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Oxytocin receptor gene polymorphisms (rs53576) and early paternal care sensitize males to distressing female vocalizations

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Abstract

The oxytocinergic system is highly involved in social bonding and early caregiver-infant interactions. Here, we hypothesize that oxytocin receptor (OXTR) gene genotype and parental bonding history interact in influencing social development. To address this question, we assessed adult males' arousal (heart rate changes) in response to different distress vocalizations (human female, human infant and bonobo). Region rs53576 of the OXTR gene was genotyped from buccal mucosa cell samples, and a self-report Parental Bonding Instrument was used (which provide information about parental care or parental overprotection). A significant gene * environment interaction between OXTR genotype and parenting style was found to influence participants' social responsivity to female cry vocalizations. Specifically, a history of appropriate paternal care in participants accentuated the heightened social sensitivity determined by G/G homozygosity, while higher vs lower paternal overprotection lead to distinct levels of physiological arousal particularly in A carriers individuals. These results add to our understanding of the dynamic interplay between genetic susceptibility and early environmental experience in shaping the development of appropriate social sensitivity in males.

Keywords: Parental attachment; oxytocin receptor gene; social abilities; Gene * Environment; physiological responses to social distress

Introduction

Early bonds formed with caregivers have a lasting impact on social interactions later in life. Individuals develop different social sensitivities as a result of a dynamic interplay between their genetic blueprint and their environmental experiences. To better understand the development of different sensitivities to social signals, a multilevel approach is needed to account for the influence of both genetic factors at an individual level and environmental factors at an experiential level. The neuropeptide oxytocin is involved in the modulation of key social behaviors such as bonding and attachment (Kendrick et al., 1987; Ross and Young, 2009; Ebstein et al., 2012). In a previous study we saw an effect of the interaction between a specific single nucleotide polymorphism on the oxytocin receptor gene (rs2254298) and early social experiences in moderating adults' responses to social stimuli (Esposito et al., 2016). However, previous researches have shown that one more single-nucleotide polymorphism (rs53576) in the oxytocin receptor gene (OXTR) is linked to the expression of different social behaviors, including empathy and social cognition (Rodrigues et al., 2009; Park et al., 2010; Wu et al., 2012). Most notably, previous studies have highlighted that the two alleles, G and A, show specific and differential influence on social development. The G allele has been associated with successful social development while the A allele has been linked to less adaptive social traits (Thompson et al., 2011; Wu et al., 2012). For example, individuals who are G/G homozygous for OXTR have greater dispositional empathy (Rodrigues et al., 2009; Smith et al., 2014). In addition, G/G individuals have higher levels of overall empathy and pro-social characteristics (Rodrigues et al., 2009; Tost et al., 2010), as well as increased autonomic arousal in response to a social stressor (Norman et al., 2012). In contrast, the A allele has been associated both with reduced positive affect (Lucht et al., 2009) and reduced empathic accuracy (Rodrigues et al., 2009), reflective of poorer social development.

On the other hand other studies found opposite or no associations between rs53576 genotype and social traits. For example, a study from Apicella and colleagues (2010) found no association between the genotype in 9 SNPs in the OXTR gene and individuals' performances in two economic games, the dictator and the trust game, involving real monetary rewards. Also, two recent meta-analysis (Bakermans-Kranenburg & van Ijzendoorn, 2008; Li et al., 2015) could not confirm the presence and the direction of this association. The exact role of this polymorphism in moderating social behaviors is therefore still to be fully elucidated. This uncertainty however is probably due to the moderation of participants' ethnic group and to the fact that genetic predispositions rather than being direct risk or protective factors for environmental factors may moderate individuals' sensitivity to them. While genetics play a core biological role in development, the quality of an individual's relationship with their parents is a key experiential factor that influences individual social sensitivity to stressful situations (Sbarra & Hazan, 2008). The natural social development and adaptive abilities of humans are highly dependent on parental attachment (Bowlby,1999). Indeed, sensitive parenting is a well-documented key determinant of young children's socio-emotional development with many long-lasting consequences (Sroufe, 2006). Parental care which successfully nurtures and attends to children's physiological and emotional needs fosters a secure attachment style which eventually underpins a child's ability to regulate their emotions and cope with and adapt to stressful situations (Fraley, 2002). Parental overprotection, on the other hand, breeds excessive dependence on parents, which may eventually compromise a child's ability to cope with stressful situations (van der Bruggen et al., 2008). Furthermore, differences in sensitive parenting are associated with molecular genetic differences that may involve the production of oxytocin. Although oxytocinergic system activity may not be a necessary nor sufficient condition for sensitive parenting, experimental research showing that oxytocin improves 'mind reading' suggests that it may nevertheless facilitate parental sensitivity not only during periods

surrounding the birth of offspring, but at any stage in the lives of parents. More broadly speaking, OXTR genotype in the investigated region was found to be generally involved in the parent-infant interactions moderating both children's and parents' attitudes, child negativity and parents' confidence specifically (Kryski et al., 2014). G/G homozygotes in the rs53576 region show higher likelihood of developing depressive traits compared to A carriers when participants experienced high levels of maltreatment in childhood and therefore seems to be more affected by seriously ill early-life environment (McQuaid et al., 2013). On the other hand, in a longitudinal research G/G homozygotes showed higher coherence between early attachment with parents and adult attachment styles underlying how A carriers may be in general more sensitive to environmental experiences across lifetime (Raby et al., 2013).

