al., 2000, 2010). However, its exact role in paternal care remains largely unclear, making AVP an obvious candidate for closer examination in the context of how males respond to infant signals.

Sexually dimorphic roles of AVP have been found in both humans (e.g., Thompson et al., 2006) and animals (e.g., see Terranova et al., 2017). For example, in response to watching an interaction with one's own child, activations in social-cognitive circuits were correlated with fathers' but not mothers' salivary AVP levels (Atzil et al., 2012). Additionally, the male mandarin vole has been found to show differential behavioral, hormonal, and neural responses to own versus unknown pups, with AVP neurons

specifically responding to the voles' own pups (Yuan et al., 2018). Considering its crucial role in protective aggression as a part of paternal care (Van Anders et al., 2011; Bakermans-Kranenburg and Van IJzendoorn, 2017), it is likely that paternal AVP plays a role in the physiological response and emotional regulation when exposed to infant crying (Meyer-Lindenberg et al., 2011). Specifically, AVP might be implicated in making the evolutionary beneficial distinction between one's own versus unrelated offspring. Indeed, in rodents, AVP is associated not only with male bonding, defensive and territorial behavior (Bielsky et al., 2005), but also with social recognition (Caldwell et al., 2008). In humans, AVP has also been found to play an important role in social recognition and face perception (Guastella et al., 2010). For instance, AVP-dependent paternal brain activations and hormonal responses have been suggested to underlie fathers' ability to interpret others' intentions in order to accurately defend offspring (Thompson et al., 2006; Atzil et al., 2012). By fostering selective protection, AVP may facilitate successful fathering in humans and other mammals (Carter, 1998). The effect of AVP on responses to infant cries may therefore depend on the presence of kinship cues. Additionally, AVP administration increases salience processing in the brain (Brunnlieb et al., 2013; Feng et al., 2015) and can therefore be expected to play a role in highlighting the salience of infant cry signals, particularly in periods with marked AVP sensitivity.

Expectant fathers can undergo physical changes that prepare them for fatherhood, which are, at least in part, due to changes in various hormone levels (see Wynne-Edwards, 2001). Coinciding with an increase in caregiving behaviors and caregiving attitudes in expectant fathers (Cohen-Bendahan et al., 2015), robust changes in prolactin, cortisol and sex steroids have been found during the prenatal period (e.g., Storey et al., 2000; Berg and Wynne-Edwards, 2001; Edelstein et al., 2015). Also, basal levels of testosterone and cortisol, as well as prolactin have been shown to relate to responsiveness to infants and to prenatal quality of caregiving in expectant fathers (Storey et al., 2000; Bos et al., 2018). One study found that although basal levels of OT and AVP are no different in fathers-to-be compared to non-expecting men, administration of AVP to fathers-to-be results in an increase of parenting behaviors whereas administration to non-expecting males does not (Cohen-Bendahan et al., 2015). These findings suggest an increase of sensitivity to AVP in fathers during the prenatal period.

To our knowledge, the current exploratory study is the first to examine whether, in expectant fathers, administration of AVP affects the use of excessive handgrip force in response to infant crying paired with images representing one's own or an unknown infant. To this end, a double-blind, placebo-controlled, within-subject design was used. On the basis of the literature described here, it can be expected

that fathers-to-be would use more excessive force during cry sounds (i.e., a salient and aversive stimuli) compared to neutral sounds and more excessive force while viewing an unknown versus their own infant under crying conditions. Considering the limited literature on the effects of AVP in expectant fathers, we examined if AVP administration would differentially affect these responses. Considering findings indicating that experienced caregiving in parents' own childhood alter performance on a parenting-related handgrip task (Bakermans-Kranenburg et al., 2012) as well as neural responses to cry sounds after AVP administration (Thijssen et al., 2018) we will take these experiences into account.

Material and methods

Participants

Twenty-five first-time expectant fathers were recruited through midwives and ads on Leiden University affiliated webpages. Sample size was determined by the ethics approval request for a first study with AVP administration in our lab. Participants cohabitated with their pregnant partners, spoke Dutch, and were screened and excluded for self-reported neurological, neuroendocrine and psychiatric disorders, and alcohol and substance abuse. The mean age of the participants was 31.92 years (*SD* = 4.30). The mean gestational age of the unborn infants was 27.02 weeks (*SD* = 4.91). See Table 4.1 for information on demographics. This experiment was part of a larger study (see also Thijssen et al., 2018; Van 't Veer et al., 2019). Permission for this study was obtained from the Ethics Committees of the Institute for Education and Child Studies at Leiden University and the Leiden University Medical Centre, as well as the Dutch Central Committee on Research Involving Human Subjects. All participants gave informed consent.

Procedure

Participants visited the lab twice with an intervening period of 1 week. They self-administered a single dose of 20 IU AVP or placebo nasal spray at the start of each session (counterbalanced) using a syringe with a MAD NasalTM Device. Dosage was chosen based on previous studies of AVP effects on behavior and brain activation (e.g., Pitman et al., 1993; Thompson et al., 2006; Rilling et al., 2012; Uzefovsky et al., 2012; Tabak et al., 2015). This dose has been found to result in elevations in plasma equivalent to those produced by an intravenous dose of 0.025 IU (Pietrowsky et al., 1996). After administration participants first completed tasks in an MRI scanner (i.e., a resting state scan, a working memory task, a task involving labeled cry sounds, see Thijssen et al., 2018, and a task with video vignettes, see Van 't Veer et al., 2019), followed by three behavioral tasks, starting with the handgrip paradigm described

here. On average the handgrip paradigm took place 125.5 min (*SD* = 8.5) after nasal spray administration. Of the 24 participants who answered the question about which substance they thought they were given during the second session (placebo, AVP, or unsure), only 10 were correct. In the week between the two sessions, participants filled out online questionnaires at home including the Conflict Tactics Scale (CTS, Straus et al., 1998) and a subscale of the Children's Report of Parental Behavior Inventory (CRBI, as used in Huffmeijer et al., 2011), which serve as our measures of early caregiving experiences of the fathers-to-be.

Table 4.1. Demographic information of the sample (*N* = 25)

		M(SD)/N(%)	**Min**	**Max**
Age (years)		31.92 (4.30)	24.65	43.04
Gestational age (weeks)		27.02 (4.91)	20.43	36.14
Education	Secondary	5 (20%)		
	Higher	20 (80%)		
Income	< €3200	6 (24%)		
	€3200 - €4000	10 (40%)		
	> €4000	9 (36%)		
Handedness	Right handed	23 (92%)		
Condition session 1	AVP	13 (52%)		
Time between nasal spray and handgrip paradigm (min)	Placebo	126 (9)	1:53	2:30
	AVP	125 (8)	1:52	2:28

Measures

Handgrip Dynamometer. Participants were exposed to infant crying and images representing either their own or an unknown infant while they were asked to squeeze a handgrip dynamometer (similar to Bakermans-Kranenburg et al., 2012).

In order to create suitable images for the handgrip paradigm, participants either provided a full-color digital photograph of themselves prior to the first session, or a picture was taken at the beginning of the first visit. The participant's picture met the following criteria: it showed their face, en face, with a neutral expression, a light and neutral background, without piercings, make-up, or glasses. Photographs were edited using Adobe Photoshop CS in order to remove unwanted facial features (e.g., facial hair). Subsequently, morphed images representing participant's own infant were created by combining 75% of an average infant image (created by the authors of Hahn et al., 2015, from 10 female and 10 male infant faces) and 25% of participant's own picture, using Fantamorph 5 Deluxe1. Similarly, the morphed image of an unknown infant was created by combining 75% of the average infant image and 25%

of a male unknown to the participants, after which all images were resized to 640 × 480 pixels. Finally, images were masked with a black face contour. Participants were familiarized with their morphed own infant image before onset of the task with the explanation that a future infant of theirs might look similar to this image. The same own and unknown infant images were also used during one of the fMRI tasks (see Van 't Veer et al., 2019) prior to the handgrip paradigm. During this fMRI task, and contrary to the handgrip paradigm, the images were presented alongside text inviting the participants to imagine seeing their own or an unknown infant, respectively.

A total of three cry sounds were used from two infants, one male (two sounds) and one female (one sound) recorded with a TasCam DR-05 solid state recorder with a 44.1 Khz sampling rate and 16 bit. All sounds were recorded within the first two prenatal days. Individual sounds were scaled, the intensity was normalized to the same mean intensity and sounds were edited using PRAAT software (Boersma and Weenink, 2017). For each cry sound a neutral auditory control stimulus was created by calculating the average spectral density over the entire duration of the original sound. A continuous sound of equal duration was re-synthesized from the average spectral density and amplitude modulated by the amplitude envelope, extracted from the original sound. After this procedure, all auditory stimuli and control stimuli were intensity matched. Using this procedure, the neutral auditory control stimuli were identical to the original auditory stimuli in terms of duration, intensity, spectral content, and amplitude envelope, but lacking the emotional meaning associated with a cry sound.

During the task participants were seated comfortably in front of a computer screen wearing headphones while holding a dynamometer in their dominant hand. During an initial training period, participants were asked to squeeze the handgrip dynamometer at full and half strength while they received feedback from a monitor indicating the strength they used graphically. Once participants could reliably alternate between full and half strength (half strength being 50% of the strength used at full strength), the actual task began in which participants received no further feedback on their performance.

The task was administered using E-Prime software (version 2.0; Psychology Software Tools, Inc., Sharpsburg, PA, United States) and hand squeeze intensities (in kg) were transferred directly from the dynamometer to AcqKnowledge software (version 4.3.1; Biopac Systems, 2004). First, a baseline measure of three maximum strength trials each followed by half strength trials was administered. Then, four randomly presented conditions of three max-half trials were presented; (1) viewing a morphed image of own infant while hearing control (scrambled) sounds (Own Neutral); (2) viewing a morphed image of own infant while hearing cry sounds (Own Cry); (3)

viewing a morphed image of an unknown infant while hearing control (scrambled) sounds (Other Neutral); (4) viewing a morphed image of an unknown infant while hearing cry sounds (Other Cry). Handgrip force measures were reliable (α = 0.75 – 0.89) in all four conditions consisting of three trials each, across both placebo and AVP sessions. Therefore, the three trials per condition were averaged as an indicator of handgrip force in each condition. Sounds and images were presented throughout each trial lasting 12 s. Eight seconds after the beginning of each trial, participants were prompted to squeeze maximally (instructions displayed for 1 s). After an interval of 2 s, participants were prompted to squeeze at half strength (instructions were displayed for 1 s). A fixation cross was shown for 3 s between each trial.

Similar to previous studies (Bakermans-Kranenburg et al., 2012; Riem et al., 2012; Compier-de Block et al., 2015), grip strength modulation was calculated by dividing half-strength squeeze intensity by the preceding full-strength squeeze intensity, meaning that scores of over 0.50 indicated excessive force on the half-strength squeeze attempt. We examined the effects of AVP on this ratio of handgrip strength at half force and handgrip strength at maximum force, which can be considered an implicit measurement of reactive force in response to infant signals. Matlab (version 8.0.0.783, Mathworks, Natick, MA, United States) was used to identify peak intensities for each squeeze.

Mood. In order to assess possible mood induction by the preceding fMRI tasks and a potentially differential effect of hormone administration, the current emotional status of participants was measured using the Positive and Negative Affect Schedule (PANAS; Watson et al., 1988) in between MRI and behavioral measurements.

Associations With Early Caregiving Experiences. Early caregiving experiences were considered to be possible related to our outcome measures. Participants completed the Conflict Tactics Scale – Parent Child (CTS, Straus et al., 1998), which assesses experienced abuse and neglect during the participants' childhood, and the Love Withdrawal subscale of the Children's Report of Parental Behavior Inventory (CRPBI, Schludermann and Schludermann, 1983; Beyers and Goossens, 2003), see Supplementary Material for details of these measures.

Results

Positive mood scores were roughly the same in the AVP (M = 32.04, SD = 6.56) and placebo (M = 31.96, SD = 7.52) conditions. Similarly, negative mood scores were roughly the same in the AVP (M = 13.96, SD = 3.63) and placebo (M = 13.32, SD = 2.98) conditions.

Measures of early caregiving experiences were not found to correlate strongly with mean handgrip force ratio's (see Supplementary Material). Under baseline conditions (i.e., no sounds or images presented), as well as in all other conditions, the mean handgrip force ratio was just above the instructed 0.5, see Table 4.2. Mean handgrip force ratio during the AVP baseline was slightly lower than handgrip force ratio during placebo baseline, see Table 4.2.

In order to examine the patterns in the data for the effect of AVP on the use of excessive handgrip force while listening to infant cry sounds as well as viewing one's own and an unknown infant images, a repeated measures analysis of variance with condition (AVP versus placebo), sound (cry versus control sounds), and familiarity (unknown versus own infant image) as factors and mean handgrip force ratio as the dependent variable was conducted. A Shapiro–Wilk test indicated that all data was normally distributed ($p > 0.1$ for all conditions).

Results did not show main effects of condition (AVP versus placebo, $F[1,24] = 0.68$, $p = 0.42$, $\eta^2_p = 0.03$), sound (cry versus control sounds, $F[1,24] = 1.46$, $p = 0.24$, $\eta^2_p = 0.05$), or familiarity (unknown versus own infant image, $F[1,24] = 0.00$, $p = 0.98$, $\eta^2_p = 0.00$).

However, the two-way interaction between condition and familiarity was significant ($F[1,24] = 6.27$, $p = 0.02$, $\eta^2_p = 0.21$). We present the estimated marginal means and standard errors for this interaction in Figure 4.1. Compared to placebo, AVP had a differential effect on handgrip force while watching one's own versus an unknown infant. As can be seen in Figure 4.1, the interaction between condition and familiarity was such that, in contrast with placebo, AVP administration elicited more excessive force while viewing an unknown infant image compared to viewing one's own infant's image, while the reverse was true for placebo administration. In other words, under AVP there was less excessive handgrip force while viewing an image representing one's own infant compared to while viewing an unknown infant.

Upon reviewer suggestion we also ran post hoc t-tests on the familiarity means within each condition separately. This revealed that, with medium effect size, while viewing the unknown infant image participants tended to used more excessive handgrip force in the vasopressin condition ($M = 0.66$, $SE = 0.03$) compared to placebo condition ($M = 0.62$, $SE = 0.03$), $F(1,24) = 3.51$, $p = 0.07$, $\eta^2_p = 0.13$, 95% CI [–0.004,0.086]. In contrast, while viewing one's own infant image, there was not such a difference in handgrip force in the vasopressin condition ($M = 0.63$, $SE = 0.03$) and the placebo condition ($M = 0.65$, SE = 0.02), $F(1,24) = 0.32$, $p = 0.58$, $\eta^2_p = 0.01$, 95% CI [–0.05,0.03].

Table 4.2. Mean handgrip force ratio's for all conditions, calculated by the ratio between half strength and maximum strength.

	M(SD)
Placebo, baseline	.63 (.11)
AVP, baseline	.58 (.09)
Placebo, own infant, control sound	.63 (.12)
AVP, own infant, control sound	.63 (.14)
Placebo, own infant, cry sound	.66 (.13)
AVP, own infant, cry sound	.64 (.13)
Placebo, unknown infant, control sound	.62 (.15)
AVP, unknown infant, control sound	.66 (.13)
Placebo, unknown infant, cry sound	.62 (.13)
AVP, unknown infant, cry sound	.66 (.14)

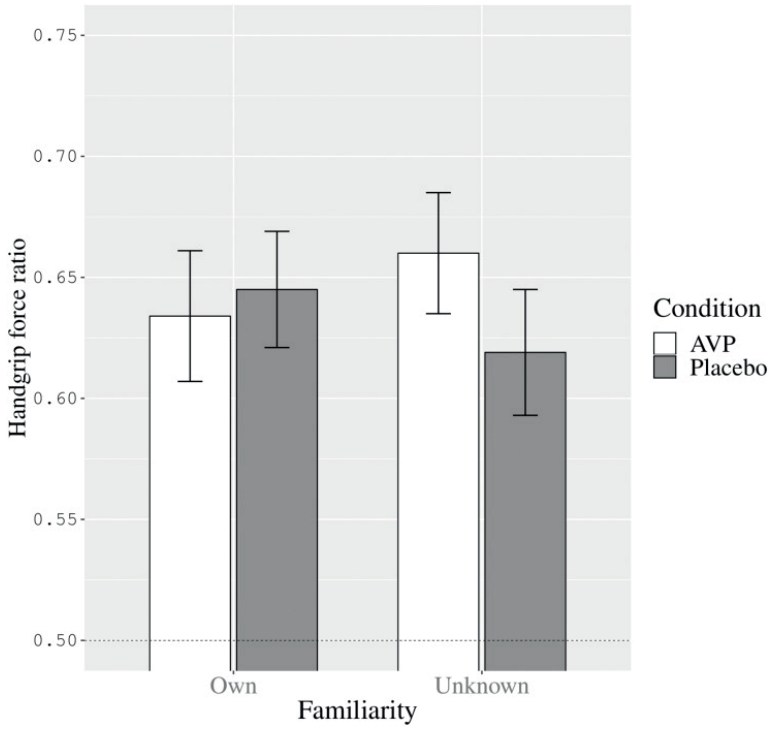

Figure 4.1. The interaction between condition (AVP versus placebo) and familiarity (own versus unknown infant image) on participants' handgrip force ratio (Estimated marginal means and Standard errors). The dashed line represents control over handgrip force in line with the instructions to first squeeze as hard as possible and then squeeze at half that strength (corresponding to a handgrip force ratio of 0.50).

