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

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Key words: fathers, testosterone, fMRI, infant crying, handgrip force, parental sensitivity

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 et 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 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 the 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 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 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 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 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 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 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 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.

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 for a design overview of the study.

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 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 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 1-4.

Results

Descriptive results

Results on differences and correlations between prenatal and postnatal mean-levels are reported in Table 1, and concurrent associations are shown in Table 2 and 3. Correlations between lower prenatal measures and higher level postnatal measures can be found in Table 4. All correlations of $r \geq .50$ are depicted in Figure 3.

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 1.

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 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 radiata descending into the left frontal operculum cortex. See Supplemental Materials Figures 1-7 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 1.

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 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 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 1.

Concurrent relations

Bivariate correlations between prenatal measures were found to be low and are reported in Table 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 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 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 time in the perinatal period. However, the neural response to infant crying changed remarkably 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 1-4. We also have 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 motor 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 radiata 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 remarkably 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.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CRediT author statement

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

Acknowledgements

This study was supported by a European Research Council grant [ERC AdG 669249] awarded to M.J.B-K.

Declarations of interest: none.

Figure 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).

EXPLORING THE TRANSITION INTO FATHERHOOD

Figure 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 baseline 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.

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Figure 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

Table 1 Results for prenatal-postnatal differences and correlations for all measurements.

	<i>N</i>	<i>M</i> (<i>SD</i>)	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

Table 2 Prenatal concurrent associations between the measurements (Pearson's r).

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

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

Table 3 Postnatal concurrent associations between the measurements (Pearson's *r*).

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

Table 4. Prenatal to postnatal correlations (Pearson’s *r*).

	Post	Post bi	Post l	Post in r	Post r body	Post l	Post	Post
	midbrain	auditory	supraCal	precentral	and	antCorRad	handgrip	sensitivity
		cortex	cortex	gyrus	splenium of		force	
					CC			
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.

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