Therefore, given the key roles that both OXTR and parental attachment play in social development it is important to understand the biological mechanisms underlying the interaction between these two factors to highlight how genes moderate individuals' sensitivity to environment. Indeed, this study aims to shed light on the possible interaction of these factors with measures of physiological arousal (heart rate - HR) in response to distressing stimuli in the form of female crying vocalizations. Such physiological responses, markers of overall autonomic nervous system activation reflective of psychological stress, may lie at the critical intersection of genetic and environmental influences on an individual's social development. While genes establish initial patterns of physiological responsiveness, early experiences provide key information which may modify and remodel these initial patterns, allowing the developing individual to best adapt to their evolving and complex environment. In light of recent findings on OXTR rs53576 variation, we predict that G/G homozygotes, as compared to A allele carriers, should display more sensitiveness to distressing social stimuli.

Materials and Methods

Participants. Forty-two non-parent adult males (*M* = 24.7 years, *SD* = 5.05) were recruited through a database of volunteers available through the University of Trento website. Given the evolutionary significance that cry stimuli and to avoid possible confounding effects due to females' specific responses to infant cries (De Pisapia et al., 2013; Messina et al., 2016), only males were included in the present study. The group was ethnically homogenous and all participants had Italian nationality. To prevent external non-experimental factors from influencing heart rate, all participants were required to refrain from drinking coffee or smoking on the day of the experiment, and to refrain from performing any sports activity 24 hours before the start of the experiment. No participant was involved in agonistic sports at the time of the experiment. Informed consent was obtained from all participants and the study was conducted in accordance with the Declaration of Helsinki. The genetic assessment was conducted on anonymized bio-samples at the University of Nagasaki (Japan), and followed the procedures approved by the IRB guidelines of the University of the Nagasaki Graduate School of Medicine.

Stimuli. The stimuli consisted of 30 15-second audio clips of distressing vocalizations, including female, infant and bonobo cries. Cries were chosen as stimuli because of their strong social significance and because they have been found to elicit distress and specific physiological responses in adults (Messina 2016). Bonobo cries were included as control stimuli. Bonobo cries were chosen because these are non-human vocalization whose acoustic characteristics bear some similarities with human and because bonobos' vocal tract is similar to that of humans. Within each category, ten different clips were presented (30 stimuli = 3 type of distress vocalizations x 10 different clips). There was no significant differences ($F(2,27) = .28$; *ns*) for the mean fundamental frequency of each category of cry was for female cries *f*0 M = 480Hz (*f*0 range = 280Hz-705Hz), infant cries *f*0 M = 482Hz (*f*0 range = 334Hz-736Hz), bonobo cries *f*0 M = 384Hz (*f*0 range = 355Hz-431Hz). All

vocalizations were normalized for intensity (M = 85dB; range = 65dB-90dB) and the volume was kept constant during presentation to all participants. Each audio clip was preceded by 10 seconds of silence. Audio clips were organized into three different randomized sequences and presentation order of the three sequences was balanced across participants. Stimulus sequences were created using open source software Audacity.

Procedure. The study was conducted in three parts. First, participants completed an on-line self-report questionnaire to assess their attachment status. Next, in the laboratory, participants' heart rate (HR) was recorded. To measure participants' HR baseline, a gray screen with a fixation point was presented for 60s while participants were instructed to only look at the screen and relax. Then, 30 audio clips were presented and the participants' (HR) was recorded throughout the entire stimuli presentation. The overall HR recording lasted about 13 minutes. Finally, a buccal mucosa for DNA analysis sample was collected from each participant.

Attachment. The Parental Bonding Instrument (PBI; Parker et al., 1979) is a 50-item self-report questionnaire developed to measure the principal parental dimensions of care and overprotection. This self-report measure gives information about perceptions of how one was parented during childhood and adolescence. Measures of 'care' reflect parental attention to children's needs, while measures of 'overprotection' reflect parental protectiveness and anxiety. Both are measured on continuous scales and values range from 0 to 3. Within our sample, the PBI Cronbach's alpha average was .74.

Heart Rate. HR was measured to assess participants' levels of arousal and stressful or calming states using a pulse oximeter (CONTEC CMS60D) placed on participants' left

index finger. An LED which emits light in two wavelengths is placed on participants' index finger. Light passes through the finger and the part of it not absorbed by the tissues is measured by a photodetector. The difference between the emitted light and the light entering the detector gives information about the type of tissues the light encountered during its path. Specifically, the two emitted wavelengths are absorbed respectively by oxygenated hemoglobin and deoxygenated hemoglobin. The pulse oximeter is therefore able to measure the blood volume in the finger and an increase in blood volume occurs in correspondence to each heartbeat. The Oximeter (CONTEC CMS60D) collect measurements at 64 Hz. Then, once per second, the device automatically calculates the frequency of heartbeat per minute. Therefore, the frequency of the device's output signal is 1Hz (one heart rate value per second). A HR increase from baseline in response to a specific stimulus reflects an increase in attention and readiness to action, whereas a HR decrease from baseline in response to a specific external stimulus reflects a calming response (Bernston et al., 1997; Bradley, 2009). For completeness, the Heart Rate Variability (HRV) indexes were also computed and analyzed. Specifically, the Root Mean Square of Successive Differences (RMSSD), the Low Frequency (LF) power, the High Frequency (HF) power, and the ratio between low and high frequencies (LF/HF) have been calculated. Contrary to Heart Rate results which showed a higher influence of parental care on G/G homozygotes, HRV indexes' analysis showed an overall higher effect of parental care on A carriers RMSSD and LF compared to G/G homozygotes. Moreover, a higher influence of maternal overprotection on A carriers was found on RMSSD changes. No significant effect for HF and LF/HF was found. The related methods and results are shown in the Supplementary Materials.