Results did not show a significant two-way interaction effect between condition and sound (F[1,24] = 0.17, p = 0.68, η^2_p = 0.01), nor between infant and sound (F[1,24] = 0.62, p = 0.44, η^2_p = 0.03). The three-way interaction between condition, sound, and familiarity was not significant either (F[1,24] = 0.95, p = 0.34, η^2_p = 0.04).

Discussion

In a randomized controlled within-subject experiment we tested the effect of AVP administration on the use of excessive handgrip force during exposure to infant crying and images of one's own versus an unknown infant in fathers expecting their first child. Contrary to our expectation, expectant fathers did not use significantly more handgrip force during infant cry sounds versus control sounds. Results indicated that AVP administration affected the use of handgrip strength differently depending on whether a morphed image representing participant's own infant or an unknown infant was shown. More specifically, compared to placebo, fathers used more handgrip force under AVP when looking at an image representing an unknown infant than when looking at an image representing their own infant, while under placebo it was the other way around. That is, under AVP the mean ratio of handgrip force (a proxy for control over behavioral responses) increased while viewing and unknown infant but decreased while viewing one's own infant. These findings were independent of the accompanying sound (i.e., cry versus control sounds).

The follow-up analyses illustrating and exploring the interaction effect of hormone administration and image showed that compared to placebo, the administration of AVP in expectant fathers increased handgrip force in response to an unknown (but not own) infant. This finding is in line with indications from previous literature. Long known from clinical and behavioral studies, men are more likely to provide care for biologically related children and less likely to abuse them compared to unrelated children (e.g., Daly and Wilson, 1988; Burch and Gallup, 2000), with the exception of adoptive fathers (Van IJzendoorn et al., 2009). Assessing paternal resemblance, starting soon after birth, has been shown to be an important mechanism in estimating the chances of paternity (Daly and Wilson, 1982, 1998; Lacy and Sherman, 1983). Interestingly, even the unconscious determination of self-resemblance in a child's face may affect attitudes and intended care toward the child. For instance, studies have found that morphed child images bearing resemblance to participants were rated as more attractive, were more likely to be adopted in a hypothetical situation, and received more hypothetical time and money by male (but not female) participants (Platek et al., 2002, 2004; but see DeBruine, 2004 for methodological considerations on the gender difference for these effects). This idea is supported by findings that males

show differential brain responses to resembling versus non-resembling child images, supposedly underlying either heightened attention allocated to assess resemblance, or increased reward related activation when the child is likely to be genetically related (e.g., Platek et al., 2005, 2008). AVP administration may magnify such differentiating processes. Whether the differential effect of AVP on reactions to own versus unknown infants was based on conscious or unconscious recognition of the images cannot be determined since participants were not asked to identify or rate the images.

Additionally, our findings are in line with previous suggestions proposing that changes in sensitivity to AVP during the prenatal period, and changes in AVP expression postnatally, promote paternal behavior (e.g., see Gettler, 2014 resp.; Cohen-Bendahan et al., 2015). In accordance with the Steroid/Peptide Theory of Social Bonds (Van Anders et al., 2011) this study supports the notion that AVP may be involved in a critically important but understudied part of paternal care, namely protective aggression. Our finding concerning the use of more excessive force while viewing an unknown versus one's own infant image may speculatively be related to an increase in protective parenting behaviors induced by the administration of AVP. Under such circumstances, the evolutionary beneficial recognition of related offspring could result in preferential allocation of resources to their own infant rather than a unrelated infant. The presence of aversive and now increasingly salient infant crying could have prompted our expectant fathers to relatively high levels of intolerance for crying unrelated infants. Future studies can further parse out whether AVP indeed underlies mechanisms of protective aggressive responses to non-kin in expectant fathers.

We did not find a significant effect of cry sounds (versus control sounds) on fathers' handgrip force. Even though exposure to infant crying (versus control sounds) increased activation in the bilateral auditory cortex and posterior medial cortex in the same group of participants (Thijssen et al., 2018), these effects do not seem to relate to behavioral change as measured in the present study by the handgrip paradigm outside the scanner. In accordance with the results presented here, Thijssen et al. (2018) found no effect of AVP on these neural responses to infant crying. However, AVP did selectively affect the neural processing of infant cries coupled with an emotional context label (e.g., 'this infant is sick') compared to cry sounds coupled with a neutral label (e.g., 'this is an infant'). Effects of AVP can be highly context-dependent (Van Anders et al., 2011; Gettler, 2014), and real-life cry sounds are usually coupled with contextual information that may push caretakers toward protective or caretaking behavior. The absence of contextual information accompanying the cry sounds presented in the handgrip paradigm may play a role in explaining why we did not find an AVP effect on responses to cry sounds.

The current study has several limitations that should be addressed in future research. One important limitation is that conclusive information about the optimal dose of AVP and the best time interval between administration and behavioral effects is lacking. Based on the literature at hand it cannot be determined with certainty that our chosen dose and time interval were ideal. Also, due to the varying duration of other assessments, the exact time interval between hormone administration and the handgrip task varied somewhat among participants, which may have influenced the results. The exact mechanism of the effect of exogenous AVP on behavior, and the consequences for timing protocols, remain elusive and should be studied more extensively. Additionally, individual variation in the basal levels of, and sensitivity to, AVP might influence its behavioral effects, similar to what has been found for other hormones such as OT (see Bos, 2017 for a review), and future research may take these individual differences into account. Another important limitation is the sample size; we were only able to detect medium to large effects. Studies with larger sample sizes are warranted to confirm and extend these findings, preferably including participants in various phases of fatherhood (e.g., without children, early and late prenatal, early and late postnatal). Ultimately, more studies including physiological measures, such as was done here, are needed for the accumulation of knowledge about the (neuro) biological mechanisms underlying paternal care.

Author Contributions

MB-K designed and directed the project. KA-vD wrote the manuscript with support from AvV and MB-K. JW devised the auditory stimuli and JW and AvV programmed the task. KA-vD devised the visual stimuli. KA-vD, AvV, WM, AL, and JW performed the experiments. KA-vD, AvV, and AL analyzed the data. All authors provided critical feedback and helped shape the research and manuscript.

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Chapter 5

Development and feasibility of the Prenatal Video-feedback Intervention to promote Positive Parenting for expectant fathers

Alyousefi-van Dijk, K., de Waal, N, van IJzendoorn, M. H., & Bakermans-Kranenburg, M. J. (2021). Development and feasibility of the Prenatal Video-feedback Intervention to promote Positive Parenting for expectant fathers. Journal of Reproductive and Infant Psychology. https:/doi.org/10.1080/02646838.2021.1886258

Abstract

The transition period in which men become fathers might provide an important window of opportunity for parenting interventions that may produce long-term positive effects on paternal care and, consequently, child development. Existing prenatal programs traditionally focus on maternal and infant health and seldom involve the father. This paper describes an interaction-based prenatal parenting intervention program for first-time fathers using ultrasound images, the Prenatal Video Feedback Intervention to promote Positive Parenting (VIPP-PRE). We randomized a group of expectant fathers ($N = 73$) to either the VIPP-PRE or a control condition. Expectant fathers thought the VIPP-PRE was more helpful and influenced their insights into their babies to a greater extent than the control condition. Expectant fathers receiving the VIPP-PRE reported that they particularly liked seeing and interacting with their unborn children as well as receiving feedback on these interactions. The intervention was well received and was considered feasible by both expectant fathers and sonographers and midwifes. We discuss the VIPP-PRE based on the experiences and perspectives of fathers, interveners, and sonographers and midwifes.

Introduction

The Video-feedback Intervention to promote Positive Parenting (VIPP; Juffer, Bakermans-Kranenburg, and Van IJzendoorn, 2008; 2017) is an evidence-based parenting intervention program aimed at improving parenting sensitivity as defined in attachment theory (Ainsworth, Bell, and Stayton, 1974). The intervention attempts to increase the caregiver's ability to accurately observe and interpret the signals of a child, and to react promptly and appropriately to the child's attachment-related behaviours and explorations. VIPP is a brief, home-based intervention that uses videotaped recordings of individual parent-child dyads for reinforcing and building upon existing positive interactions. In the past 25 years, the intervention has been successfully adapted for various clinical and non-clinical populations (e.g., Hodes, Meppelder, Schuengel, and Kef, 2014; Iles, Rosan, Wilkinson, and Ramchandani, 2017; Poslawsky et al., 2014; Stein et al., 2006; Van den Broek et al., 2017). Moreover, a meta-analysis showed a combined effect size of d = 0.47 for twelve randomized controlled trials (RCT) evaluating the effects of VIPP on parenting sensitivity (Juffer et al., 2017). Whereas mothers are the most common participants, some pilot work indicated that VIPP is also feasible and potentially successful for fathers (Lawrence, Davies, and Ramchandani, 2012). Here, we describe the development of the first prenatal VIPP in a particularly important and understudied period and population: men in the transition to fatherhood.

Fathers have been found to contribute substantially to child development, in some aspects even over and above mothers' influences (Cabrera, Shannon, & Tamis-LeMonda, 2007). Even in the prenatal period, fathers' influence on children's wellbeing is substantial. Fathers' perinatal behaviour and involvement during pregnancy is known to benefit maternal health behaviours and foetal outcomes (see Alio, Salihu, Kornosky, Richman, and Marty, 2010 and Lamb, 2004, for reviews) and the quality of later affective and behavioural involvement with his children (e.g., Cabrera, Fagan, and Farrie, 2008; Cook et al., 2005; Fagan et al. 2007; Witte, Bakermans-Kranenburg, Van IJzendoorn, Szepsenwol, and Shai, 2019). Additionally, parenting sensitivity originates in the prenatal period (Leifer, 1977; Lucassen et al., 2015; Steele, Steele, and Fonagy, 1996) and early postnatal parenting quality is likely founded on prenatal mental representations of the unborn child as well as the caregiver's imagined (future) relationship with the child (Siddiqui and Hägglöf, 2000; Vreeswijk, Maas, Rijk, and Van Bakel, 2014). Importantly, prenatal paternal sensitivity, measured during the third trimester using a life-like infant simulator, has been found to predict postnatal paternal sensitivity six weeks after birth (Hechler, Beijers, Riksen-Walraven, and De Weerth, 2019). Despite these findings, few parenting programs focus on fathers, the perinatal period, or both.

The existing parenting interventions that include (but are not limited to) prenatal sessions are characterized by high numbers of sessions and a broad focus (e.g., self-care, mental health, social networks) with no or little focus on improving parenting quality (e.g., Kitzman et al, 1997; Larson, 1980; Olds et al., 1998). Very few studies have involved fathers in prenatal parenting interventions that focus directly on parent-child interaction quality. In one study, it was found that three prenatal 'Growing as a Couple and Family' (GCF) sessions led to favourable, albeit different, outcomes for first-time mothers and fathers (Bryan, 2000). In this study, prenatal GCF classes focused on positive parent-child interactions by showing videotapes of unknown mothers and fathers interacting with an infant, stimulating group discussion on changing roles and identities, and offering information on the physical and behavioural capabilities and needs of a newborn. While mothers in the intervention group were found to be more sensitive to infant cues postnatally, intervention-group fathers provided more affective support in the first two years postpartum (Bryan, 2000). Additionally, a couple-focused perinatal educational program with four sessions prenatally and four within the initial postnatal months has been shown to positively affect first-time fathers' interactional skills with their infants (i.e., observed warmth/emotional support, intrusiveness, positive affect, and dyadic synchrony) as well as their time investment in parenting (Doherty, Erickson, and LaRossa, 2006). These results show promise for a brief and interaction-focused intervention for expectant fathers.

Taken together, this research suggests there is a need for an effective, brief, prenatal, interaction-focused parent-child intervention, aimed at improving paternal sensitivity and stimulating paternal involvement. VIPP might be an excellent candidate for this purpose. Specifically, VIPP is both manualized and individualized: the themes of the sessions are manualized, but it uses individualized dyad-specific footage of the parent-child interaction. This has been shown to be highly valuable in promoting sensitive parenting behaviours that are vital to the optimal development of each specific child. Here, we describe the development of the first prenatal VIPP for first-time expectant fathers using live ultrasound images. In the context of a randomized controlled design, we illustrate the perceived effects of the intervention by comparing the extent to which fathers thought the intervention versus the control condition affected their insights into both their infants and their relationships with their infants. Additionally, we report on the experiences (e.g., satisfaction with content, planning, and number of sessions) of fathers participating in the intervention as well as the sonographers providing the visualization of the unborn infants during the intervention.

Materials and methods

The VIPP-PRE program

The VIPP-PRE consists of three prenatal sessions in which the intervener discusses the following themes with the expectant father in the respective sessions: 1) attachment and exploration; 2) speaking for the child; and 3) sensitivity chains. (See Supplementary Materials for a more detailed description of the VIPP-PRE protocol per session.) During each session one or two video recordings are made while the father performs interaction-based tasks that are specific to the current session (i.e., reading, touching, singing, talking, free play). These videos are then used at the next appointment to provide feedback based on the interactions specific to each individual father-child dyad. During the recordings, sonographers are asked to create a recognizable live image of the foetus (i.e., profile) using ultrasound images (Philips Lumify 2017, Best, the Netherlands) and to interfere as little as possible. Each father is seated next to the mother's abdomen, where he is close to the child and can see the ultrasound images. The resulting recordings contain both the ultrasound images as well as a frontal view of the father's upper body. During the interactions between the father and his unborn child, the mother is asked to stay aloof and read a magazine. Consequently, both verbal communication and facial expressions of the mother are kept to a minimum during these interactions. To satisfy mothers' wishes to see their unborn children, the sonographers guided both parents during each session in detecting foetal position before and after the intervention activities.

During the recordings of fathers' interactions with their unborn children, interveners provide live feedback in line with the current theme being discussed, during which an effort is made not to disrupt ongoing interactions but subtly support the father to read the child's signals. Given the limitations in visualizing the child's signals, interveners are careful in interpreting the images. For example, instead of '*she is listening to what you are saying,*' a more typical VIPP-PRE comment would be '*Your baby stopped moving when you started talking, Maybe she is listening. At this age she is certainly capable of hearing and recognizing your voice.*' Additional effort is put into encouraging fathers to let the babies lead the interactions; teach father is encouraged to act according to his child's current behaviour (e.g., playing when the child is active, but softly supporting the child when he/she is resting). After the recordings, the father is invited to review the recordings of the previous session together with the intervener and is provided with feedback on these recordings as prepared by the intervener in the period between the sessions. Throughout the intervention, the intervener not only shows empathy for the child (e.g., '*It's very tiring to grow so fast, so no wonder that he/she sleeps very often!*'), but also for the parent (e.g., '*Some behaviours of your child might be a bit difficult to see or*

interpret now, but that will get easier once he/she is born.'). Fathers were also encouraged to interact with their unborn children outside of the intervention during fathers' own time for at least 5-10 minutes per day.

Upon request of the relevant ethics committee, sessions were scheduled at a prenatal screening facility and only took place at participants' homes when no other options were available. The VIPP-PRE only took place in case of uncomplicated singleton pregnancies where no abnormalities were discovered on standard 20-week scans. Ideally, the VIPP-PRE sessions were scheduled between 20 and 30 weeks' gestation when foetal behaviour can be easily visualized by use of ultrasound, with one to two weeks in between sessions.

Control condition

In order to examine expectant fathers' experiences with the VIPP-PRE , all expectant fathers described here were randomly assigned to either the VIPP-PRE intervention or a control condition (as is typically done in VIPP intervention trials, e.g., Juffer et al., 2008). The control condition consisted of three phone conversations during which the pregnancy and upcoming fatherhood were discussed; any interaction-related information and encouragement were excluded. See Supplementary Materials for a more detailed description of the control condition.

Intervener criteria and training

All VIPP-PRE interveners (i.e., first and second author and one research assistant named in the acknowledgements) were behavioural scientists trained as interveners in a Video-feedback Intervention to promote Positive Parenting and Sensitive Discipline (VIPP-SD) training. After successful completion of the VIPP-SD training, they were trained in the VIPP-PRE by the first and last authors of this paper. Frequent supervision was used to provide ongoing support and quality control.

Sonographers

The sonographers were employees of the partnering prenatal clinic *Verloskundig Centrum De Poort* in Leiden, the Netherlands. Most, but not all, sonographers were also midwives. They were asked to indicate foetal position to the parents, and remain silent throughout the remainder of the session. The sonographers did not answer any questions regarding the wellbeing of the mother or child, unless they noticed something clinically relevant on the images, in which case the parents were instructed to contact their midwife. This happened in none of the cases.

