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Effects of vasopressin on neural processing of infant crying in expectant fathers

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ABSTRACT

In a randomized, double blind, placebo-controlled, within-subject magnetic resonance imaging study, we examined the effect of 20 IU intranasal vasopressin on the neural processing of infant crying in 25 fathers-to-be. We explored whether familial background modulates vasopressin effects, and whether vasopressin differentially affects cry processing coupled with neutral or emotional contextual information. Participants listened to cries accompanied by neutral ('this is an infant') or emotional ('this infant is sick/bored') contextual information, and neutral control sounds ('this is a saw'). Additionally, participants reported on their childhood experiences of parental love-withdrawal and abuse. Infant crying (vs control sounds) was associated with increased activation in the bilateral auditory cortex and posterior medial cortex. No effects of vasopressin were found in this 'cry network'. Exploratory whole-brain analyses suggested that effects of vasopressin in the anterior cingulate cortex, paracingulate gyrus and supplemental motor area were stronger in fathers who experienced lower (vs higher) levels of love-withdrawal. No interaction was observed for abuse. Vasopressin increased activation in response to cries accompanied by emotional vs neutral contextual information in several brain regions, e.g. the cerebellum, brainstem (midbrain), posterior medial cortex, hippocampus, putamen, and insula. Our results suggest that the experience of love-withdrawal may modulate the vasopressin system, influencing effects of vasopressin administration on cry processing. Results further suggest a role for vasopressin in the processing of cry sounds with emotional contextual information.

1. Introduction

Whether they are cold, sick, or tired, crying is one of the infant's most important means of soliciting parental attention and care. However, crying can also elicit aversion and anger in the parent, and can trigger child abuse and neglect (Barr et al., 2006). How parents process infant cry sounds, therefore, constitutes an important area of study. In recent years, fathers have significantly increased their participation in child caretaking. Even though there remains large variation in paternal involvement (Hrdy, 2009) and quality of caregiving (Lucassen et al., 2011; van IJzendoorn and DeWolff, 1997), a father's parental role is highly relevant for child development (Kok et al., 2015; Ramchandani et al., 2005). The transition to fatherhood is a gradual process taking place over the course of the pregnancy (Edelstein et al., 2015; Finnbogadóttir et al., 2003). Already during his partner's pregnancy, a man's hormonal response to infant crying has been found to be associated with variation in paternal responsiveness (Storey et al., 2000). In the past decade, a relatively large literature on the neural underpinnings of the processing of infant crying in mothers has become available (e.g. Groh et al., 2015; Parsons et al., 2017; Wright et al., 2017), however, little is known about the way fathers or expectant fathers process these cues of infant distress (Li et al., 2017; Mascaro et al., 2014; Seifritz et al., 2003). Following-up on the Li et al. (2017) study on the effects of neuropeptides oxytocin (OT) and vasopressin (AVP) on the processing of infant signals in fathers of toddlers, the present study examined the effect of AVP on processing of infant cry sounds in a different yet equally important group of men: expectant fathers, and explored whether this effect of AVP is moderated by the father's childhood parenting experiences. Moreover, we examined whether accompanying contextual information affects expectant fathers' neural processing of cry sounds, and whether AVP administration modulates this effect of context.

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Quality of parenting skills may in part be related to hormonal levels. In fathers, the neuropeptide vasopressin has been suggested to play a special role (Taylor et al., 2010). Both in rodents and in non-human primates, the transition to fatherhood has been associated with changes in AVP signaling (Bamshad et al., 1993; Kozorovitskiy et al., 2006; Wang et al., 2000). In male prairie voles, AVP injections into the lateral septum elicit paternal behavior (i.e. crouching over pups, Wang et al., 1994), and AVP-immunoreactive staining in the bed nucleus of the stria terminalis has been associated with paternal behavior in California mice (Bester-Meredith and Marler, 2003; but see Taylor and French, 2015 who found no effects of intranasal AVP administration on responsiveness to infant stimuli in male marmosets).

Associations between AVP and parenting have also been observed in humans, but results have been inconsistent. In expectant fathers, vasopressin administration increased fathers' implicit caregiving interests (Cohen-Bendahan et al., 2015). However, in a sample of 15 fathers of 1–2-year-old children, AVP administration (compared to placebo administration) did not affect neural processing of infant cry sounds nor of own infant photos (Li et al., 2017). As this is one of the few studies examining AVP effects in human fathers—and with a relatively small sample—we revisit the questions posed in the Li et al. (2017) study (does AVP administration affect processing of infant crying and is its effect modulated by familial background?) with a larger sample in a different group of fathers (fathers-to-be instead of fathers of toddlers). Moreover, we extend the literature by examining the effect of contextual information describing the reason for the infant's distress (e.g. “this infant is sick”), on cry sound processing in fathers and by assessing whether AVP modulates such a ‘context effect’.