Genetic Assessment. DNA extraction and genotyping were conducted by ACGT, Inc. (Wheeling, IL). DNA was extracted from each kit using the Oragene DNA purification

reagent. DNA concentrations were evaluated using spectroscopy (NanoDrop Technologies, USA). Each DNA sample was polymerase chain reaction (PCR) amplified for the rs53576 region target with the primers 5′-GCCCACCATGCTCTCCACATC-3' and 5'-GCTGGACTCAGGAGGAATAGGGAC-3'. A PCR reaction of 20 ll was performed, consisting of 1.5 ll of genomic DNA from the test sample, PCR buffer, 1 mMeach of forward and reverse primers, 10 mM deoxyribonucleotides, KapaTaq polymerase, and 50 mM MgCl2. Cycling conditions included an initial 15 min denaturation step at 95 °C, and 35 cycles of 94 °C (30 s), 60 °C (60 s), 72 °C (60 s), and a final extension of 72 °C for 10 min. PCR reactions were genotyped with an ABI 3730xl Genetic Analyzer (Applied Biosystems Inc.) and normalized with GeneScan 600 LIZ (Applied Biosystems, Inc.) size standards for each sample. Genotype data were analyzed using GeneMapper ID (Applied Biosystems, Inc.). Participants possessing at least one A allele (A/A or G/A) were grouped into a single A carrier group. In the general population, the distribution of different genotypes for this DNA region is 40-50% of G/G homozygous and 50-60% for A carriers. The distribution in our sample was 43% for G/G homozygous and 57% for A carriers. Genotype frequencies were as follows: A/A = 8 (19.02%), A/G = 16 (38.10%), G/G = 18 (42.86%). This genotype distribution is in Hardy-Weinberg Equilibrium (X^2 (1) = 1.55, *ns*). Participants' age did not significantly differ between the two groups, G/G vs A ($t(40) = 1.25$, $p = 0.22$).

Analysis. An average baseline HR value was calculated for each participant. The linear model between HR values and the average baseline was then computed. The residuals of the model were considered as difference from the baseline. Then, for each participant, one average HR value was calculated for each condition. The different distress vocalization sounds (female, infant, and bonobo) were considered separately to test participants' reactions to the three distinct types of distress calls. All further analyses were conducted based on the computed averaged values, which represent the dependent variables. One

multivariate ANCOVA was performed with HR values as the dependent variable, the distress type (woman, infant, and bonobo) as a within-subjects factor, the OXTR (rs53576) gene genotype (G/G and A carriers) as a between-subjects factor and the PBI dimensions all together (maternal care, maternal overprotection, paternal care, and paternal overprotection) as continuous covariates. Correlations were run as post hoc tests and Pearsons' *r* coefficients were used to analyze the strength of the effect of the covariate on the dependent variable and Cohen's *d* was used to evaluate the magnitude of effects which were found to be significant.

Results

Attachment and Genotype

The distribution of genotypes, GG vs A carriers was not significantly different between high vs low paternal care (X^2 (1) = 0.47, *ns*) and between high vs low paternal overprotection (X^2 (1) = 1.76e-31, *ns*). High vs low groups were divided applying the median split procedure.

Heart Rate

Paternal Care. A significant interaction between paternal care, genotype and vocalization type was found for HR ($F(1,41) = 4.07$, $p < .05$, $d = .63$). Post-hoc statistical power calculated with GPower software was adequate, being equal to .95 [Fig. 2a-c]. The effect of paternal care was present only in homozygous G/G variants especially in response to female crying sounds. The higher the paternal care, the higher the HR increase ($r = .36$, $p = 0.14$). No significant main effect of paternal care was found.

Paternal Overprotection. A significant interaction between paternal overprotection, genotype and vocalization type was found for HR ($F(1,41) = 3.60$, $p < .05$, $d = .59$). Post-hoc statistical power calculated with GPower software was acceptable, being equal to .92

[Fig. 3a-c]. The effect of paternal overprotection was present only in A carriers especially in response to female crying sounds. The higher the paternal overprotection, the higher the HR decrease (r = -.28, p = 0.19). No significant main effect of paternal overprotection was found.

Maternal Care, Maternal Overprotection. No main effect nor significant interaction was found between maternal care, maternal overprotection, genotype, or vocalization type.