Current study

First-time expectant fathers were assessed for eligibility after responding to recruitment invitations distributed via midwives and (online) advertisements. Fathers had to cohabitate with first-time expectant partners and speak Dutch; they were excluded if they self-reported current psychiatric symptoms or medication. Partners had to have an uncomplicated pregnancy of a singleton with a pregnancy duration of 18-31 weeks at the time of inclusion. Fathers were excluded when their partners used alcohol, tobacco, or illicit drugs during the pregnancy or had a BMI over 30 kg/m^2 before pregnancy. Additionally, participants were excluded when abnormalities were found during the 20-week ultrasound examination or in case of known birth defects in the families of either parent that caused excessive worry for the current pregnancy. Included fathers (N = 73) were randomly assigned to the intervention or control group based on their study identification number. Ninety-six percent of fathers were born in the Netherlands. The average duration of education was 8.79 (SD = 1.44) years past primary education. Ninety-five percent of couples had planned this pregnancy, and 89% conceived naturally. Seventy-four percent of couples had not experienced a previous abortion or miscarriage.

After completion of the intervention all expectant fathers were asked to fill out an online questionnaire, with questions regarding an evaluation of their experiences (i.e., VIPP-PRE or dummy intervention) and the perceived effects of the intervention. VIPP-PRE fathers were given additional questions assessing their experiences with the VIPP-PRE. Additionally, sonographers were presented with a questionnaire pertaining to their experiences with the VIPP-PRE intervention. All questions were designed for the current study; existing VIPP evaluation questionnaires were not suitable for the prenatal period. Where possible, t-tests are used for testing differences between groups with regard to their evaluation of the intervention and its effects. In all other cases a description of the results is given for illustrative purposes. Effects of the intervention on parenting sensitivity and involvement will be reported elsewhere. The study in which the VIPP-PRE was embedded was approved by the Ethics Committee of the Leiden University Medical Centre and the Department of Education and Child Studies at Leiden University. All participants gave informed consent.

Results

Results are presented in three sections. First, we provide a brief description of the sample of expectant fathers. Then we list their evaluations of the intervention's perceived effects, feasibility, and experiences, followed by the evaluations of the sonographers.

Description of the sample

Of the 73 expectant fathers, 39 were randomly assigned to the VIPP-PRE (M_{Age} = 32.60, SD = 2.91) and 34 to the control condition (M_{Age} = 32.73, SD = 3.76). Randomization was performed before the start of the study using a computer generated randomization sequence. Due to logistical problems we had to stop the inclusion of participants earlier than expected. Keeping the random assignment, this led to somewhat unequal numbers in the experimental and control group. In the VIPP-PRE group, 12 fathers were expecting boys, 18 fathers were expecting girls, and 9 fathers did not know the gender of their unborn children. In the control group, 11 fathers were expecting boys, 18 fathers were expecting girls, and 5 fathers did not know the gender of their unborn child. Attrition overall was small and similar in both groups. Two participants (1 VIPP-PRE, 1 control) dropped out of the study due to pregnancy complications. One VIPP-PRE participant participated in the intervention but did not fill out questionnaires. During the first intervention session the gestational age for fathers ranged between 22 and 33 weeks in the VIPP-PRE condition and between 21 and 32 weeks in the control condition. Fifty percent of fathers were in the second trimester (i.e., <28 weeks) at the start of the intervention for the VIPP-PRE group compared to 68% for fathers in the control group. See Figure 5.1 for an overview of the timeline of the intervention.

Fathers' evaluation of the intervention

Participants in both groups were asked about the perceived effects of the intervention by indicating whether the intervention gave them more insight into 1) their relationship with the babies, 2) their understanding of the babies, 3) their communication with the babies, and 4) their understanding of the feelings of the babies. All items were rated on a scale ranging from 1 = 'not at all' to 5 = 'very much.' VIPP-PRE fathers thought the intervention improved their insights into their babies more than fathers in the control condition; see Table 5.1. Also, fathers were asked to rate whether or not they found the intervention helpful on a 5-point rating scale (ranging from 1 = 'not at all' to 5 = 'very much'). Fathers in the VIPP-PRE group found the appointments more helpful (t[63.04] = 4.89, p < .001); see Table 5.1. See Supplemental Material Table 5.1 for the same analysis excluding the participants who had filled out the questionnaires postnatally.

Additionally, participants in both groups reported on the intervention by evaluating their experiences with the planning and number of sessions as well as interaction with the intervener; see Table 5.2. Not surprisingly, control-condition fathers receiving phone conversations (M = 4.42, SD = 1.03) experienced less difficulties planning the appointments compared to the VIPP-PRE fathers attending sessions at the prenatal clinic (M = 3.08, SD = 1.21), t[66] = 4.86, p < .001, 95% CI [0.79, 1.89], Hedges' g = 1.17. Expectant fathers in both groups reported overall positive experiences with the intervener. Most fathers found the number of sessions and the time in between sessions 'just right.'

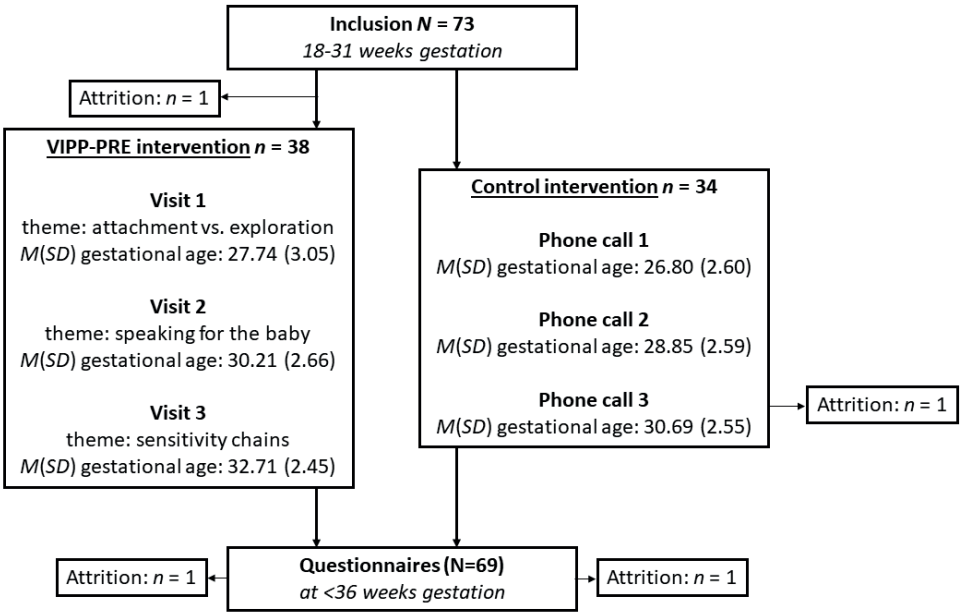

Figure 5.1. Timeline for the VIPP-PRE intervention as well as the feasibility data collected through a questionnaire. The mean gestational age of the unborn child is reported for all intervention appointments. Participants were randomly assigned to one of the groups.

Table 5.1. Expectant fathers' perceived effects of the VIPP-PRE intervention and the control condition.

	VIPP-PRE (*n* = 37)	Control (*n* = 31)	Independent sample t-test				
	M (SD)	*M (SD)*	*t*	*df*	*p*	*95% CI*[a]	*Hedges's* s_g
Relation with the baby	3.16 (1.14)	1.84 (0.86)	5.44[c]	65.31	< .001	[0.84, 1.81]	1.28
Understanding of the baby	3.11 (1.17)[b]	2.00 (0.97)	4.21	65	< .001	[0.58, 1.64]	1.01
Communication with the baby	3.41 (1.14)	1.94 (0.81)	6.18[c]	64.46	< .001	[0.99, 1.95]	1.45
Understanding of the feelings of the baby	2.81 (1.28)[b]	2.00 (1.03)	2.80	65	< .01	[0.23, 1.38]	0.68
Helpfulness	3.36 (1.17)[b]	2.13 (0.86)[d]	4.89[c]	63.04	< .001	[0.73, 1.17]	1.17

Note. Participants indicated to what extend (i.e., ranging from 1 = 'not at all' to 5 = 'very much') they thought the interventionaffected their insight into their relationship with, understanding of, and communication with the baby. Also, participants indicated on the same scale to what extent they thought the VIPP-PRE session or phone conversations were helpful. [a]Confidence interval of the difference between means, [b]Data available for 36 participants, [c]Unequal variances according to the Levene's test, [d]Data available for 30 participants

Fathers in the VIPP-PRE group were asked some additional questions regarding their experiences with the intervention; see Table 5.2 for answers to the multiple choice questions and this paragraph for their responses to open-ended questions. (Open-ended questions are listed in the Supplemental Materials.) Some fathers indicated that they would have liked to know in advance when they would be asked to sing for their babies. Likewise, when asked about what they liked least about the VIPP-PRE, 18% of expectant fathers reported having to sing. Other least favourite aspects of the intervention were logistic difficulties with the appointments at the prenatal clinic due to limited available time slots, heavy traffic or the amount of time invested, the instructions for the video recordings in general, the quality of the ultrasound images, and the mother not being allowed to join the reviewing of the ultrasound images. When asked about the most positive elements of the VIPP-PRE, 82% of expectant fathers said they particularly liked seeing and / or interacting with their unborn children. Other elements perceived as positive were: the feedback provided by the intervener, the instructions for the video recordings, and receiving information about their children's development and capabilities. Surprisingly, some fathers found that the presence of ultrasound images made the interactive activities such as reading or touching more difficult. Two fathers in the VIPP-PRE group reported that the presence of their partners made carrying out the instructions for the videos somewhat or a lot more difficult.

Sonographers' evaluation of the intervention

The sonographers involved with the VIPP-PRE who filled out an evaluation form (N = 5) reported that they had received sufficient information about the intervention beforehand. Also, they reported that achieving a recognizable image of the foetus was somewhat or very doable (on a 3-point scale ranging from not doable to very doable). In order to create recognizable images some sonographers would have preferred using their own equipment (n = 3) or to see all participants exclusively before 30 weeks' gestation (n = 1). On a 5-point scale (i.e., ranging from 1 = 'not good at all' to 5 = 'very good'), they indicated that they were positive about fathers having a central position in the intervention (M = 4.60, SD = 0.55).

Sonographers' opinions on interactions between fathers and their unborn children in general did not change. Three out of five of the sonographers would not opt to include father-foetus interaction in standard medical practice. The sonographers who were open to include father-foetus interaction in standard medical practice (if given enough time to do so), indicated that the results of an RCT testing the effects of the intervention would be crucial in determining whether this would be appropriate. Two sonographers, including one who was slightly less positive about fathers' playing a central role in the intervention, indicated they would not opt for including this

Table 5.2. Expectant fathers' evaluation of the feasibility and experiences of the VIPP-PRE or control condition sessions.

		VIPP-PRE (*n* = 37)	Control condition (*n* = 31)
How difficult was it to plan the sessions?			
	Very difficult	5.4%	0%
	A bit difficult	37.8%	12.9%
	Neutral	13.5%	0%
	Easy	29.7%	19.4%
	Very easy	13.5%	67.7%
What did you think of the time between sessions?			
	Too long	0%	0%
	Just enough	94.6%	96.8%
	Too short	5.4%	3.2%
What did you think of the number of sessions?			
	Too few	2.7%	6.5%
	Just enough	89.2%	93.5%
	Too many	8.1%	0%
How did you experience the interaction with the researcher?			
	Very unpleasant	0%	0%
	A bit unpleasant	0%	0%
	Neutral	5.4%	3.2%
	A bit pleasant	24.3%	9.7%
	Very pleasant	70.3%	87.1%
Did the ultrasound images make performing the tasks (e.g., reading, talking to the baby) easier or more difficult?			
	A lot harder	0%	
	A bit harder	13.5%	
	Made no difference	32.4%	
	A bit easier	29.7%	
	A lot easier	24.3%	
Did the presence of your partner make performing the tasks more difficult or easier?			
	A lot harder	2.8%	
	A bit harder	2.8%	
	No difference	77.8%	
	A bit easier	11.1%	
	A lot easier	5.6%	
Did you miss any specific information before onset of the intervention?			
	No	81.1%	
	Yes	18.9%	

interaction into standard practice, saying that fathers might have sometimes felt uncomfortable during the intervention and that a home setting could aid in improving parent-child interactions. Three out of five sonographers indicated that they thought that fathers would likely be more involved in parenting after the VIPP-PRE. Some indicated that the fathers participating in this study were likely already very involved and therefore might not benefit from the intervention. Lastly, sonographers reported that their interaction with the intervener was pleasant, as was based on a 5-point scale ranging from very unpleasant (i.e., 1) to very pleasant (i.e., 5), (M = 4.80, SD = 0.45).

Discussion

In this paper we described the Prenatal Video-feedback Intervention to promote Positive Parenting (VIPP-PRE), aimed at improving parenting quality and stimulating involvement in expectant fathers. Based on reports of participating fathers and sonographers, we conclude that the VIPP-PRE is feasible and positively evaluated.

Expectant fathers receiving the VIPP-PRE reported that they particularly liked seeing and interacting with their unborn children as well as receiving feedback on these interactions. The number of appointments, as well as the time in between appointments, was deemed 'just right'. Being able to see their children through live ultrasound images was helpful to most fathers in the intervention. Importantly, expectant fathers receiving the VIPP-PRE reported more insight into their relationship with the babies, better understanding of the babies and the babies' feelings, and more insight into their communication with the babies than fathers in the control condition. Also, fathers found the VIPP-PRE more helpful than the control condition.

Sonographers also reported overall positive experiences with the VIPP-PRE. Providing live and recognizable images of the foetuses was feasible. Interactions with the interveners were rated as pleasant, and sonographers felt they had received sufficient information on the intervention beforehand. They suggested that if the VIPP-PRE improves expectant fathers' parenting sensitivity and/or involvement, then it could be considered to offer these sessions, perhaps in a more private and home-based environment where fathers feel more at ease. They also suggested to start the sessions preferably before 30 weeks of gestation due to difficulties with imaging near the end of pregnancy. Even though the sonographers' opinions on the role of father-foetus interactions did not change after the intervention, they were very positive about the fact that fathers played a central role. Some sonographers indicated that using more high-grade equipment would have resulted in more recognizable images.

Previously, prenatal parenting interventions have predominantly focused on achieving positive health and psychosocial outcomes in high risk samples. Such interventions are scarce, and they do not make clear which element(s) contributed to these positive outcomes. For example, Bryan (2000) evaluated a broad intervention that included videotaped examples of unknown fathers and mothers interacting with a child, group discussions about parental roles, and parenting education. This compound of potentially effective components leaves open the question of the specific part of the intervention which brought about the change. In contrast, the VIPP-PRE is a brief and focused intervention aimed at supporting interactions between the father and his own baby.

With the VIPP-PRE we build on the theories of attachment and mentalization that are the basis for our video-feedback parenting interventions. Because of this theoretical foundation, the intervention focuses on the core elements of the future attachment relationship, namely parental sensitive responsiveness (Ainsworth et al., 1978) and on the enhancement of paternal mentalizing capacity (Fonagy et al., 2002). The latter enables fathers to take the perspective of the foetus and the new-born, and to project an emerging mind on the baby that needs his attention and protection. Whereas mothers have been prepared for their mothering role by carrying the foetus and by pregnancy-induced hormonal and neural changes, fathers have had less opportunity to be neurobiologically and behaviourally prepared for the arrival of a newborn (Bakermans-Kranenburg et al., 2019). They might profit from prenatal exposure to the foetus and video feedback around this exposure.

Several potential weaknesses of the intervention arising from the evaluations warrant some discussion. First, a number of expectant fathers receiving the VIPP-PRE seem to have had difficulty with the unannounced proposal to sing to their unborn children in the presence of the mothers, sonographers, and interveners, while being recorded. Therefore, we would suggest replacing this activity with another activity for example, an additional 'free play' situation.

Secondly, several fathers reported that the live ultrasound images made carrying out the activities more difficult. This might be due to the fact that fathers had to multitask during recordings and might have felt like they did not have sufficient time to look at the images closely enough. This might have been especially the case when they were asked to read from a book or when they made eye contact with the intervener. However, the feedback given based on previous recordings in one-to-one conversations with the father was well received. We would therefore suggest to keep reviewing the ultrasound recordings with feedback in the VIPP-PRE and to perhaps put more emphasis on the feedback based on earlier recordings, such as is the case

with the other modules of the VIPP. If advances in prenatal imaging allow for making more easily recognizable images of the foetus (e.g., 3D imaging) within the time window needed for this intervention, then this could certainly be considered for the VIPP-PRE.

Lastly, a small percentage of fathers had some difficulty planning the appointments due to limited availability at the prenatal clinic. Considering the limited available spots (e.g. working days only, 8am-4pm), and given that most of our expectant fathers and mothers worked full time, the attrition in the intervention group was surprisingly low. However, if the VIPP-PRE is to be implemented in primary health care, it might be helpful to search for options that circumvent the flexibility shown by our participants. One such solution could be offering home sessions, which might be feasible with portable ultrasound equipment, such as the type used in this study.