Previous studies from our lab have shown that effects of OT are dependent on experienced care, such that positive effects of OT are found in individuals coming from a supportive background only (Bakermans-Kranenburg et al., 2012; Riem et al., 2013; van IJzendoorn et al., 2011). For example, OT administration decreased excessive force on a hand-grip dynamometer when listening to infant cry sounds, but only in individuals who experienced low levels of harsh discipline (Bakermans-Kranenburg et al., 2012). Although there is no direct evidence that effects of AVP may also be dependent on experiences of childhood care, the association between experienced care and own caregiving skills suggest that these experiences affect biological properties important to parenting (Kovan et al., 2009; Madden et al., 2015). There may be a variety of biological mechanisms explaining increased or decreased susceptibility to extraneous hormones, for example, endogenous hormone levels or receptor properties. Through gene methylation, experiences of harsh and neglectful care may affect properties of systems involved in parenting such as OT, but also AVP (Mulder et al., 2017).

As the cause of the infant's distress may be difficult to discern from the infant's cry, contextual information can be an important determinant of parental action. For example, the parental response to crying is delayed when the infant has just been fed (Leger et al., 1996), or when the adult is told that the infant needs sleep (Wood and Gustafson, 2001). Effects of contextual information have also been found on the neural processing of cry sounds (Riem et al., 2014). In a sample of nulliparous women, the amygdalae showed an increased response to the same cry sound labelled as originating from a sick infant compared to a bored infant. In the insula and inferior frontal gyrus, a comparable effect was found after administration of OT, a neuropeptide similar to AVP in molecular structure but with different behavioral correlates. However, similarly to OT, AVP has been found to alter the interpretation of social stimuli (Thompson et al., 2004), and therefore, modulating effects on the processing of contextual information may also be expected of AVP administration.

The present study assessed the effect of AVP administration on the neural processing of infant cry sounds in 25 fathers-to-be. Based on the existing literature in females, we expected expectant fathers to show increased activation in response to infant crying (compared to control sounds) in regions associated with social information processing, such as the amygdala, insula, cingulate cortex and inferior frontal gyrus (Laurent and Ablow, 2012a, 2012b; Riem et al., 2014; Riem et al., 2011). We hypothesized that activation in these regions would be affected by AVP administration and by contextual information accompanying the cry sound. Finally, we explored whether experiences of harsh and neglectful parenting modulate the effect of AVP administration on the processing of infant cry sounds.

2. Methods

2.1. Participants

Participants were recruited through midwives and ads on Leiden University affiliated webpages. They cohabitated with their pregnant partners, spoke Dutch, were in good health, without psychiatric, neuroendocrine or neurological disorders, and were screened to exclude excessive smoking and/or alcohol use, and recreational drug use within 6 months prior to participating. Twenty-five first time expectant fathers participated in the study. The mean age of the participants was 31.9 years (SD = 4.30), and the mean gestational age of the unborn infants was 27.02 weeks (SD = 4.91). All participants provided informed consent. Participants were instructed to abstain from alcohol and excessive physical activity during the 24 h before the start of each session, and from caffeine on the day the session took place. Both sessions took place at similar times of day. This study was approved by 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.

2.2. Procedure

In a randomized, double blind, placebo-controlled, within-subject trial, fathers-to-be participated in two sessions in which they self-administered either a nasal spray containing AVP (20 IU) or placebo (PL) using a syringe with a MAD (Mucosal Atomization Device) Nasal™ Device. After nasal spray administration, participants completed several questionnaires and were familiarized with the fMRI protocol outside of the MRI environment. Prior to the cry paradigm, participants performed a working memory fMRI paradigm also involving cry sounds as well as a paradigm aimed at measuring protective parenting, to be reported separately. The cry sound paradigm commenced approximately 94 min after nasal spray administration in both the AVP and placebo sessions. In a study examining cerebrospinal fluid (CSF) AVP concentrations up to 80 min after intranasal administration of AVP, 80 and 40 IU of intranasal AVP resulted in a significant increase in CSF AVP after 10 and 60 min, respectively (Born et al., 2002). For both dosages, AVP was still significantly increased after 80 min. More prolonged subsampling in a subset of participants receiving the higher dose of 80 IU suggested that AVP was still elevated at 100–120 min after administration. We, therefore, believe that the 94 minute delay after administration of 20 IU of AVP in the present study is an appropriate delay.

2.3. Measures

2.3.1. fMRI paradigm

For a visual representation of the cry paradigm, see Fig. 1. Contextual information (emotional: ‘this infant is sick’ or ‘this infant is bored’, neutral: ‘this is an infant’) was presented as a white text on a black screen for a duration of 2 s. In order to assure that participants remained attentive throughout the task, they were instructed to press a button with their index right finger when they finished reading the context information. The context information was followed by the presentation of a fixation cross hair. After 500 ms, the auditory stimulus was presented (10 s), while the fixation cross hair remained on the screen. Trials were separated by an inter stimulus interval (ISI) of