Discussion and Conclusions

In this study, several broad results are of interest. Firstly, participants were found to respond preferentially only to the distressing vocalizations of females rather than infants or bonobos. Given that participants were males at peak mating age (M = 24.7 years), preferential responsiveness to the vocalizations of potential mating partners may represent an adaptive behavior. In addition, participants' social sensitivities were found to be more influenced by paternal than maternal caregiving style. This may be due to the male gender of the study participants, who may be preferentially emulating the adaptive behavior of their same-gender parent because of a stronger identification with him/her as suggested in the classical work of Bandura (1961)—however, further studies are warranted to fully explain this. For instance, this particular finding may arise from several factors, such as an interplay between paternal and maternal characteristics or cultural stereotypes on gender behaviors which may differentially affect the interactions (Eccles et al., 1990; Martin et al., 2010). Further studies will need to test the presence of this directionality also in females and across cultures. Beyond broad results, several key findings are of importance to the central hypothesis. G/G homozygotes who experienced good paternal care were the only experimental group to display heightened physiological arousal to female crying. OXTR variants have previously

been linked to proficiency in social processing, with G/G homozygotes displaying superior emotional identification skills (Rodrigues et al, 2009), as well as increased autonomic arousal in response to socially distressing stimuli (Norman et al., 2012). Consistent with these findings, among individuals who experienced a constructive early social environment in the form of good paternal care and attachment style, G/G homozygous males of mating age displayed increased physiological arousal responses to female cries, while G/G homozygotes who experienced poor paternal care displayed decreased physiological arousal in response to female cries. G/G homozygosity may as such represent a genetic factor which promotes proficient socio-emotional information processing as well as, and as a result, increased physiological arousal in response to external social distress.

In contrast, A allele carriers, who have been shown to experience decreased empathetic accuracy (Rodrigues et al., 2009), showed greater interaction with paternal overprotection in response to female distress. A carriers who experienced low levels of paternal overprotection, and thus a more positive early social environment, reacted more intensely to female cries, while A carriers who experienced high levels of paternal overprotection, reflective of a compromising early social environment, showed an opposite reaction reacted to female cries, a decreased heart rate. The genetic factor of carrying an A allele in the OXTR gene, compounded with the environmental factor of experiencing paternal overprotection, reinforces an individual's lack of response to female distress—in this context, this decreased physiological arousal in males of mating age to female distress may be interpreted as a maladaptive response underlying less promptness to action. This being said, it may still also be conceived as an adaptive response, with its calming character allowing for better response planning. A study from Schwartz and colleagues (1981) indeed highlighted how situations eliciting personal distress are related to an increase in heart rate, while situations eliciting sympathy and empathic concern are related to a decrease in heart rate. However, in this study the authors asked their participants to think about a particular

emotion, while actually perceiving an external stimuli involve motor responses and other researches showed how being ready to move in response to positive or negative emotional stimuli relate to high emotional empathy (Sonnby-Borgström et al., 2003). The relation between physiological activations and empathy is therefore still under investigation. Further researches including also behavioral measurements of participants' attitude towards cry and other complementary physiological measures will need to be run in order to better investigate and unveil this relation. Further studies will as such need to shed light on whether low or high physiological arousal is best for coping with distressing external social stimuli and to take into account other early environmental factors which may play a role in affecting individuals' social responses, such as in utero hormonal exposure (Truzzi et al., 2016).

It is necessary to highlight that the specific functionality of the single-nucleotide polymorphism in the region rs53576 of OXTR is still unknown and it may also be null. However the presence of relations between the genetic characteristics of this genomic region and social behaviors point towards a contribution of this region in the functionality of the oxytocin receptors. The present results, also, highlight a certain genetic predisposition to developmental sensitivity to environmental experience, as exemplified here by G/G homozygosity increasing vulnerability to poor paternal behaviors. Interestingly, a similar genetic predisposition to higher environmental sensitivity was found in variations of the promoter region of the serotonin transporter gene 5-HTTLPR (Truzzi et al., 2017), as well as in variations of the rs22254298 region and the same rs53576 region of OXTR (Esposito et al., 2016; Senese et al., 2016). Together, these previous and current findings are consistent with the increasingly prevalent concept that specific alleles in certain 'plasticity genes' may confer a heightened susceptibility to both positive (constructive) and negative (destructive) early environmental experiences in youth, while different alleles may decrease this susceptibility causing individuals to be more protected to negative environmental experiences but also less receptive to positive ones (Belsky et al., 2009).

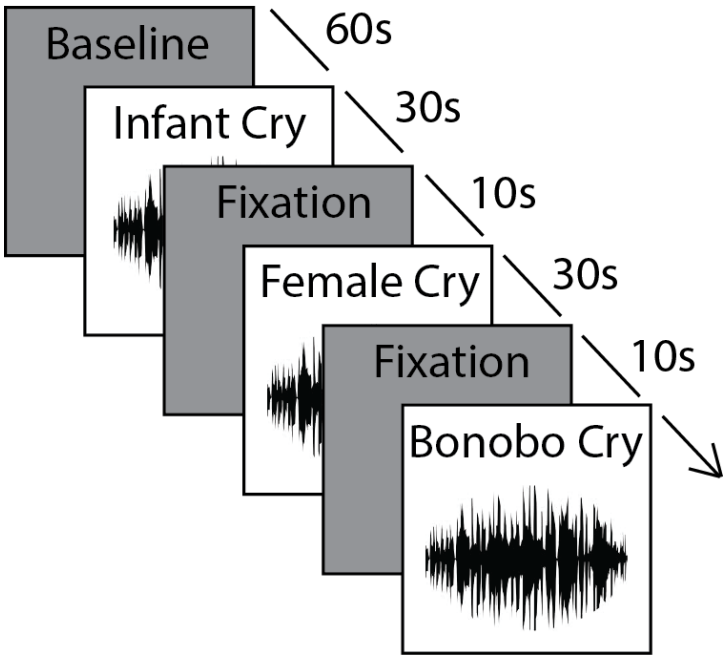

Figure 1. Representation of the experimental procedure and data acquisition periods.