The following limitations of the current study should be noted. First, the fathers included in the study do not necessarily represent the general population and are likely relatively involved parents. However, for the purpose of testing feasibility of the intervention this group of fathers was suitable as potential confounding factors, such as the strains and stresses of poverty, were absent. To further test the acceptability and effectiveness of the VIPP-PRE, future studies could include a more diverse group of fathers. Secondly, the effects of getting extra ultrasound scans are intertwined with the intervention, and it is difficult to disentangle the effects of both components of the intervention. Importantly, the intervention's efficacy needs to be interpreted with this possible confounding in mind, and future studies may be advised to include a control condition with the extra scans but without the interactions and feedback.

The effects of the VIPP-PRE on fathers' quality and quantity of care should guide future efforts on expanding the use of the intervention. Possible mediators, moderators, and secondary outcomes (e.g., fathers' mentalizing abilities, neural and hormonal functioning, parents' childhood experiences with maltreatment, postnatal depression) should be considered and might point towards those who would benefit most from the VIPP-PRE.

In summary, both researchers and clinicians have recently started to include partners of pregnant women in perinatal care. The development of a first interaction-based, brief, prenatal interventions aimed directly at improving parenting quality and quantity helps to include family context in perinatal health care.

Author Contributions (CRediT)

Conceptualization, MJB-K, MHvIJ and KA-vD ; Methodology, KA-vD, MHvIJ and MJB-K; Formal analysis, KA-vD and NdW; Investigation, KA-vD and NdW; Data curation, KA-vD and NdW; Writing – original draft, KA-vD; Writing – review & editing, NdW, MHvIJ and MJB-K; Visualization, KA-vD and MJB-K; Supervision, MJB-K and MHvIJ ; Project administration. KA-vD and MJB-K; Funding acquisition, MJB-K and MHvIJ .

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Chapter 6

General discussion

Summary of results

The main goal of this thesis was to investigate the development of perinatal parenting behaviours in first-time fathers, as well as to study the hormonal and neural processes involved. We investigated this through both correlational research as well as via a hormonal and a behavioural intervention, providing insight into the relatively understudied workings of paternal care. First, we explored changes and concurrent associations between and within paternal behaviour, hormonal levels, and neural activation in response to infant crying from the prenatal to the postnatal period (Chapter 2). Secondly, we examined the relation between new and expectant fathers' experiences of childhood maltreatment and their behavioural response to infant crying, as well as moderation of this relationship by structural brain connectivity (Chapter 3). Thirdly, we examined the effects of vasopressin (AVP) administration on paternal behavioural responses to infant crying (Chapter 4). Lastly, we reported on the development of a prenatal parenting intervention aimed at improving paternal involvement and parenting sensitivity (Chapter 5). The summary of results is followed by a General discussion, conclusions and future directions.

Chapter 2 - Exploring the transition into fatherhood

In Chapter 2 we built on existing knowledge from cross-sectional studies by conducting a longitudinal study of first-time fathers assessing changes in, and concurrent associations between, behavioural, hormonal, and neural aspects of paternal caregiving, following calls to study the biobehavioural changes that take place in this important period (Saxbe, 2017). In this study, we investigated parenting sensitivity, handgrip force, and neural activation in response to infant cry sounds, in addition to testosterone baseline levels, both before and after the birth of fathers' first child (N = 25). Our results indicate that paternal sensitivity, handgrip force in response to infant crying, and testosterone baseline levels are stable over time in the perinatal period. However, fathers' neural response to infant crying was found to change noticeably from the prenatal to the postnatal period, indicating that some neural processes evoked by infant crying (e.g., those involved in visual imagery) emerge after the birth of their child. We also found that behavioural, hormonal, and neural measures were not highly correlated in the prenatal period, but neural activation in response to infant crying in several areas (i.e., the right precentral gyrus and the right body and splenium of the corpus callosum) were interrelated postnatally. Moreover, we found that postnatal neural activation in response to infant crying in the right precentral gyrus was strongly related to postnatal parenting sensitivity, possibly indicating an important role for neural reactivity in response to infant signals in the foundation of parenting quality. In turn, this postnatal activation in response to infant crying in the right precentral gyrus was found to be highly correlated to prenatal

activation in the bilateral posterior cingulate cortex (PCC). This finding suggests that prenatal reactivity to infant signals in the PCC might be an indirect neural predictor for early postnatal parenting quality in new fathers. In conclusion, fathers' behavioural responses to infant crying (i.e., observed sensitivity and handgrip force), as well as baseline testosterone, seem to have been shaped before late pregnancy, and we propose that future studies test these hypotheses. In line with previous theoretical work (Bakermans-Kranenburg, Lotz, Alyousefi-van Dijk, van IJzendoorn, 2019; Saxbe, 2017), the birth of fathers' first child seems to be a major life event which triggers large changes in the brain's neural responses to infant signals. Importantly, these changes are likely functionally relevant and play an important role in the constitution of paternal care behaviour in the early postnatal period.

Chapter 3 - Childhood maltreatment, paternal behaviour, and brain connectivity

In Chapter 3 we reported on a study in which we examined the association between fathers' experienced childhood maltreatment, control over behavioural responses to infant crying (i.e., handgrip force), and brain connectivity (i.e., white matter integrity) in first-time new and expectant fathers (N = 121). As predicted, fathers' childhood maltreatment experiences were associated with behavioural responses; fathers who had experienced more maltreatment during their own childhood used more excessive handgrip force while listening to infant crying than fathers who had experienced less maltreatment. Additionally, the association between experienced maltreatment and handgrip force was moderated by an index of white matter integrity in the bilateral uncinate fasciculus (UF); experienced childhood maltreatment was only predictive of handgrip force during infant cry exposure in fathers with low structural integrity in the bilateral UF. Unexpectedly, we found no statistically significant relation between maltreatment exposure and white matter integrity. These results indicate that fathers who have been maltreated in their own childhood show inadequate inhibitory control over their behavioural responses and / or emotional hyperreactivity towards infant crying in the peripartum period. Moreover, this effect is only present for fathers with low structural connectivity between the prefrontal cortex and the amygdala, a tract previously found to be crucial for inhibitory control over emotionally driven responses (Depue, Orr, Smolker, Naaz, and Banich, 2016; Versace et al., 2015) as well as for resilience towards the detrimental effects of childhood maltreatment (Crone et al., 2020). Importantly, these findings suggest that detrimental behavioural effects of negative caregiving experiences are present in fathers during a period when they are (about to be) frequently exposed to infant crying. In order to develop effective early intervention programs for at-risk-parents, a more thorough understanding of the biological factors contributing to quality of paternal care is needed.

Chapter 4 - The effects of AVP on fathers' handgrip force in response to infant crying

In Chapter 4 we reported on a double-blind, placebo-controlled study using a within-subject design examining the effect of AVP administration on the use of handgrip force in response to infant crying (N = 25 first-time expectant fathers). Considering its role in protective aggression, and its involvement in social recognition and face perception, it is possible that AVP aids fathers in the evolutionary beneficial detection of kinship cues (e.g., facial resemblance). Therefore, fathers looked at morphed images representing their own infant (i.e., bearing resemblance to the father) or an unknown infant while listening to the infant cry or control sounds. We found that AVP administration led to more excessive force (a proxy for a lack of control over autonomic responses) while viewing an unknown infant image compared to viewing an image representing fathers' own infant, while the opposite was true under placebo. These findings were independent of whether images were accompanied by cry or control sounds; expectant fathers did not use more handgrip force during infant cry sounds compared to control sounds. In conclusion, these findings indicate an AVP-induced increase in protective aggressive behaviours based on preference for facial resemblance in offspring.

Chapter 5 - Prenatal Video-feedback Intervention to promote Positive Parenting (VIPP-PRE)

In Chapter 5 we reported on the development and feasibility of the first prenatal, interaction-focused parenting intervention for fathers. We developed the Prenatal Video-feedback Intervention to promote Positive Parenting (VIPP-PRE) with the aim of improving postnatal parenting quality and stimulating involvement in expectant fathers. With the use of ultrasound images, fathers-to-be interacted with their unborn children (e.g., singing, touching, reading) and were given feedback aimed at improving their ability to detect and understand their child's behavioural signals as well as reinforcing fathers' timely sensitive responses to those signals. Importantly we embedded the intervention in a large sample randomized controlled trial (RCT) examining hormonal, neural, and behavioural aspects of paternal care during the transition into fatherhood, which can shed light on the relevant processes involved in (changed) paternal caregiving behaviours. Based on the evaluation of participating fathers (N = 73 first-time expectant fathers) and sonographers, we concluded that the VIPP-PRE is feasible and is received positively by those involved, see Figure 6.1 for quotes from fathers receiving VIPP-PRE. Moreover, we found that fathers receiving the VIPP-PRE, compared to those receiving a control intervention, reported to have gained more insight into their relationship with their child, a better understanding of their child and its feelings, and more insight into their communication with their

child. The effects of VIPP-PRE on fathers' parenting sensitivity and involvement are to be reported in the near future and will guide future implementation of the intervention.

"I liked the explanation of the videos most, so that you can see what your child is doing, and understand or speculate why it's doing that. I think the bond with the baby became stronger because of that. Also, the guidance of the intervener was pleasant, everything was explained in an easy going and clear manner with lots of understanding for expectant parents."

"I liked being able to actually see the reaction of my daughter as I was playing with her. It opened a new dimension to how I play with her at home."

"Discussing the videos mainly provided a lot of insight into how important you are as father in guiding your child from the beginning of pregnancy through her development, in bonding with the father, and in being in contact with the world. I really underestimated this before these appointments."

"It was wonderful to have a moment to admire my son. To see how he reacts to my presence and to follow his development in more detail. These were precious moments to me."

"Fantastic to watch! At first I felt awkward signing to a belly while being videotaped, but eventually we had a great time. The session inspired me to read more to the baby at home and to become a member of the local library."

Figure 6.1. Quotes of fathers receiving the VIPP-PRE intervention.

Discussion

VIPP-PRE

In this thesis, we discussed the development and protocol of the first interaction-based prenatal parenting intervention for fathers, embedded in a RCT examining the neuroendocrine and behavioural modalities relevant for the transition into fatherhood (Chapter 5). Although the efficacy of the intervention (i.e., improving paternal sensitivity and involvement) has yet to be reported (preregistered here: osf.io/487xc), we found the program to be feasible, helpful, and to be associated with an

improvement in fathers' understanding of their (unborn) child. Nowadays, fathers in Western countries are more involved in parenting than ever before and are expected to participate from pregnancy onwards (Alio, Lewis, Scarborough, Harris, and Fiscella, 2013; Bakermans-Kranenburg et al., 2019). However, even willing fathers often still struggle in accessing perinatal health care and early parenting activities (Lever Taylor et al., 2018; Shorey et al., 2019; Steen et al., 2012; Widarsson et al., 2015). Additionally, fathers have fewer opportunities to bond with their child than mothers do, both during pregnancy (Van Bakel et al., 2013; Vreeswijk et al., 2014), as well as postnatally, in part due to the limited amount of parental leave fathers are offered in many countries (Moss and Deven, 2019). Prenatal paternal behaviour is known to affect child outcomes as well as fathers' postnatal parenting behaviours (e.g., Cabrera, Fagan, and Farrie, 2008; Cook et al., 2005; Fagan, Bernd, and Whiteman, 2007; Hechler, Beijers, Riksen-Walraven, and De Weerth, 2019; Zvara et al., 2013; and see Alio, Salihu, Kornosky, Richman, and Marty, 2010 and Lamb, 2004, for reviews), and the prenatal period might therefore provide an important window of opportunity for interventions aimed at long term effects on paternal behaviour and child development (Condon, Corkindale, Boyce, and Gamble, 2013). The VIPP-PRE seems an excellent candidate to improve paternal caregiving that transcends into the postnatal period, as it focusses on fathers' ability to interact with his unborn child, emphasizes the importance of his involvement for child development, and reinforces positive interactions.

Paternal hormones

AVP. Another important avenue of research we investigated surrounded some of the hormones that play a role in early paternal behaviour and brain activation. In a pilot study we explored the effects of AVP administration on first-time expectant fathers. As discussed in Chapter 4, we found that AVP administration aided the evolutionary beneficial distinction between infant with and without facial resemblance to the father (Alyousefi-van Dijk et al., 2019). In accordance with theoretical frameworks such as the Steroid-Peptide Theory (van Anders, Goldey, & Kuo, 2011), we showed that AVP administration in expectant fathers is associated with behaviours that are relevant for paternal caregiving. Likewise, others have shown similar results in different tasks (i.e., orienting gaze towards infant avatars), whereas this effect is not present in non-expectant men (Cohen-Bendahan et al., 2015). Supporting the idea that AVP is functionally related to quality of paternal care, another study found that men who show more stimulatory play with their infants have higher levels of AVP (Abraham and Feldman, 2018; Apter-Levi et al., 2014). However, not all aspects of paternal care seem to relate to higher levels of AVP, as we also found that AVP administration did not affect expressed emotion or emotional content when fathers talked about their expected child, but that the birth of fathers' first child greatly influenced the way fathers speak about their relationship with the child (Lotz et al., 2020b). Speculatively,

the administration of AVP mimics the increase of the hormone after the birth of a child (e.g., Gray et al., 2007). Possibly, the neuroendocrine system has started to prepare for functional adaptation in the prenatal period and has therefore become sensitive to certain hormone fluctuations that normally are brought on by exposure to the new-born (see also Cohen-Bendahan et al., 2015). Some controversy exists however, to which degree the found effects are due to AVP alone or by an interaction with other hormones (e.g., for a review see Storey, Alloway, and Walsh 2020). Lastly, we discovered that the effects of AVP administration on the neural processing of infant crying differed according to expectant fathers' own history of parental love withdrawal (Thijssen et al., 2018), and it might therefore be relevant to take the degree of parents' experienced maltreatment into account when examining the associations between parenting hormones, brain, and behaviour (e.g., see also Swain and Ho, 2017).

Testosterone. In Chapter 2 we discussed how baseline levels of testosterone were found to be unaffected by the birth of fathers' first child (Alyousefi-van Dijk et al., 2020), adding to the controversy in literature on the exact role of testosterone in paternal care. Although it is generally assumed that nurturing parenting behaviours, as well as the transition into fatherhood, are associated with a decrease in testosterone, the effect size is modest at best (see for meta-analyses; Grebe, Sarafin, Strenth, & Zilioli, 2019; and Meijer et al., 2019). The variation found in parenting studies focussing on testosterone might in part be due to the fact that testosterone decreases are only found when fathers are involved in child care activities (see Storey, Alloway, and Walsh 2020 for a review). Considering our specific sample and cultural setting, this explanation for an absence of testosterone decrease probably does not apply to the unchanged testosterone baseline levels in the perinatal period we found. It was concluded based on our pilot examination, that in addition to baseline levels, hormone reactivity to child signals should be added to future, well-powered, studies in the perinatal period. This suggestion was confirmed by our recent report based on a larger sample that there were no significant associations between hormonal baseline levels (i.e., testosterone and AVP) and paternal care (i.e., protective behaviour and neural response to infant threat) in new fathers (Lotz et al., 2020a). We also found no noteworthy associations between basal testosterone levels and parenting behaviours (i.e., sensitivity and handgrip force in response to infant crying) in the late prenatal and early postnatal phase (Alyousefi-van Dijk et al., 2020a). One of the few longitudinal studies on this subject also reported that the relation between testosterone and paternal quality of care might be more nuanced than commonly thought, as they found a negative relation between the rebound of paternal testosterone from 3 to 9 months postnatally and involvement, but a positive relation between this rebound and parenting quality (Corpuz, D'Alessandro, S., and Collom, 2020). Therefore, we are now well underway

to report on findings of hormonal responses to child signals (e.g., testosterone, AVP, oxytocin) in first-time fathers before and after the child's birth based on the VIPP-PRE study. In this thesis (i.e., Chapter 2) we also discussed how the association between hormones and paternal behaviour and / or neural activation in response to infant crying might not be linear and that it might be worth to look into more detailed types of coding for paternal behaviour (e.g., distinguishing irritation from apathy in insensitive parenting) when attempting to uncover hormonal mechanisms. Lastly, interactions with psychological traits (e.g., self-control), other hormones (e.g., cortisol), and context (i.e., harmonious vs. challenging situation) have been found to interact with testosterone baseline and reactivity, when examining associations with paternal quality of care (Bos et al., 2018; de Vries et al., 2019; van der Pol et al., 2019).