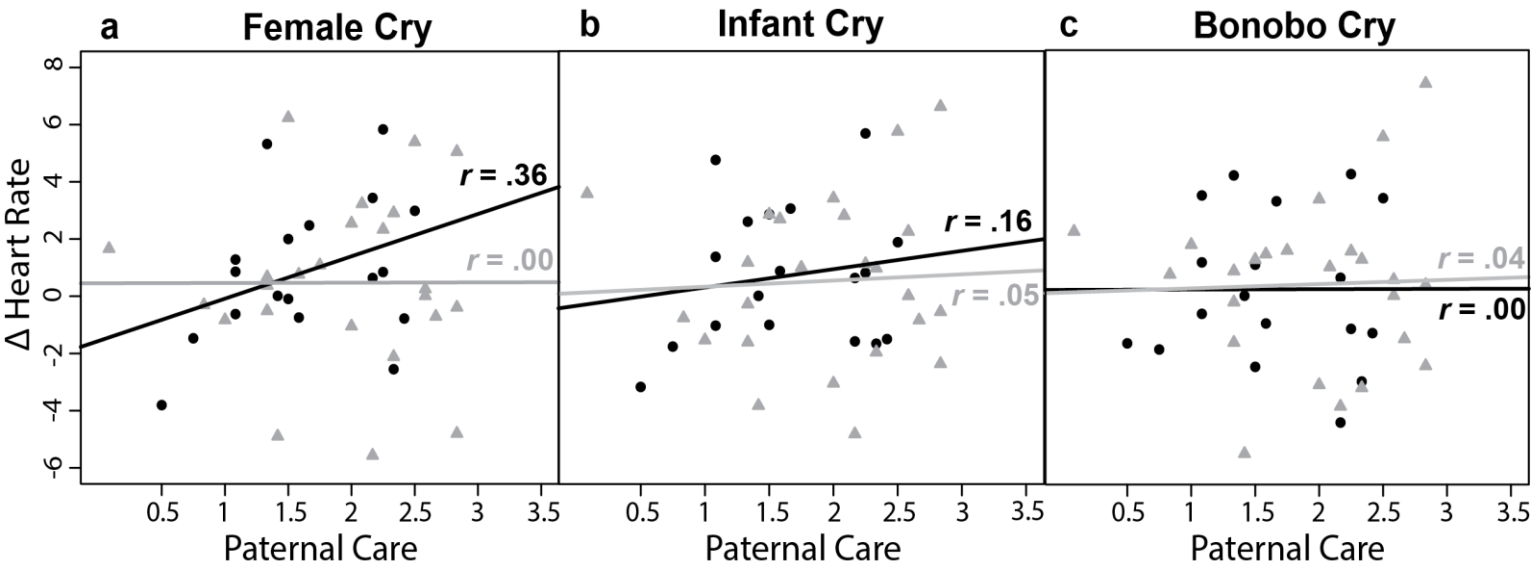

Figure 2a-c. Correlations between HR changes (calculated as the difference from baseline) and experienced paternal care in response to distinct cry types. In the figure, HR values averaged per participant and condition are represented. Paternal care values ranged from 0 to 3. Black circles = G/G homozygous; grey triangles = A carriers. Lines represent the linear models for G/G homozygotes (black) and A carriers (grey). The reported *r*-values represent Pearson's *r* correlations. (a) HR responses to female cry. Influence of paternal care on HR responses to female cries accordingly to genotype. (b) HR responses to infant cry. (c) HR responses to bonobo cry.