Paternal brain

Brain activation in response into infant signals. The second level of modalities relevant for paternal behaviour we investigated was the paternal brain. Based on our pilot study we proposed that the paternal brain demonstrates widespread activation patterns in reaction to infant crying postnatally (Chapter 2: Alyousefi-van Dijk et al., 2020a), as compared to prenatally (Khoddam et al., 2020; Thijssen et al., 2018). Unlike (biological) mothers, fathers do not undergo the physiological changes associated with pregnancy, parturition, or breastfeeding, which play a role in preparing parents for parenting behaviours. Although some preparatory biological mechanisms are detectable in expectant fathers (see also Paternal hormones), many neuroendocrine processes relevant for paternal care are thought to 'come online' after birth when fathers are able to spend time with the infant (e.g., Abraham et al., 2014). As discussed in Chapter 2, we speculate that this is the case for the paternal brain. Recently, this was partially confirmed by a study including both expectant and non-expectant males, in which it was found that most of the neural parental caregiving network is not activated in expectant fathers (as compared to non-expectant males) when they are faced with infant-interaction videos in early pregnancy (Diaz-Rojas et al., 2021). Infant-scene related activation in some areas however (i.e., inferior frontal gyrus, and the amygdala), was found to correlate with the duration of the partner's pregnancy, suggesting that there might be some level of neural adjusted to men's brain happening during pregnancy. Importantly, very little is known about the functional significance of these changes for paternal behaviour (for a review see Feldman, Braun, and Champagne, 2019). Noticeably, we found that prenatal paternal brain activation in response to infant signals does not relate strongly to paternal behaviour or testosterone levels. Likewise, others have shown that paternal neural activation in response to infant crying is not related to expectant fathers' subjective perception of these sounds (Khoddam et al., 2020). However, just as Li et al. (2018) found an association between perceived irritation and neural activation in fathers postnatally,

we detected concurrent associations between neural activation in response to infant crying and paternal behaviour after the birth of fathers' first child (Chapter 2: Alyousefi-van Dijk et al., 2020a). We hypothesize that neural processes involved in visual imagery, action preparedness, and empathy, arise in the early postnatal period for fathers, and specifically, that activation in the right precentral gyrus is functionally relevant for early postnatal parenting sensitivity in fathers. Although this hypothesis remains to be tested, it seems plausible that this specific area is involved in parenting behaviour as it is known to activate more strongly in parents compared to non-parents (Witteman et al., 2018) and it has been implicated to play a role in motion preparedness while listening to infants' distress (Bornstein et al., 2017; Messina et al., 2016). Additionally, we concluded that well-powered experimental studies are lacking in the field of paternal neurobiology (in particular those including neural activation in response to infant signals by expectant fathers), leaving researchers with many small and correlational studies with seemingly contradictory findings (N = 36 in Diaz-Rojas et al., 2021; N = 34 in Khoddam et al., 2020; and N = 39 in Li et al., 2018). We felt it was important to explicitly present our pilot data as exploratory and to provide hypotheses (rather than conclusions) based on effect sizes (rather than p-values); a methodological approach which is superior at this stage but is sadly not widely accepted (e.g., Scheel, Tiokhin, Isager, and Lakens, 2020). Ideally, the small innovative exploratory studies conducted so far, could be synthesized into a to-be-tested-theory of paternal brain activation in the perinatal period (see for a mathematical model of scientific discovery: Devezer, Nardin, Baumgaertner, and Buzbas, 2019). Unfortunately, we have stumbled upon reluctance among peer-reviewed journals to publish data without firm conclusions based on traditional null hypothesis significance testing. However, open access-based online options for sharing work are now available (e.g., PsyArXiv). Additionally, the VIPP-PRE RCT will shed more light on both the development of the neurobiology of fatherhood across the peripartum, as well as gain valuable insight into the possible workings of a parenting intervention aimed at improving parenting quality which is likely associated with neurobiological modalities such as neural reactivity to relevant stimuli.

Structural connectivity. In addition to neural activation in response to infant signals, we have included measures of neural structural connectivity (i.e., diffusion tensor imaging: DTI) in the larger samples within the Father Trials project. As a result, we were able to detect a moderating role of structural integrity in the uncinate fasciculus for the relation between fathers' experienced childhood maltreatment and behavioural responses to infant crying (Chapter 3: Alyousefi-van Dijk et al., 2020b). This finding points towards an underlying mechanism of the intergenerational transmission of suboptimal parenting. Noteworthy, although a large body of evidence suggests its existence, we did not find atypical structural connectivity in the brains of father who

had endured childhood maltreatment. Upon examining the relevant literature, we found that most studies in this field made use of pre-specified anatomical ROIs, rather than clusters resulting from statistical testing for associations with maltreatment history, when extracting DTI variables (e.g., Hanson et al., 2015; Jensen et al., 2018; McCarthy-Jones et al., 2018). Next, these DTI variables are often used in various analyses testing models including other (behavioural) data, such as was done in our analysis (Chapter 3: Alyousefi-van Dijk et al., 2020b). ROI-based testing in studies examining maltreatment effects typically examine multiple combinations of data on subgroups of participants or subscales of the used questionnaires and find many non-significant associations next to the highlighted significant ones (but see McCarthy-Jones et al., 2018 for an example of extensive corrections for the number of tests as well as a comparison between continuous and categorical assessment of maltreatment). Results from this type of analyses might not be comparable to those examining whether clusters of the brain are significantly related to maltreatment scores and then basing extraction on those results. All these ROI-based studies have in common that they did not test or report whole-brain findings, leading to some doubt over the conclusions that effects of maltreatment can be found in white matter integrity of healthy adults in whole brain analyses. Although more studies using unbiased whole-brain approaches are warranted, it is possible that a direct effect of maltreatment on the brain either does not exist in healthy adults with low levels of exposure, or that publication bias has played a role in shaping the estimated likelihood of these effects existing (for a review on researchers' degrees of freedom see: Wicherts et al., 2016). The implications for the discrepancies between data resulting from whole-brain analyses and the commonly reported significant associations between ROI-based DTI variables and overall maltreatment remain unclear. Possibly, commonly applied extensive testing on subgroups and subscales based on findings that might not be methodologically comparable has promoted the reporting of false positives. Some improvements for this field, as well as in any field within neuroimaging, might lie in open reporting and standardizing of preprocessing pipelines (e.g., Botvinik-Nezer et al., 2020), using multiverse analyses (e.g., Dafflon et al., 2020), or including raw data in meta-analyses (e.g. as was done in Witteman et al., 2019).

Paternal behaviour

The third level and final level of paternal neurobiology that was of interest for this thesis was fathers' behaviour. We conducted correlational research in our pilot study by exploring associations between behavioural responses to infant crying by means of the handgrip paradigm as well as observing paternal sensitivity using an infant simulator, and other neurobiological factors before and after the birth of a first child (Alyousefi-van Dijk et al., 2020a). Although both behavioural constructs were found to be rather stable throughout the peripartum, concurrent associations (e.g., with

neural activations to the same stimuli) arose only in the early postnatal period. This finding points towards the importance of controlling for parental status (e.g., early, middle or late pregnancy, early postnatal period, etc.) in neurobiological studies, as the unaccounted heterogeneity in samples has likely contributed to contradictory findings.

Handgrip paradigm. In Chapter 3 we reported that fathers' experience of maltreatment is associated with less inhibitory control and / or insufficient emotional regulation when exposed to infant cry sounds (Alyousefi-van Dijk et al., 2020b). This finding in expectant and new fathers is relevant as the use of excessive handgrip force indicates a risk for perpetuating child maltreatment in response to infant distress (Bakermans-Kranenburg et al., 2012; Compier-de Block et al., 2015; Crouch et al., 2008). Recently, researchers using the same handgrip paradigm design have claimed that the absence of a robust difference in handgrip force during cry versus control sounds casts doubt on the usefulness or even validity of this instrument (Hechler, Beijers, Riksen-Walraven, and de Weerth, 2019; Khoddam et al., 2020). Although we have also noted that handgrip force applied by fathers does not seem to differ significantly while listening to cry versus control sounds (Alyousefi-van Dijk et al., 2019), the force in both conditions is not so highly correlated that there is merely measurement error left when controlling for the control sound in calculating the force applied during infant crying. We conclude that this instrument is of value since the handgrip response to infant crying, which has been corrected for the response to a neutral aversive control sound (a strategy adopted from Buisman et al., 2018), has been found to relate to important paternal care parameters (Alyousefi-van Dijk et al., 2020a; Alyousefi-van Dijk et al., 2020b).

Parenting sensitivity. As the modality closest to real-life parenting behaviours, we assessed paternal sensitivity using the Leiden Infant Simulator Assessment (Voorthuis et al., 2013). The first of the two main findings in regards to sensitivity discussed in this thesis is the stability of paternal sensitivity from late pregnancy to the early postnatal period (Chapter 2: Alyousefi-van Dijk et al., 2020a). Similarly, others have found prenatal sensitivity in fathers to predict postnatal sensitivity (Hechler et al., 2019). These findings indicate that intervening prenatally in fathers could be beneficial for postnatal parenting quality. Our second finding in relation to paternal sensitivity is that, unlike in the prenatal period, postnatal parenting sensitivity is strongly associated with neural activation in the right precentral gyrus during exposure to infant crying (Chapter 2: Alyousefi-van Dijk et al., 2020a, see also Paternal brain). With the VIPP-PRE intervention we aim to improve postnatal paternal sensitivity as observed while fathers interact with their own infant (for the intervention protocol see Chapter 5: Alyousefi-van Dijk et al., 2021).

Limitations

Several limitations to the work presented here should be noted. Firstly, the results based on our pilot examination (Chapters 2 and 4) are based on small samples. These studies were intended as exploratory examinations aiding to the formulation of hypotheses for larger future studies and should be interpretated in that light. Secondly, our samples of fathers are likely not representative of the general population or of the subgroups of fathers that might need or benefit from the VIPP-PRE intervening the most. Given the fact that pilot study (Chapters 2 and 4), and in particular the VIPP-PRE RCT (Chapters 3 and 5), required fathers to invest large amounts of time, and our recruitment strategy was passive (i.e., fathers had to contact us) we most likely recruited highly involved and motivated fathers. If the VIPP-PRE is proven to be effective in this particular sample, the next step would be to look at samples where the intervention should and could be applied, such as those struggling with perinatal mental health issues, or subgroups at increased risk of committing child maltreatment. Lastly, our studies did not include a non-expectant or non-fathers control group. We therefore cannot exclude that some of the found effects were due to repeating measurements in the same sample (Chapter 2), or were not exclusive to fathers (to-be) (Chapter3).

Conclusions and future directions

Although fathers are now included into parenting research more often than ever before, most of parenting research still focus on mothers only (for a review see Cabrera, 2020). Importantly, both mothers and fathers often experience the transition into parenthood as stressful, negatively impacting their wellbeing (e.g., Nelson, Kushlev, and Lyubomirsky, 2014). Unlike mothers however, fathers have little access to support within perinatal healthcare and parenting resources (e.g., Deave and Johnson, 2008; Palsson, Persson, Ekelin, Kristensson Hallstrom, and Kvist, 2017). A difficult transition into parenthood can affect fathers' mental health, a problem which frequently goes undetected and untreated (for a review about fathers' mental health see Bruno et al., 2020). Mental and emotional well-being of fathers in turn affects their capacity to provide appropriate care at a time when the infant is in great need of physical and emotional support from its caregivers (for a recent meta-analysis on fathers' effect on child development see Rodrigues et al., 2021). Within Father Trials, we aimed to put fathers at the heart of a parenting study investigating several modalities of parental care. We have shown that some of the neuroendocrine changes fathers experience after their first child is born relate to their parenting quality, and that to some extent, their parenting behaviours are under hormonal control, even during pregnancy. Additionally, our findings emphasize the effect of fathers'

own childhood experiences on his responses to infants' distress, and that this effect is dependant on fathers brain anatomy. Lastly, we developed a prenatal parenting intervention aimed at improving fathers' postnatal quality and quantity. If shown to be effective, this intervention might be of particular interest for those fathers struggling with the adjustment to parenthood. By conducting intervention studies, we will be able to discover more about the causality of neuroendocrine and behavioural processes in paternal care.

Another important area of future research exploring fatherhood lies within redefining and adjusting our measurements of parenting where needed (for a review see Volling and Cabrera, 2019). For example, beyond parenting quality measured as observed sensitivity, other behavioural aspects (e.g., stimulatory play, protective behaviours) are thought to be of particular interest in the father-child relationship (e.g., Van Bakel and Hall, 2020). Hormonal studies should take into account the relevant interactions between various paternal hormones as well as reactivity of these hormones to child stimuli or interactions. Also, relevant control groups are often missing. In order to uncover the neural and hormonal reactivity patterns relevant for paternal behaviour, future studies should adopt longitudinal designs, including pre-conception couples (such as was done for fathers' brain structure across the peripartum: Paternina-Die et al., 2020).

Lastly, as noted by others (Cabrera, 2020), the level and nature of fathers' involvement with his children should be taken into account. Despite the fact that fathers' ability to take parental leave facilitates his involvement in childcare, even after returning back to work (e.g., Tamm, 2019), Dutch fathers are given merely five days paid leave in this vital period of parenting and child development. However, in 2020 paternal leave was extended in the Netherlands, with an additional five weeks being offered during which fathers receive 70% of their salary through social security. Future studies should investigate further how the birth of a child (and importantly: time spent with the infant) affects all modalities of paternal care. This will provide a basis for a discussion on how much time men should be given to adjust to fatherhood and to form adequate father-child relationships (e.g., see also Storey, Alloway, and Walsh 2020).

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Supplemental Materials

Chapter 2 - Alyousefi-van Dijk, K., Thijssen, S., van 't Veer, A. E., Buisman, R. S. M., van IJzendoorn, M. H., & Bakermans-Kranenburg, M. J. (2020, July 7). Exploring the transition into fatherhood: behavioral, hormonal, and neural underpinnings of responses to infant crying. PsyArXiv. https:/doi.org/10.31234/osf.io/5bxk9

Neural assessment

fMRI cry paradigm. The neural data described here stems from a fMRI paradigm designed to investigate the effect of contextual information associated with cry sounds. To this end, contextual information (i.e. 'this infant is sick', 'this infant is bored', or 'this is an infant') was presented as a white text on a black screen for a duration of 2 s. For the purpose of this study, only neutral trials (i.e. cry sounds associated with the sentence 'this is an infant') were analyzed. Control sounds were presented as the sound of a saw (i.e. 'this is a saw'). After the presentation of the labeled cry sounds, a fixation crosshair was shown for 500 ms followed by the auditory stimulus that lasted 10 s, while the fixation crosshair remained on the screen. Trials were separated by an inter stimulus interval (ISI) of variable length ranging from 4.5–5.5 s. The fixation cross remained visible during the ISI. Participants received one of four pre-programmed semi-random orders. Three separate infant cry sounds were presented four times with each of the three contextual information labels. Three corresponding control sounds were also presented four times, leading to a total of 48 trials. The task was programmed in E-Prime (Schneider et al., 2002). A projector outside of the MRI suite was used to display the task on a large screen located at the back of the MRI bore, that was viewable through a mirror mounted on the top of the head coil. All responses were registered using a fiber optic response box (Current Designs, Philadelphia, PA, USA).

A total of three cry sounds were used from two infants; one male (two sounds) and one female (one sound) recorded with a TasCam DR-05 solid state recorder with a 44.1 Khz sampling rate and 16 bit. All sounds were recorded within the first two postnatal days. Individual sounds were scaled, the intensity was normalized to the same mean intensity and sounds were edited using PRAAT software (version 6.0; Boersma & Weenink, 2017). For each cry sound a neutral auditory control stimulus was created by calculating the average spectral density over the entire duration of the original sound. A continuous sound of equal duration was re-synthesized from the average spectral density and amplitude modulated by the amplitude envelope, extracted from

the original sound. After this procedure, all auditory stimuli and control stimuli were intensity matched. Using this procedure, the neutral auditory control stimuli were identical to the original auditory stimuli in terms of duration, intensity, spectral content, and amplitude envelope, but lacking the emotional meaning associated with a cry sound.

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)= 9.7 ms, echo time (TE) = 4.6 ms, flip angle = 8°, 140 transverse slices, voxel size 0.875 × 0.875 × 1.2 mm). The fMRI-task utilized a gradient-echo blood oxygen level dependent (BOLD) echo-planar imaging sequence with: TR = 2200 ms, TE = 30 ms, flip angle = 80°, 38 transverse slices, and voxel resolution of 2.75 × 2.75 × 3.025 mm (including a 10% interslice gap). The duration of the fMRI paradigm was 14 min 19 s (387 volumes). Participants listened to the cry and control sounds through MRI-compatible headphones.

fMRI preprocessing. Preprocessing and statistical analysis of the imaging data were performed using fMRI of Brain (FMRIB) Software Library (FSL, version 5.0.9; Jenkinson et al., 2012; Smith et al., 2004). Brain extraction was performed via BET (Brain Extraction Tool), and motion correction using MCFLIRT (Motion Correction FMRIB's Linear Image Registration Tool). Spatial smoothing was applied with a Gaussian kernel of 5 mm (FWHM). FMRI data from each participant were registered to their own high resolution T1 image (boundary-based registration (BBR, Greve and Fischl, 2009), 90 degree search) and then spatially normalized to MNI (Montreal Neurological Institute) space (12 degrees of freedom (DOF), 90 degree search) using FSL's FLIRT registration tool.

fMRI statistical analysis. After preprocessing, statistical analyses were performed at the single-subject level using the general linear model (GLM) within FSL's FEAT (FMRI Expert Analysis Tool). For each of the labelled sounds (i.e. infant cry labeled 'this is an infant' and a scrambled control sound labeled 'this is a saw'), temporal derivatives were added to the model, as well as both standard motion parameters and additional motion confound EVs as obtained from fsl_motion_outliers (DVARS, http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSLMotionOutliers) to address common problems resulting from motion (Power et al., 2012). In a group-level analysis, we tested the difference between cry sounds and control sounds to assess the regions involved in the processing of infant crying in both the prenatal and postnatal visit.

For all comparisons of interest, both positive and negative t-tests were performed as well as an overarching F-test to account for two-sided testing. Due to the exploratory nature of the study, statistical maps were thresholded using clusters determined by $Z > 2.3$ and a cluster corrected significance threshold of $p < .05$. Only significant results of the F-test are reported. Using Featquery, individual mean Z values were extracted for all significant clusters found in the higher level feat analysis. See Thijssen et al. (2018) for details of the analytic protocol for the prenatal placebo visit which was also used for the postnatal visit.

Behavioral assessments

Handgrip cry paradigm. Participants were exposed to infant crying and images representing either their own or an unknown infant, while they were asked to squeeze a handgrip dynamometer. During the task participants were seated in front of a computer screen wearing headphones while holding a dynamometer in their dominant hand. During an initial training period (typically lasting a 1-2 minutes) without cry sounds or images, participants were asked to squeeze the handgrip dynamometer at full and half strength while they received feedback from a monitor indicating the strength they used graphically. Once participants could accurately alternate between full and half strength (half strength being approximately 50% of the strength used at full strength), the monitor was turned away and the actual task without feedback on performance began.

In order to create suitable infant images for the handgrip paradigm, pictures of the participant and that of an unknown man were morphed with the image of an average infant image. Participants either provided a full-color digital photograph of themselves prior to the first session, or a picture was taken at the beginning of the first visit. The participant's picture met the following criteria: it showed their face, en face, with a neutral expression, without piercings, make-up, or glasses, on a light and neutral background. Photographs were edited using Adobe Photoshop CS in order to remove unwanted facial features (e.g. facial hair). Subsequently, morphed images representing participant's own infant were created by combining 75% of an average infant image (created by the authors of Hahn, DeBruine, Fischer, & Jones, 2015, from 10 female and 10 male infant faces) and 25% of participant's own picture, using Fantamorph 5 Deluxe (www.fantamorph.com). Similarly, the morphed image of an unknown infant was created by combining 75% of the average infant image and 25% of a male unknown to the participants, after which all images were resized to 640x480 pixels. The decision to include images of 'own' and 'unknown' infants' was based on the theory of evolutionary psychology that states that perceived genetic relationships influence paternal behavior, with closer genetic relationships supposed to enhance paternal investment in children. This was particularly relevant in assessing the effects

of threat to infant (see Van 't Veer et al., 2019) and the effects of vasopressin on used handgrip force (see Alyousefi-van Dijk et al., 2019). Finally, images were masked with a black face contour. Participants were familiarized with their morphed own infant image before onset of the task with the explanation that a future infant of theirs might look similar to this image. Cry and scrambled control sounds used in the handgrip cry paradigm were identical to those used in the fMRI task.

The task was administered using E-Prime software (version 2.0; Psychology Software Tools, Inc., PA, USA) and hand squeeze intensities (in kg) were transferred directly from the dynamometer to AcqKnowledge software (version 4.3.1; Biopac Systems, 2004). First, a baseline measure was administered consisting of three maximum strength trials each followed by a half strength trials. Then, four conditions of three max-half trials were randomly presented; 1) viewing a morphed image of own infant while listening to control sounds (Own Neutral); 2) viewing a morphed image of own infant while listening to cry sounds (Own Cry); 3) viewing a morphed image of an unknown infant while listening to control sounds (Other Neutral); 4) viewing a morphed image of an unknown infant while listening to cry sounds (Other Cry). Sounds and images were presented throughout each trial lasting 12 s. Eight seconds after the beginning of each trial, participants were prompted to squeeze maximally (instructions displayed for 1 s). After an interval of 2 s, participants were prompted to squeeze at half strength (instructions were displayed for 1 s). A fixation cross was shown for 3 s between each trial.

Similar to previous studies (Bakermans-Kranenburg et al., 2012; Compier-de Block et al., 2015; Riem et al., 2012), grip strength modulation was calculated by dividing half-strength squeeze intensity by the preceding full-strength squeeze intensity, meaning that scores of over .50 indicated excessive force on the half-strength squeeze attempt. Matlab (version 8.0.0.783, Mathworks, MA, USA) was used to identify peak intensities for each squeeze. Handgrip force measures have previously been shown to be reliable in all four conditions across the prenatal visits (Alyousefi-van Dijk et al., 2019). For the postnatal visit, handgrip force measures were also found to be reliable (αrange = .63 - .81). Therefore, for both prenatal and postnatal measures, the three trials per condition were averaged as indicators of handgrip force in each condition. There was no main effect of infant image presented on handgrip force during the prenatal placebo visit (Alyousefi-van Dijk et al., 2019) or the postnatal visit (unknown vs. own infant image, $F[1,19 = 0.56, p = .46, \eta p2 = .03]$. Therefore, the own and unknown infant trials were taken together for the purpose of the analyses described here.

In order to create one value representing the cry-control sound contrast, a residualized change score (see also Buisman et al., 2019) was calculated by residualizing the squeeze during cry trials for the squeeze during control trials, for both prenatal and postnatal measurements. Residualized change scores were created in order to avoid issues associated with difference scores (MacKinnon, 2012). Due to high correlations between mean handgrip force ratios for neutral and cry sounds for both prenatal and postnatal measurements (i.e. r = .89 and r = .71 respectively), we examined the robustness of the residualized change scores (see also Buisman et al., 2019). We found that the use of residualized change scores (versus the use of raw handgrip force) did not affect results and these were therefore used in further analyses.

Statistical analyses

Shapiro-Wilk tests indicated that all variables were normally distributed, except for postnatal mean Z values in the left corona radiate and the bilateral auditory cortex (p = .01 and .01 resp.) see Table 2.1 in the supplement. For these variables standardized kurtosis and skewness were checked and they were in the normal range. Postnatal mean Z values in the left supracalcarine cortex were also not normally distributed (p < .00), and although data were not particularly skewed, we found a problematic kurtosis (i.e. kurtosis / SE kurtosis = 5.4). No outliers (i.e. Z score of < -3.29 or > 3.29) were found in any of the variables.

Supplementary Table 2.1. Descriptives for all variables, including results of normality tests.

	N	M(SD)	Min	Max	Shapiro-Wilk Sig.	Standardized skewness	Standardized kurtosis
Testosterone baseline							
Pre (pg/ml)	25	54.11 (21.90)	25.35	112.00	0.11	2.26	0.89
Post (pg/ml)	20	47.95 (10.78)	34.20	76.90	0.08	-1.80	1.15
Neural activation							
Pre bi PCC (mean Z)	25	0.74 (0.75)	-1.13	2.32	0.27	-0.74	0.51
Pre l auditory cortex (mean Z)	25	1.33 (1.08)	-0.39	2.93	0.21	-0.26	-1.32
Pre r auditory cortex (mean Z)	25	1.33 (0.87)	-0.06	3.65	0.56	1.24	0.89
Pre bi auditory cortex (mean Z)	25	1.33 (0.93)	-0.14	3.06	0.71	0.07	-0.99
Post midbrain (mean Z)	19	0.62 (0.11)	0.37	0.84	0.82	-0.52	0.88
Post l auditory cortex (mean Z)	19	0.71 (0.55)	-0.16	1.58	0.04*	0.25	-1.56
Post r auditory cortext (mean Z)	19	0.80 (0.66)	-0.06	1.73	0.00*	0.40	-1.83
Post bi auditory cortex (mean Z)	19	0.75 (0.60)	-0.11	1.60	0.01*	0.37	-1.79
Post l supraCal cortex (mean Z)	19	0.65 (0.29)	-0.29	1.04	0.00*	-3.42	5.46
Post r precentral gyrus (mean Z)	19	0.65 (0.39)	-0.28	1.18	0.10	-1.98	0.81
Post r body and splenium of CC (mean Z)	19	0.74 (0.19)	0.39	1.02	0.05	-1.29	-0.75
Post l ant CorRad (mean Z)*	19	0.89 (0.59)	0.15	1.82	0.01	0.27	-1.79
Handgrip force							
Pre control sound (ratio)	25	0.63 (0.12)	0.33	0.86	0.75	-0.30	0.19
Pre cry sound (ratio)	25	0.64 (0.12)	0.37	0.86	0.75	-0.15	-0.21
Post control sound (ratio)	20	0.63 (0.10)	0.45	0.79	0.32	-1.08	-0.24
Post cry sound (ratio)	20	0.63 (0.09)	0.44	0.81	1.00	0.16	-0.13
Pre (cry ratio corrected for neutral)	25	0.00 (0.98)	-2.07	1.66	0.74	-0.50	-0.14
Post (cry ratio corrected for neutral)	20	0.00 (0.97)	-2.25	1.78	0.99	-0.55	0.17
Parental sensitivity							
Pre (score 1-10)	25	5.40 (1.67)	2.00	8.50	0.28	-0.5	0.26
Post (score 1-10)	20	5.88 (1.60)	3.00	8.50	0.47	-0.57	-0.85

Note. Pre = prenatal, Post = postnatal, bi = bilateral, l = left, r = right, antCorRad = anterior corona radiata, CC = corpus callosum, supraCal cortex = supracalcarine cortex, * = significant

Supplementary Table 2.2. Correlations (Pearson's *r*) between postnatal parental sensitivity and all other measures for both the raw scores (i.e. not imputed) and adjusted scores (i.e. imputed for $n = 1$).

		Postnatal parental sensitivity (not imputed)	Postnatal parental sensitivity (imputed)
Prenatal parental sensitivity	*r*	.53	.53
	n	19	20
Prenatal T baseline	*r*	.19	.15
	n	19	20
Postnatal T baseline	*r*	-.13	-.13
	n	19	20
Prenatal handgrip force	*r*	-.09	-.08
	n	19	20
Postnatal handgrip force	*r*	.08	.09
	n	19	20
Prenatal bi PCC	*r*	.43	.43
	n	19	20
Prenatal bi auditory cortex	*r*	-.23	-.23
	n	19	20
Postnatal l ant CorRad	*r*	.24	.25
	n	18	19
Postnatal r body and splenium of CC	*r*	.32	.31
	n	18	19
Postnatal r precentral gyrus	*r*	.60	.60
	n	18	19
Postnatal l supraCal cortex	*r*	-.45	-.45
	n	18	19
Postnatal midbrain	*r*	.06	.05
	n	18	19
Postnatal bi auditory cortex	*r*	-.36	-.36
	n	18	19

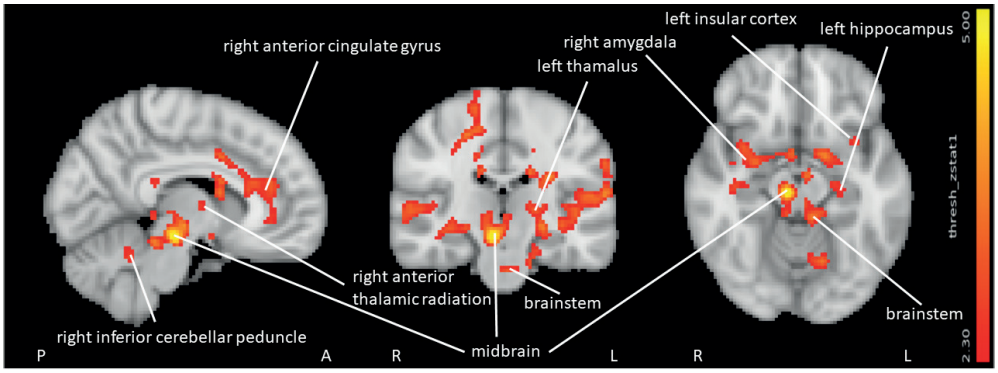
Note. T = testosterone, bi = bilateral, l = left, r = right, antCorRad = anterior corona radiata, CC = corpus callosum, supraCal cortex = supracalcarine cortex.

Supplementary Table 2.3. Results of neural activations for the postnatal contrast between infant cry sounds and scrambled control sounds (n = 19).

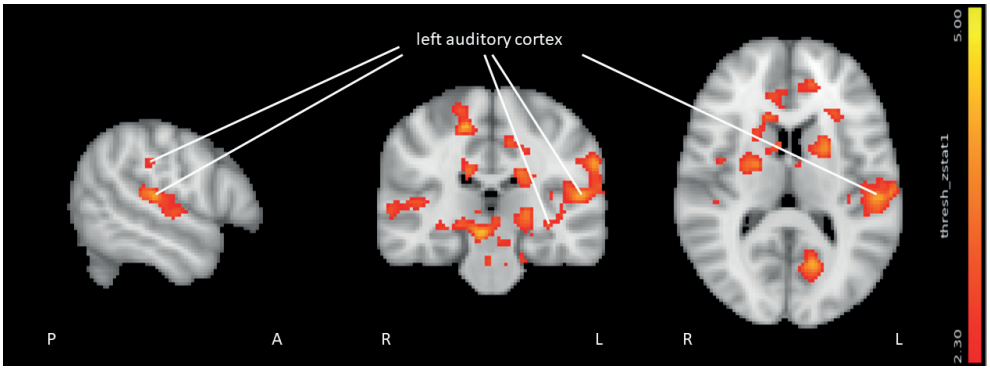
Cluster number	Region	Cluster size	MNI coordinates (mm)			*z*	*p* (corr.)
			x	y	z		
7	R Brainstem	6870	8	-22	-14	5.14	<.001
	L Anterior limb of internal capsule		-22	0	18	4.58	
	R Body of corpus callosum		16	16	20	4.48	
	L Body of corpus callosum		-10	-12	24	4.41	
	Central brainstem		0	-38	-2	4.16	
	L Middle cerebellar peduncle		-18	-34	-32	4.06	
6	L Parietal operculum cortex	1090	-54	-26	12	4.06	<.001
	L Supramarginal Gyrus, anterior division		-62	-28	32	4.05	
	L Planum polare		-48	-18	2	3.91	
	L Central Opercular Cortex		-64	-20	14	3.76	
	L WM/Planum polare		-34	-24	-6	3.35	
	L Supramarginal Gyrus, anterior division		-66	-28	18	3.12	
5	L Supracalcarine Cortex	651	-14	-66	14	4.22	<.001
	L Precuneous Cortex		-14	-66	20	3.94	
	L Posterior corona radiata		-22	-44	32	3.65	
	L Posterior corona radiata		-28	-54	22	3.08	
	L Supracalcarine cortex		-24	-60	22	3.06	
	L Cuneal cortex		-4	-74	26	3.05	
4	R Central Opercular Cortex	490	46	-4	4	3.57	<.001
	R Planum temporale		60	-18	2	3.56	
	R Planum temporale		54	-24	6	3.18	
	R Planum temporale / Heschl's Gyrus		44	-28	8	3.12	
	R Insular cortex		42	-10	-4	2.97	
	R Heschl's Gyrus		46	-20	4	2.9	
3	WM / R Precentral gyrus	350	16	-26	54	4.26	.002
	WM / R Precentral gyrus		24	-20	50	3.75	
	R Precentral gyrus		18	-20	66	3.48	
	R Precentral gyrus		20	-26	64	3.07	
	WM / R Precentral gyrus		30	-22	42	2.78	
	R Postcentral gyrus		16	-30	68	2.61	

2	R Body of the corpus callosum	327	14	-6	30	4.12	.004
	R Body of the corpus callosum		14	-24	28	3.47	
	R Splenium of the corpus callosum		12	-36	22	3.39	
	R Body of the corpus callosum		18	-22	36	2.86	
	R Splenium of the corpus callosum		6	-34	18	2.66	
	R Posterior corona radiata		26	-34	22	2.55	
1	L Anterior corona radiata	260	-22	24	26	3.99	.016
	L Anterior corona radiata		-20	22	34	3.89	
	L Frontal operculum cortex		-30	26	10	3.21	
	L Frontal Operculum Cortex		-32	30	6	2.9	

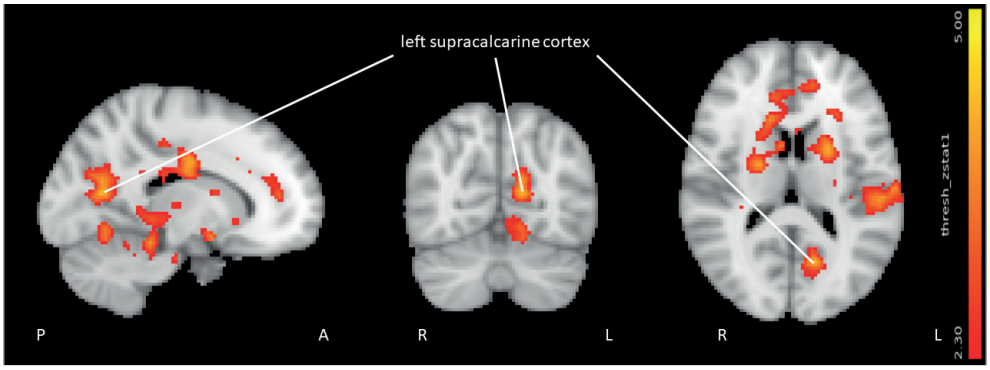
Note. Table displays the most significant voxels per contrast and is not a conclusive list of significant regions.