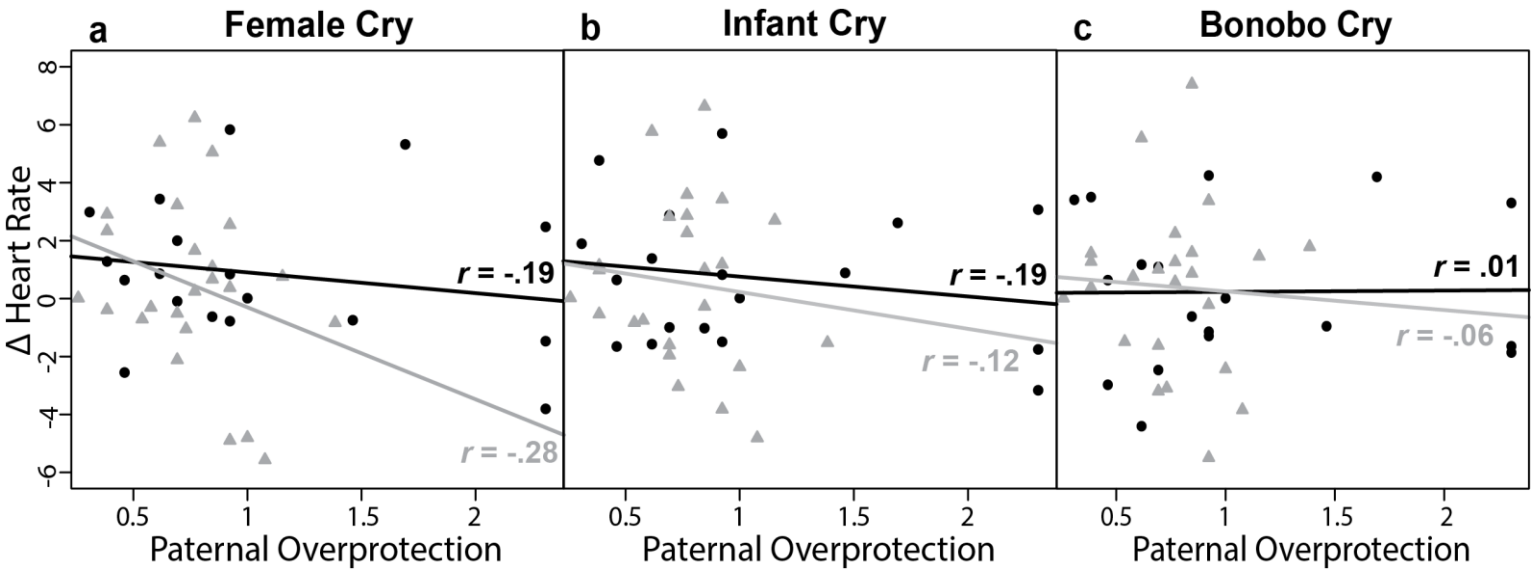

Figure 3a-c. Correlations between heart rate changes (calculated as the difference from baseline) and experienced paternal overprotection in response to distinct cry types. In the figure, HR values averaged per participant and condition are represented. Paternal overprotection values ranged from 0 to 2.5. Black circles = G/G homozygous; grey triangles = A carriers. Lines represent the linear models for G/G homozygotes (black) and A carriers (grey). The reported *r*-values represent Pearson's *r* correlations. (a) HR responses to female cry. Influence of paternal overprotection on HR responses to female cries accordingly to genotype. (b) HR responses to infant cry. (c) HR responses to bonobo cry.

Conflicts of Interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary Materials

Methods

Heart Rate Variability (HRV) Indexes. From the beat-per-minute output values obtained from the pulse-oximeter, one corresponding Inter-Beat Interval (IBI) value per second has been calculated. From the IBI values, variability and frequency indexes have been computed over 15s-long sliding time windows. Namely, the Root Mean Square of Successive Differences (RMSSD), the Low Frequency (LF) power, the High Frequency (HF) power, and the ratio between low and high frequencies (LF/HF) have been calculated. Variations in these HRV indexes reflect the functioning of the two branches of the autonomic nervous system, namely the parasympathetic and the sympathetic nervous systems (Appelhans & Luecken, 2006; Sztajzel, 2004). The activation of the parasympathetic nervous system increases heart rate variability, resulting in an increase of RMSSD and HF values. LF interpretation, on the contrary, is more controversial since they may be regulated either solely by the sympathetic system of they may be the result of a shared control between parasympathetic and sympathetic nervous systems. The LF/HF ratio, therefore, is usually more reliable because it directly gives information about the balance between the two branches of the autonomic nervous system.

Analysis. An average baseline value for each HRV index was calculated for each participant. The linear model between HRV values and the corresponding average baseline was then computed. The residuals of the model were considered as difference from the baseline. Then, for each participant, one average value for each HRV index was calculated for each condition. The different distress vocalization sounds (female, infant, and bonobo) were considered separately to test participants' reactions to the three distinct types of distress calls. All further analyses were run on the computed averaged values, which represent the

dependent variables. Multivariate ANCOVAs were performed with HRV values as the dependent variables, the distress type (woman, infant, and bonobo) as a within-subjects factor, the OXTR (rs53576) gene genotype (G/G and A carriers) as a between-subjects factor and the PBI dimensions all together (maternal care, maternal overprotection, paternal care, and paternal overprotection) as continuous covariates. Correlations were run as post hoc tests and Pearsons' *r* coefficients were used to analyze the strength of the effect of the covariate on the dependent variable and Cohen's *d* was used to evaluate the magnitude of effects which were found to be significant.

Results

Root Mean Square of Successive Differences (RMSSD)

Paternal Care. A significant interaction between paternal care and genotype was found for RMSSD values ($F(1,41) = 7.95$, $p < .01$, $d = .88$). Post-hoc statistical power, calculated with GPower software, was found to be adequate, being equal to .99 [Fig. S1]. The effect of paternal care was present only in the A carrier variant in averaged response to all crying sounds. The lower the paternal care, the higher the increase in RMSSD ($r = -.31$, $p = 0.15$). No significant main effect of paternal care or effect of the audio type was found.

Paternal Overprotection, Maternal Care. No main effect nor significant interaction between paternal overprotection or maternal care, genotype, or vocalization type was found.

Maternal Overprotection. A significant interaction between maternal overprotection, genotype and vocalization type was found for RMSSD ($F(1,41) = 4.23$ $p < .05$, $d = .64$). Post-hoc statistical power, calculated with GPower software, was acceptable, being equal to .96 [Fig. S2a-c]. The effect of maternal overprotection was more strongly present in A carriers, especially in response to infant crying sounds, while it was stronger in GG homozygotes in response to bonobo cries. In both cases, the greater the experienced maternal overprotection, the higher was the increase in RMSSD (A carriers in response to infant cry:

r = .36, *p* = 0.10; G/G homozygotes in response to bonobo cry: *r* = .28, *p* = 0.63). No significant main effect of maternal overprotection was found.

Low Frequencies (LF)

Paternal Care. A significant interaction between paternal care, genotype and vocalization type was found for LF values ($F(1,41) = 5.27$, $p < .01$, $d = .72$). Post-hoc statistical power, calculated with GPower software, was found to be adequate, being equal to .99 [Fig. S3a-c]. The effect of paternal care was more strongly present in A carriers in response to female and bonobo crying sounds, while it was stronger in GG homozygotes in response to infant cries. In both cases, the greater the experienced paternal care, the stronger was the LF decrease elicited by sounds (A carriers in response to female cry: *r* = -.39, *p* = 0.06; A carriers in response to bonobo cry: *r* = -.23, *p* = 0.27; G/G homozygotes in response to infant cry: *r* = -.20, *p* = 0.42). No significant main effect of paternal care was found.

Paternal Overprotection, Maternal Care, Maternal Overprotection. No main effect nor significant interaction was found between paternal overprotection, maternal care, maternal overprotection, genotype, or vocalization type.

No main effect nor significant interaction effect of the independent factors on high frequencies (HF) of on the ratio between low and high frequencies (LF/HF) was found.

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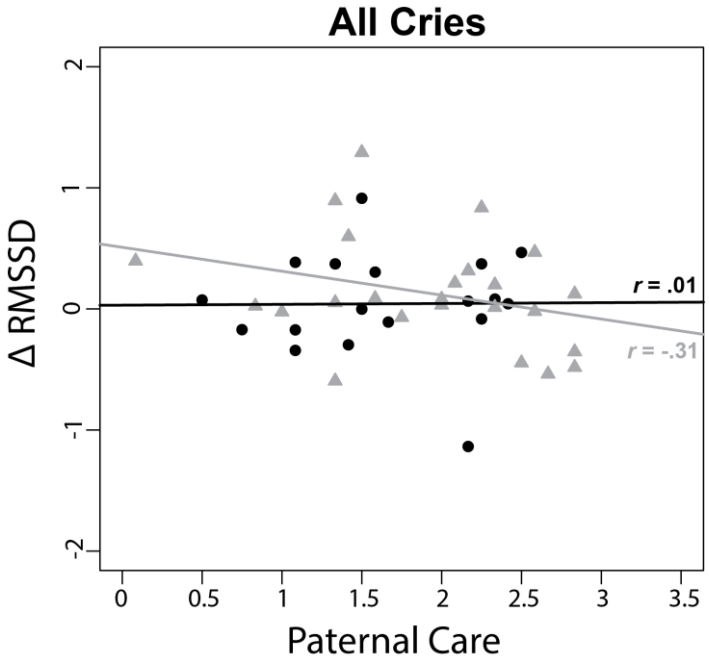

Figure S1. Correlations between changes in RMSSD (calculated as the difference from baseline) and experienced paternal care in response to all cry types. In the figure, RMSSD values averaged per participant are represented. Paternal care values ranged from 0 to 3. Black circles = G/G homozygous; grey triangles = A carriers. Lines represent the linear models for G/G homozygotes (black) and A carriers (grey). The reported *r*-values represent Pearson's *r* correlations.