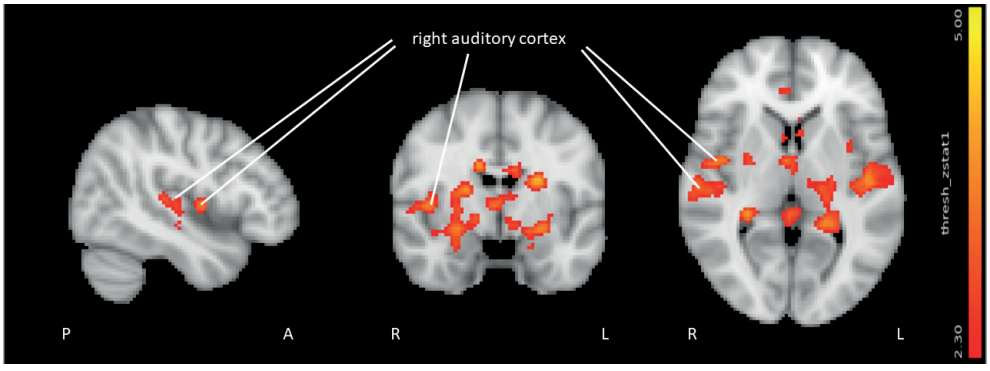
Supplementary Figure 2.1. First cluster in postnatal neural correlates of infant crying versus scrambled control sounds; spanning several distinct brain regions, including, but not limited to, the midbrain (containing the highest levels of activation), left paracingulate gyrus, bilateral anterior cingulate cortex, body and genu of the corpus callosum, left accumbens, bilateral caudates, bilateral insular cortices, bilateral amygdalae, bilateral thalami, bilateral hippocampi, left precentral gyrus, bilateral superior cerebellar peduncles, and left lingual gyrus. Indicated here are several areas within this cluster.



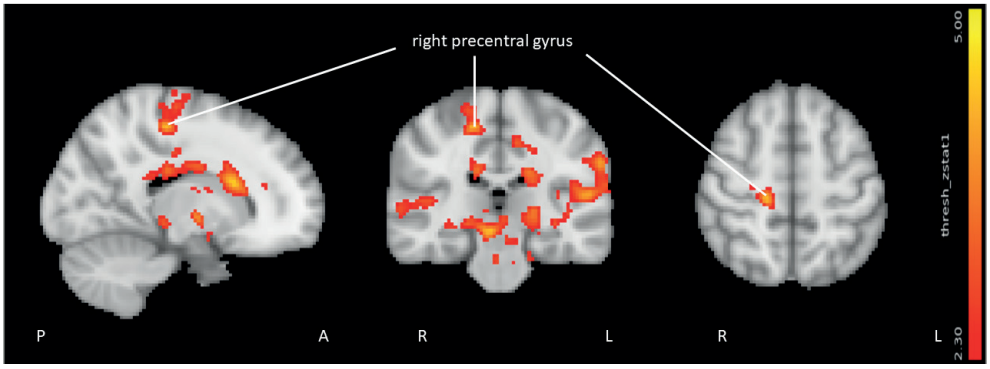
Supplementary Figure 2.2. Second cluster in postnatal neural correlates of infant crying versus scrambled control sounds; corresponding to the left auditory cortex (including the parietal operculum cortex, supramarginal gyrus, and planum polare), also extending slightly into the insular cortex. Indicated here are several areas within this cluster.



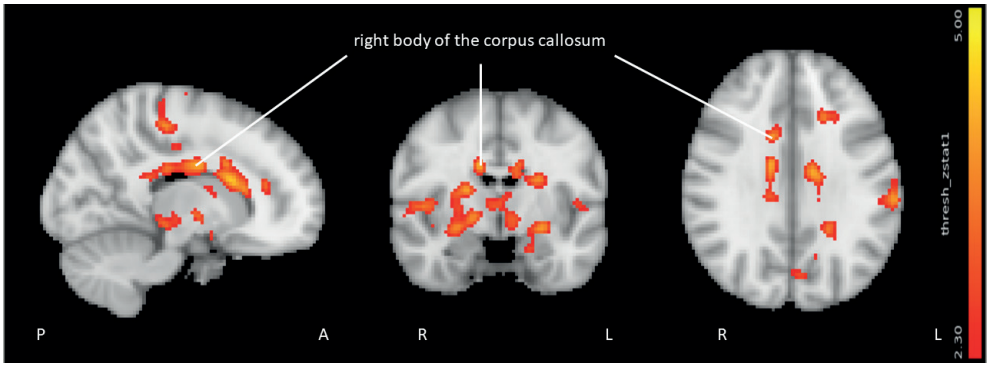
Supplementary Figure 2.3. Third cluster in postnatal neural correlates of infant crying versus scrambled control sounds; corresponding to the left supracalcarine cortex bordering on the cuneal and precuneous cortex. Indicated here is the Z-max location.



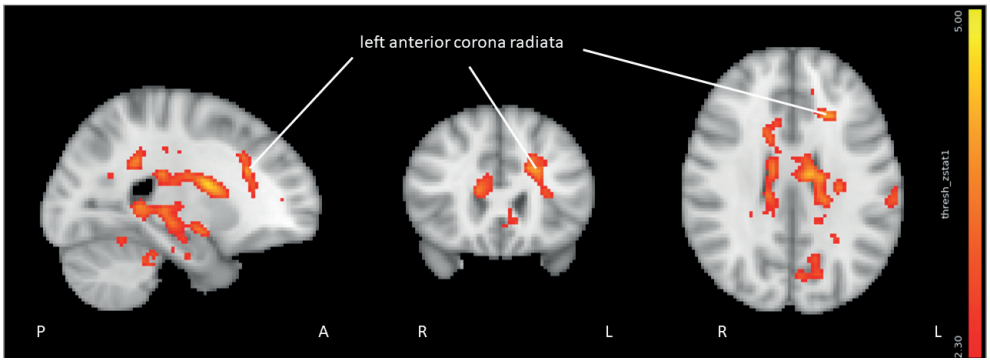
Supplementary Figure 2.4. Fourth cluster in postnatal neural correlates of infant crying versus scrambled control sounds; corresponding to the right auditory cortex (including the central opercular cortex, planum temporale, and Heschl's gyrus) extending also into the insular cortex. Indicated here are several areas within this cluster.



Supplementary Figure 2.5. Fifth cluster in postnatal neural correlates of infant crying versus scrambled control sounds; corresponding to the right precentral gyrus extending slightly into the right postcentral gyrus as well as ventrally into the right superior longitudinal fasciculus and corticospinal tract. Indicated here is the Z-max location.



Supplementary Figure 2.6. Sixth cluster in postnatal neural correlates of infant crying versus scrambled control sounds; corresponding to the right body and splenium of the corpus callosum extending into the right posterior corona radiata and retrolenticular part of internal capsule. Indicated here is the Z-max location.



Supplementary Figure 2.7. Seventh cluster in postnatal neural correlates of infant crying versus scrambled control sounds; corresponding to the left anterior corona radiata descending into the left frontal operculum cortex. Depicted here is the Z-max location.

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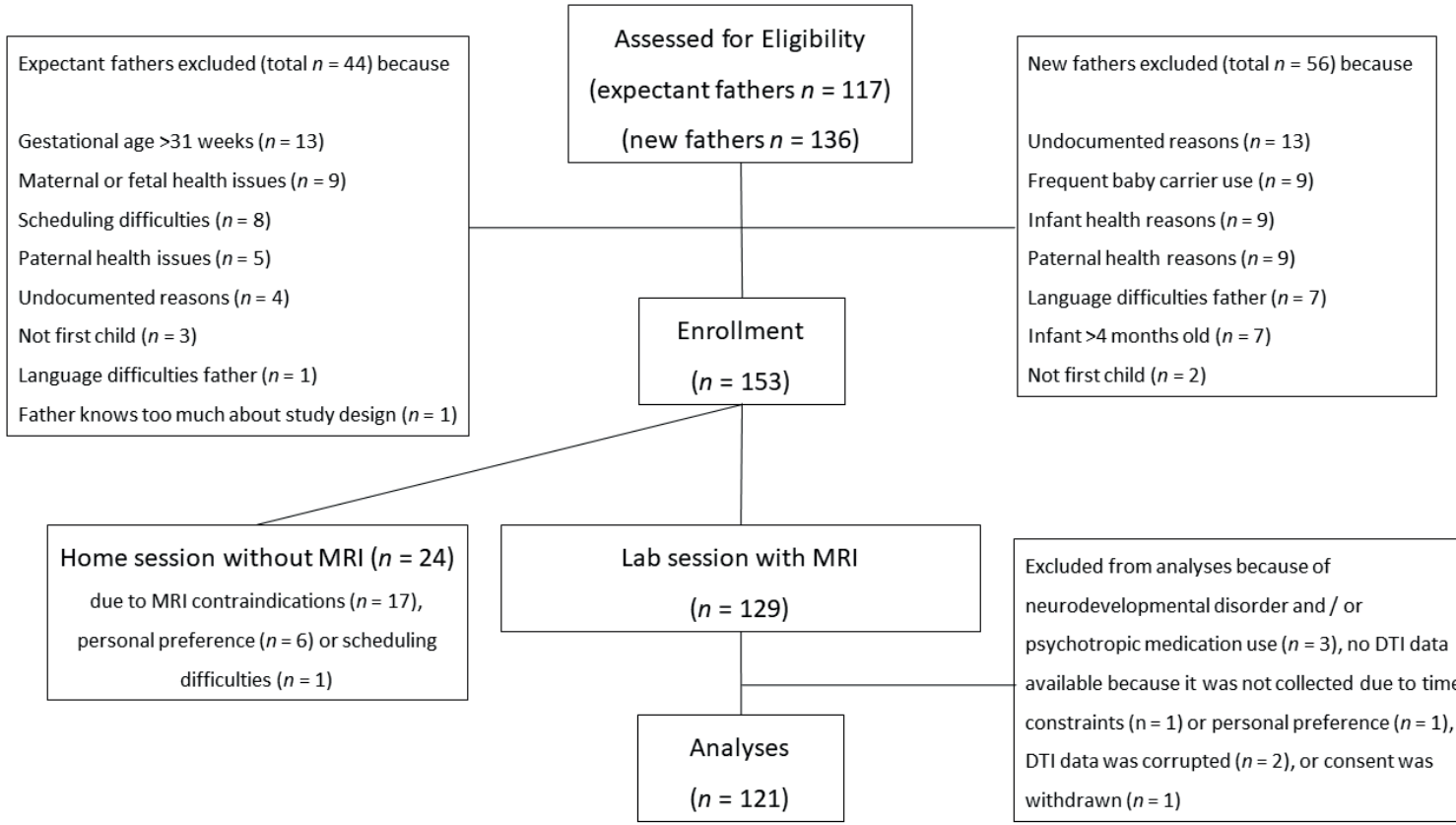

Supplementary Figure 3.1. Flow chart depicting numbers for participant enrolment, allocation, and data analysis.

Supplementary Table 3.1. Correlations of the observed variables in the non-imputed dataset.

		Age	Edu	EPDS	Maltr	HG	CC	Bi cingulum	Bi inf FOF LF	Bi sup FOF	Bi sup LF	Bi UF
Age	r		-0.04	-0.07	0.08	-0.05	-0.08	0.02	-0.06	-0.14	-0.19*	0.01
	N		120	116	116	118	121	121	121	121	121	121
Edu	*r*			0.03	-0.18	0.15	-0.04	0.01	-0.03	-0.01	-0.08	-0.08
	N			116	116	118	120	120	120	120	120	120
EPDS	*r*				0.15	0.01	0.09	0.08	0.05	0.03	0.07	-0.12
	N				116	114	116	116	116	116	116	116
Maltr	*r*					0.22*	0.04	0.00	0.11	-0.04	-0.09	0.01
	N					114	116	116	116	116	116	116
HG	*r*						-0.06	0.01	-0.01	-0.07	0.08	0.00
	N						118	118	118	118	118	118
CC	*r*							0.64**	0.57**	0.48**	0.57**	0.43**
	N							121	121	121	121	121
Bi cingulum	*r*								0.52**	0.38**	0.49**	0.40**
	N								121	121	121	121
Bi inf FOF LF	*r*									0.41**	0.45**	0.36**
	N									121	121	121
Bi sup FOF	*r*										0.43**	0.26**
	N										121	121
Bi sup LF	*r*											0.38**
	N											121
Bi UF	*r*											
	N											

Note. Edu = educational level, EPDS = Edinburgh Postnatal Depression Scale, Maltr = experienced childhood maltreatment, HG = residualized handgrip force ratio, CC = corpus callosum, Bi = bilateral, inf = inferior, FOF = fronto-occipital fasciculus, LF = longitudinal fasciculus, sup = superior UF = uncinate fasciculus, * = p<.05 (2-tailed), ** = p<.01 (2-tailed)

Supplementary Table 3.2. Results for the exploratory moderation analyses in the non-imputed dataset for the UF (N = 113), testing direct effects of white matter integrity (i.e., mean skeletonized FA values) on handgrip force in reaction to infant crying, as well as interaction effects with experienced maltreatment scores on handgrip force.

	B (SE)	*t*	*p*	*CI*
Constant	0.00 (0.09)	-0.04	.97	[-0.18, 0.17]
Age	0.00 (0.02)	0.06	.95	[-0.04, 0.05]
Edu	0.10 (0.05)	1.91	.06	[0.00, 0.21]
EPDS	-0.02 (0.03)	-0.52	.60	[-0.07, 0.04]
Maltreatment	0.28 (0.11)	2.66	.01	[0.07, 0.49]
Bi UF	-0.54 (2.70)	-0.20	.84	[-5.90, 4.82]
Bi UF x Maltreatment	-8.38 (3.01)	-2.78	.01	[-14.35, -2.41]

Note. Edu = Educational level, EPDS = Edinburgh Postnatal Depression Scale, Bi = bilateral, UF = uncinate fasciculus

Supplementary Table 3.3. Pooled results for the exploratory moderation analyses for the UF in expectant fathers only (N = 57), testing direct effects of white matter integrity (i.e., mean skeletonized FA values) on handgrip force in reaction to infant crying, as well as interaction effects with experienced maltreatment scores on handgrip force.

	B (SE)	*t*	*p*	*CI*
Constant	0.07 (0.14)	0.52	.60	[-0.20, 0.34]
Age	-0.02 (0.05)	-0.46	.65	[-0.12, 0.07]
Edu	0.12 (0.10)	1.15	.25	[-0.08, 0.31]
EPDS	0.01 (0.04)	0.16	.87	[-0.08, 0.09]
Maltreatment	0.32 (0.17)	1.91	.06	[-0.01, 0.66]
Bi UF	1.83 (4.21)	0.43	.66	[-6.43, 10.08]
Bi UF x Maltreatment	-5.71 (6.04)	-0.94	.34	[-17.55, 6.14]

Note. Edu = Educational level, EPDS = Edinburgh Postnatal Depression Scale, Bi = bilateral, UF = uncinate fasciculus

Supplementary Table 3.4. Pooled results for the exploratory moderation analyses for the UF in new fathers only (*N* = 64), testing direct effects of white matter integrity (i.e., mean skeletonized FA values) on handgrip force in reaction to infant crying, as well as interaction effects with experienced maltreatment scores on handgrip force.

	B (SE)	***t***	***p***	***CI***
Constant	-0.05 (0.13)	-0.35	.73	[-0.30, 0.21]
Age	-0.01 (0.03)	-0.23	.82	[-0.06, 0.05]
Edu	0.11 (0.07)	1.45	.15	[-0.04, 0.25]
EPDS	-0.04 (0.04)	-0.79	.43	[-0.12, 0.05]
Maltreatment	0.28 (0.16)	1.77	.08	[-0.03, 0.59]
Bi UF	-1.63 (4.15)	-0.39	.70	[-9.77, 6.52]
Bi UF x Maltreatment	-8.40 (3.81)	-2.21	.03	[-15.86, -0.94]

Note. Edu = Educational level, EPDS = Edinburgh Postnatal Depression Scale, Bi = bilateral, UF = uncinate fasciculus

Chapter 4 - Alyousefi-van Dijk, K., van 't Veer, A. E., Meijer, W. M., Lotz, A. M., Rijlaarsdam, J., Witteman, J., & Bakermans-Kranenburg, M. J. (2019). Vasopressin differentially affects handgrip force of expectant fathers in reaction to own and unknown infant faces. Frontiers in behavioral neuroscience, 13. https:/doi.org/10.3389/fnbeh.2019.00105

Early Caregiving Experiences – Methods

Participants completed the Conflict Tactics Scale – Parent Child (CTS, Straus et al., 1998), which assesses experienced maltreatment during the participants' childhood. We used items from the subscales Psychological aggression, Minor physical assault, Severe physical assault, and Neglect, resulting in a total of 18 items. Items were answered on a 7-point scale (0 ='never',1 = 'once', 2 = 'twice', 3 = '3–5 times', 4 = '6–10 times', 5 = '11–20times', 6 = 'more than 20 times'). Averaging scores on the minor and severe physical assault scales resulted in a Physical assault score, which combined with the scores on Psychological aggression formed an Abuse score. An overall CTS score was computed by averaging the Abuse and Neglect scales (M = 0.53, SD = 0.34), which was used for further analysis. One outlier (Z = 4.09) was winsorized to match the second highest score. The CTS total score was positively correlated with the Abuse scale, r= 0.92, p < .001, and with the Neglect scale, r = 0.53,p = .006. Additionally, participants completed seven items from the Withdrawal of Relations subscale of the Children's Report of Parental Behavior Inventory (CRPBI, Beyers and Goossens, 2003; Schludermann and Schludermann, 1983) of which two items were slightly adapted for a smoother translation. To obtain a more comprehensive measurement of parental love-withdrawal, the questionnaire was complemented with four items from the Parental Discipline Questionnaire (PDQ, Patrick and Gibbs, 2007, see Huffmeijer et al., 2011 for the resulting scale). Participants rated how well each of the statements described their mother's or father's behavior on a 5-point scale ranging from 1 (not at all) to 5 (very well). A parental love-withdrawal score was computed by averaging the 11 maternal and 11 paternal scores (M = 1.72, SD = 0.47). The maternal and paternal scores correlated with the total score r = 0.74, p < .001, and r = 0.67, p < .001, respectively. See Thijssen et al., 2018 for use of the same questionnaires.

Early Caregiving Experiences – Results

Correlations between mean handgrip force ratio's and both CTS and parental love-withdrawal were found to be low (*r* ranging from .01 to .28), see Supplementary Table 1.

Supplementary Table 4.1. Correlation matrix for mean handgrip force ratio's and early caregiving experiences.

	CRBI Love Withdrawal	CTS Abuse and Neglect
Placebo – baseline	.072	.088
AVP – baseline	.176	.040
Placebo – own infant, control sound	.004	-.107
AVP – own infant, control sound	.119	.017
Placebo – own infant, cry sound	-.043	-.127
AVP – own infant, cry sound	.075	-.009
Placebo – unknown infant, control sound	.184	.058
AVP – unknown infant, control sound	.278	-.127
Placebo – unknown infant, cry sound	-.152	-.050
AVP – unknown infant, cry sound	.179	.029

Chapter 5 - Alyousefi-van Dijk, K., de Waal, N, van IJzendoorn, M. H., & Bakermans-Kranenburg, M. J. (2021). Development and feasibility of the Prenatal Video-feedback Intervention to promote Positive Parenting for expectant fathers. Journal of Reproductive and Infant Psychology. https:/doi.org/10.1080/02646838.2021.1886258

Methods – VIPP-PRE protocol

VIPP-PRE session 1

Live feedback - Attachment and exploration. First, the expectant father receives brief information about the sensory abilities of his unborn child. He is told that the brain and auditory system of his child develop over the course of pregnancy, and that his child can now hear voices from outside the mother's body. Also, the father is told that if the unborn child hears his voice often enough he/she can distinguish that voice from other male voices at some point during the pregnancy (Lee and Kisilevsky, 2014). As is the case when the child is born, his unborn child is capable of directing sustained attention towards voices (e.g. Granier-Deferre, Bassereau, Ribeiro, Jacquet, and DeCasper, 2011). Second, the expectant father is told that his unborn child is incapable of doing two things at the same time, and that he/she is either discovering the surroundings (e.g. playing with a toe) or seeking contact with a caregiver (e.g. listening to father's voice). The intervener emphasizes throughout the intervention that it is beneficial for the child to be given the space and time needed to discover the world, while his/her father is around whenever he/she seeks contact. Next, the father is asked to read from the children books brought by the intervener for 3 min while the interaction between him and his unborn child is recorded. After this recording, the father is asked to softly massage the mother's abdomen for 2 min while the second video is being recorded. When appropriate, the intervener points out precursors of exploration or attachment related behaviours shown by the unborn child, such as '*look, he/she moved his/her head when you started reading*', '*he/she might be listening*', or '*he/she is drinking some amniotic fluid at the moment*', '*he/she might not hear you right now but he/she loves having you there!*'. During recordings in all sessions, the intervener uses the technique of 'speaking for the child' by highlighting what the child is doing, thinking, or feeling, see Figure 5.1 for examples.

VIPP-PRE session 2

Live feedback - Speaking for the baby. First, the expectant father receives brief information about the sensory abilities of his unborn child. He is told that that just as when the baby is born, he/she calms down while being exposed to familiar sounds, such as rhymes (e.g. DeCasper, Lecanuet, Busnel, Granier-Deferre, and Maugeais, 1994). Next, fathers are asked to sing for their child for 2 min while the first recording

is being made. When fathers struggle to come up with a song, they are given a flyer with lyrics of well-known children songs. Singing songs other than children's songs is also welcomed. For the second recording of this session, expectant fathers are asked to talk to their unborn child for 3 min. When they struggle to find a topic, they are suggested to talk about what they want to do together after the baby is born. During recordings the intervener uses the 'speaking for the baby' technique, by providing appropriate subtitles for the child's behaviour (e.g. '*he/she likes hearing your voice*', '*he/she is busy moving around*', '*he/she seems to be sleeping*').

Video feedback - Attachment and exploration. During the video feedback the intervener attempts to make the expectant father aware of (precursors of) exploration and attachment behaviours of his unborn child. Based on the videos recorded in session1 (i.e., reading and touching), the intervener highlights the importance of supporting the child's exploration without interfering, the added value of having a loving and perceptive parent around, and the parent's role in providing sensitive interactions. Emphasis is put upon stimulating the father to detect whether the child is active or resting and how the father can best support the child in both cases.

VIPP-PRE session 3

Live feedback - Sensitivity chains. First, fathers are given information on sensitivity chains; situations in which the child provides a signal, followed by an appropriate response by the caregiver, which in turn leads to the child feeling understood and supported. For example, when the unborn child is restless, the father can read a story, and then the baby will slow down its movements and return to a more restful state while listening to the father's familiar voice. The intervener explains to the father that observing, interpreting, and adequately responding to the child is essential for his/her development. Where possible, all sensitivity chains visible in the live recording are pointed out by the intervener and when needed, the intervener suggests possible responses. Fathers are told that by showing that they have an interest in and recognize their child's signals, the child will develop confidence in his/her self and feel safe enough to explore new things. Second, fathers are given information about the fact that the sense of touch of their baby is rapidly developing and that the distance between the father's hand on the mother's abdomen and the baby gets increasingly smaller as pregnancy progresses. Father are then invited to interact with their unborn child for 5 min in a free play.

Video feedback - Speaking for the baby and sensitivity chains. For the first time, interveners offer corrective messages in which observed insensitive behaviour of the father is carefully discussed and alternative, more sensitive, behaviours are suggested. Based on the videos recorded in session 2 (i.e., singing and talking), interveners use

'speaking for the baby' techniques, and highlight sensitivity chains where possible. Also, the intervener promotes involvement of the father by asking what he thinks his baby is doing, thinking or feeling.

- *"He/she can hear your voice."*
- *"He/she is hearing all sorts of sounds and is trying to focus on a sound."*
- *"He/she felt that touch and moved towards it."*
- *"He/she recognizes your voice and calms down when he/she hears it."*
- *"He/she is very busy moving around right now."*
- "*He/she is relaxing or maybe even sleeping."*

Supplementary Figure 5.1. Examples of 'speaking for the child' comments that are used throughout all sessions in the VIPP-PRE.

Methods – control condition

For the control condition, three phone conversations were scheduled during pregnancy. At the start of all control intervention appointments, fathers are given information about the physical developmental stage of their unborn child at that particular week in the pregnancy. Next, fathers are asked several questions about the pregnancy, the baby, and upcoming fatherhood. The semi-structured phone conversations are designed to be a pleasant 5-10 min interaction between father and intervener with the pregnancy and the child being the focal topics, while at the same time the intervener does not explicitly encourage any type of interaction between the father and the unborn child. The questions discussed in the control condition are: '*How did it go with the pregnancy in the past week?*', '*Where there any appointments concerning the pregnancy in the past week?*', '*Did you buy, arrange, or prepare anything for the baby in the past week?*', and '*Did you speak to anybody about the pregnancy in the past week?*'.

Results – Fathers' evaluation of the intervention

Open end questions on the VIPP-PRE intervention experience.

1. Is there specific information that you would have liked to receive at the beginning of the ultrasound visits? If so, which information would you have liked to receive?
2. What did you like most about the ultrasound visits?
3. What did you like least about the ultrasound visits?

Supplementary Table 5.1. Expectant fathers' perceived effects of the VIPP-PRE intervention and the control condition.

	VIPP-PRE (*n* = 30)	**Control (*n* = 29)**	**Independent sample t-test**				
	M (*SD*)	*M* (*SD*)	*t*	*df*	*p*	95% *CI*[a]	Hedges's g
Relation with the baby	3.27 (1.14)	1.90 (0.86)	5.22[b]	53.80	< .001	[0.84, 1.90]	1.34
Understanding of the baby	3.20 (1.19)	2.07 (0.96)	4.01	57	< .001	[0.57, 1.69]	1.03
Communication with the baby	3.50 (1.17)	2.00 (0.80)	5.77[b]	51.51	< .001	[0.98, 2.02]	1.47
Understanding of the feelings of the baby	2.90 (1.35)	2.07 (1.03)	2.65	57	.01	[0.20, 1.46]	0.68
Helpfulness	3.33 (1.18)	2.17 (0.85)	4.34[b]	52.60	< .001	[0.62, 1.70]	1.11

Note. Participants indicated to what extend (i.e., ranging from 1 = 'not at all' to 5 = 'very much') they thought the intervention affected their insight into their relationship with, understanding of, and communication with the baby. Also, participants indicated to what extent they thought the VIPP-PRE session or phone conversations were helpful. Here, participants who did not fill out the evaluation before but rather after the birth of their child were excluded from the analyses. All significant findings reported in the paper remained significant.
[a]Confidence interval of the difference between means
[b]Unequal variances

Summary

Even though the relatively limited available scientific literature indicates that fathers are important for child development from the earliest stages of parenthood onward, (clinical) family services, as well as parenting research, still predominantly focus on mothers only. Importantly, prenatal precursors of paternal behaviour have been documented, but the underlying mechanisms and developmental trajectories of perinatal paternal care are still poorly understood. In this thesis, we report on findings resulting from a series of randomized controlled trials investigating neurobiological parameters across men's transition into parenthood; the *Father Trials*. Specifically, we focus on (influences on) the development of perinatal parenting behaviours, as well as some of the hormonal and neural processes involved.

In Chapter 2, we report that fathers' behavioural responses to infant crying, as well as baseline testosterone, are stable across the perinatal period. In contrast, fathers' neural response to infant crying was found to undergo a noteworthy change from the prenatal to the postnatal period, indicating that some neural response to infant crying (e.g., those involved in visual imagery) emerge after the birth of their child. We also found that postnatal neural activation in response to infant crying in the right precentral gyrus was strongly related to postnatal parenting sensitivity, possibly indicating an important association between neural reactivity in response to infant signals and parenting quality. Lastly, our findings suggest that prenatal reactivity to infant signals in the bilateral posterior cingulate cortex might be an indirect neural predictor for early postnatal parenting quality in new fathers.

In Chapter 3 we report our finding that fathers' own childhood experiences are associated with paternal behaviour; experiences of childhood maltreatment were found to be associated with inadequate inhibitory control over behavioural responses and / or emotional hyperreactivity in response to infant crying in the perinatal period. Specifically, this effect was only present for fathers with low structural connectivity between the prefrontal cortex and the amygdala (i.e., uncinate fasciculus). These findings suggest that detrimental behavioural correlates of negative caregiving experiences are present in fathers during a period when they are (about to be) frequently exposed to infant crying, and that fathers are more or less resilient to these effects dependent upon their brain's white matter structure.

In Chapter 4 we report on the behavioural effects of arginine vasopressin (AVP); a hormone which has been proposed to play a vital role in fatherhood. AVP administration in expectant fathers was found to lead to more excessive handgrip force (a marker for inadequate inhibitory control over behavioural responses and

/ or emotional hyperreactivity to stimuli) while viewing an unknown infant image compared to viewing an image representing fathers' own infant, while the opposite was true under placebo. These findings suggest that AVP may be involved in the evolutionary selected ability to detect kinship and possibly induces an increase in protective aggression based on preference for facial resemblance in offspring.

In Chapter 5 we report on the development and feasibility of the Prenatal Video-feedback Intervention to promote Positive Parenting (VIPP-PRE), aimed at improving postnatal parenting quality and stimulating involvement in first-time fathers. With the use of real-time ultrasound images, expectant fathers interacted with their unborn children and were given feedback aimed at improving their ability to detect and understand their child's behavioural signals as well as reinforcing fathers' timely sensitive responses to those signals. Based on the evaluation by participating fathers and sonographers, we concluded that the VIPP-PRE is feasible and is received positively. Moreover, we found that fathers receiving the VIPP-PRE, compared to those receiving a control intervention, reported to have gained more insight into their relationship with their child, a better understanding of their child and its feelings, and more insight into their communication with their child. The effects of VIPP-PRE on fathers' parenting sensitivity and involvement are to be reported in the near future and will guide future implementation of the intervention.

In conclusion, we have found support for the claim that several neurobiological processes (i.e., neural reactivity to infant signals and the vasopressin system) play a role in preparing expectant fathers for parenthood. Our studies indicate that after the birth of fathers' first child several neurobiological processes 'come online' and orchestrate the necessary changes for facilitating the transition into parenthood. However, fathers' quality of care is associated with their own childhood experiences, depending upon fathers' brain architecture. Although there has been a sharp increase in studies examining paternal behaviour and its underlying mechanisms, there is still much unknown about the development, and threats to optimal development, of fatherhood. Importantly, both mothers and fathers often experience the transition into parenthood as stressful, and fathers specifically have little access to support within perinatal healthcare and parenting resources. A difficult transition into parenthood can affect fathers' mental health and ability to parent at a time when the infant needs physical and emotional support from its caregivers. Within the *Father Trials* project, we aimed to put fathers at the heart of studying parenting and have provided an evidence-based, prenatal, and interaction-focused parenting intervention aimed at providing support during the transition into fatherhood.

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Curriculum Vitae

Kim Alyousefi-van Dijk was born on October 26th, 1987 in Amsterdam, the Netherlands. She enrolled in academic education in 2007 and obtained a Bachelor of Science degree in Psychobiology in 2010 from the University of Amsterdam. Simultaneously, she studied Psychology, for which she also obtained a Bachelor of Science degree in 2011 at the same university. In 2011, she was admitted into the selective Research Master programme Brain and Cognitive Sciences at the University of Amsterdam. In 2012, she completed a thesis on the modulating effects of stimulus intensity on early somatosensory processing during observation of others' pain, under supervision of prof. M. J. A. M. van Putten at the Department of Clinical Neurophysiology of the Institute for Biomedical Technology and Technical Medicine Twente. In 2014, she completed a thesis on predicting acute trauma-related symptoms in recently traumatized individuals at increased risk for post-traumatic stress disorder using brain tractography, under the supervision of prof. M. Olff at the Department of Psychiatry at the Academic Medical Center Amsterdam. She obtained her Master's degree in 2014. From 2013 to 2016, she worked as a research assistant for the Netherlands Brain Bank for Psychiatry and the Department of Psychiatry at the Academic Medical Center Amsterdam, focussing on the neurobiology of stress-related psychopathology under the supervision of prof. M. Olff. In 2016, she started her PhD programme at Leiden University and the Vrije Universiteit Amsterdam, working on unravelling the neurobiology of fatherhood under the supervision of prof. M. J. Bakermans-Kranenburg, prof. M. H. van IJzendoorn, prof. C. Schuengel and dr. M. M. E. Riem. Within her PhD she worked on the development and testing of the Prenatal Video-Feedback Intervention to promote Positive Parenting (VIPP-PRE) for first-time fathers. Kim is currently employed as a Trial Manager at the Anna Freud Centre in London (UK), under the supervision of prof. Peter Fonagy and dr. Camilla Rosan, working on a nationwide RCT investigating a Circle of Security Intervention in community perinatal mental health settings.

Publications

1. **Alyousefi-van Dijk, K.,** de Waal, N, van IJzendoorn, M. H., & Bakermans-Kranenburg, M. J. (2021). Development and feasibility of the Prenatal Video-feedback Intervention to promote Positive Parenting for expectant fathers. Journal of Reproductive and Infant Psychology. https://doi.org/10.1080/02646838.2021.1886258

2. **Alyousefi-van Dijk, K.**, van der Knaap, N., Buisman, R.S.M., Horstman, L.I., Lotz, A.M., Riem, M.M.W., 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. https://doi.org/10.1002/dev.22058

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8. Horstman, L.I., Riem, M.M.W., **Alyousefi-van Dijk, K.**, Lotz, A.M., & Bakermans-Kranenburg, M. J. (under review). Fathers' involvement in early childcare is associated with their amygdala resting-state connectivity.

9. 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., & Bakermans-Kranenburg, M. J. (under review). Mind-mindedness, sensitivity, and involvement in first-time expectant and new fathers

10. Verhees, M. W. F. T., van IJzendoorn, M. H., **Alyousefi-van Dijk, K.**, Lotz, A. M., Bakermans-Kranenburg, M. J. (under review). Child maltreatment affects fathers' response to infant crying, not mediated by cortisol or testosterone.

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