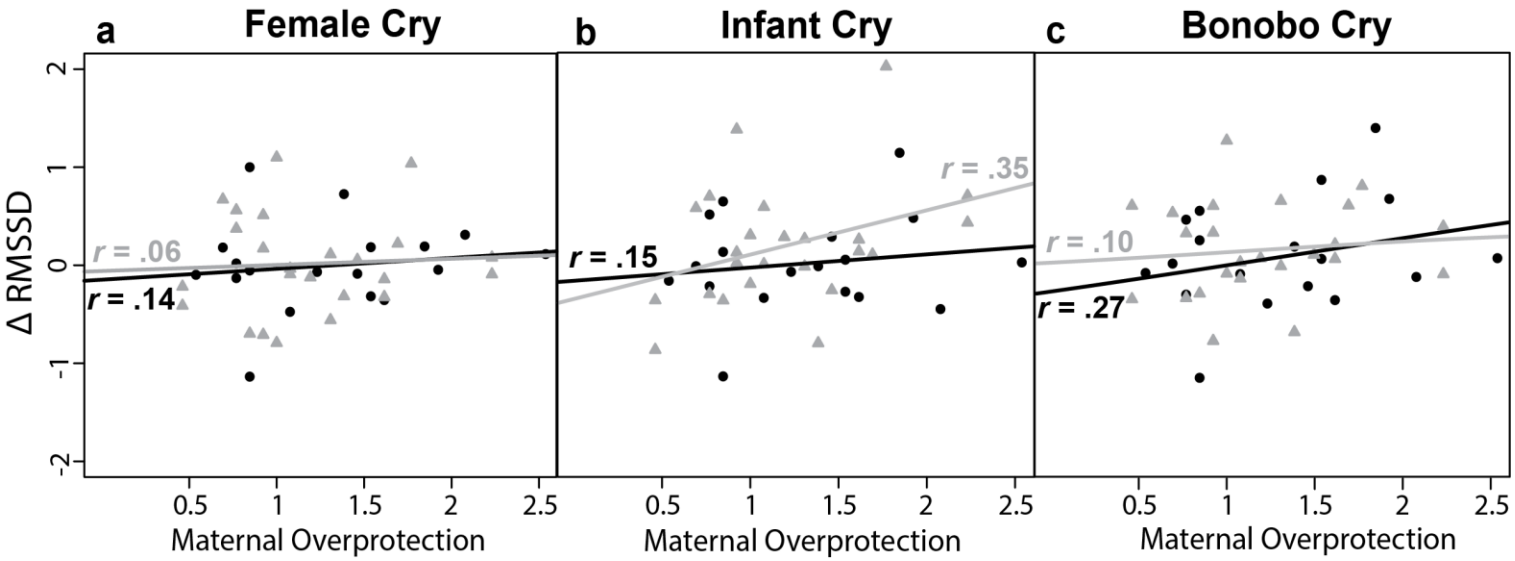

Figure S2a-c. Correlations between changes in RMSSD (calculated as the difference from baseline) and experienced maternal overprotection in response to distinct cry types. In the figure, RMSSD values averaged per participant and condition are represented. Maternal overprotection values ranged from 0 to 2.5. Black circles = G/G homozygous; grey triangles = A carriers. Lines represent the linear models for G/G homozygotes (black) and A carriers (grey). The reported *r*-values represent Pearson's *r* correlations. (a) RMSSD values to female cry. Influence of paternal overprotection on RMSSD values to female cries accordingly to genotype. (b) RMSSD values to infant cry. (c) RMSSD values to bonobo cry.

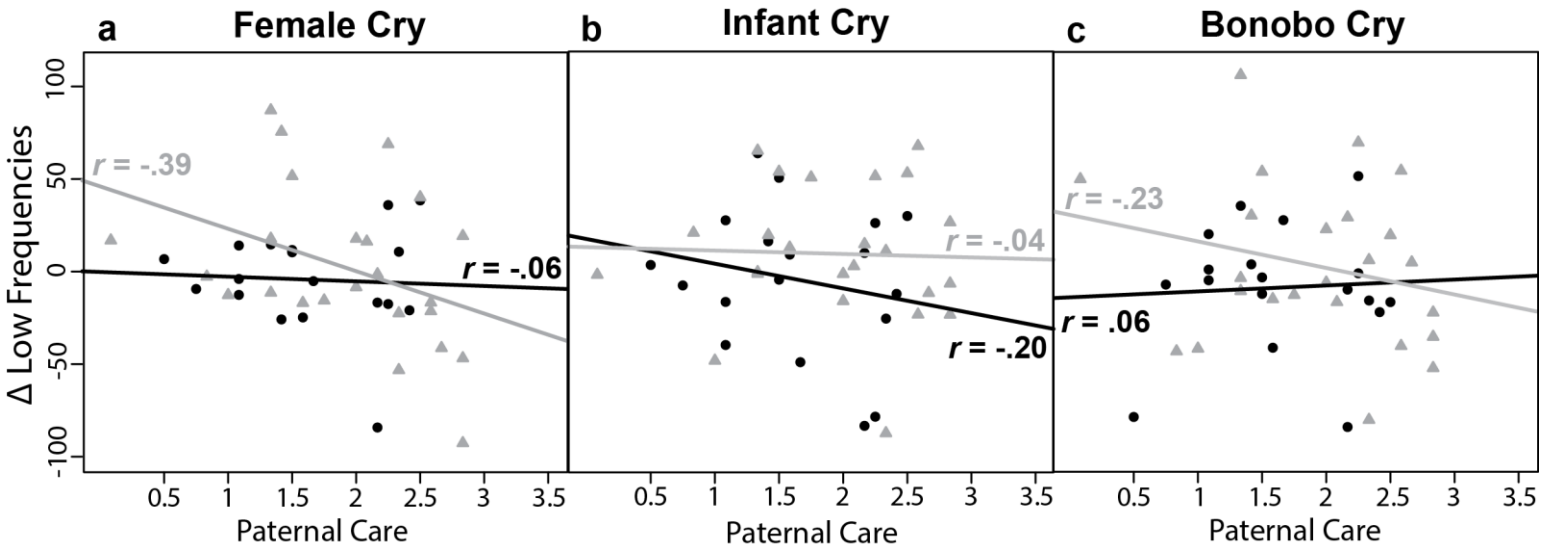

Figure S3a-c. Correlations between LF changes (calculated as the difference from baseline) and experienced paternal overprotection in response to distinct cry types. In the figure LF values averaged per participant and condition are represented. Paternal overprotection values ranged from 0 to 2.5. Black circles = G/G homozygous; grey triangles = A carriers. Lines represent the linear models for G/G homozygotes (black) and A carriers (grey). The reported *r*-values represent Pearson's *r* correlations. (a) LF values to female cry. Influence of paternal overprotection on LF values to female cries accordingly to genotype. (b) LF values to infant cry. (c) LF values to bonobo cry.