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Abstract

Parenting qualities are known to transmit across generations, but less is known about genetic processes that may modify how strongly parenting quality carries across generations. We examined in prospective data whether oxytocinergic genes of offspring moderate the intergenerational transmission of warm and accepting parent–child relationship qualities. The sample comprised 1167 Finnish parents (G2, 62% female) and their mothers (G1). At the study baseline, G1 mothers ($M_{age} = 38$) reported parent–child relationship qualities towards G2 children (age range 3-18). After 28-34 years, G2 offspring reported parent–child relationship qualities towards their own children using the same questionnaire. A cumulative genetic score was computed for G2 by summing up previously identified four alleles associated with non-optimal parenting or social impairments across *OXTR* (rs1042778, rs2254298, rs53576) and *CD38* (rs3796863) genes. Results indicated no interaction effects of G2 cumulative genetic score on the transmission of parent–child relationship qualities. Among single polymorphisms in *OXTR*, the interaction effects of rs53576 and rs1042778 were found. G1 maternal emotional warmth was associated with higher G2 emotional warmth among G2 participants with the *OXTR* rs53576 AA/AG genotype, but not among those with the GG genotype. G1 maternal acceptance was associated with higher G2 acceptance among those G2 participants with the *OXTR* rs1042778 GG/GT genotype, but not among those with the TT genotype. Oxytocinergic genes may influence sensitivity to quality of parent–child relationship, although this needs replication in future studies.

Keywords: intergenerational transmission, parent–child relationship qualities, warmth, acceptance, oxytocin receptor gene (*OXTR*), *CD38* gene, gene-environment (GxE) interaction

Several studies have shown that individuals' experience with their caregivers early in life is likely to shape their future parenting with their own children (for reviews, see Conger et al., 2009; Putallaz et al., 2001; Serbin and Karp, 2003; Van IJzendoorn, 1992), thus pointing to intergenerational transmission of parenting quality. A key issue of current research is to study factors that might determine how strongly parenting quality is transmitted across generations (Conger et al., 2009). In this context, it is especially important to elucidate genetic processes that may contribute to similarities in parenting qualities between parents and offspring when they become parents themselves (Conger et al., 2009; Mileva-Seitz et al., 2016). A recent meta-analysis of behavioral genetic research has revealed significant effects of parental genetic makeup on diverse aspects of parenting behavior (Klahr and Burt, 2014). Genetic estimates were moderate ranging from 28 to 37 percent for parental negativity and warmth, while not making significant contributions to parental control. A particularly promising area is gene-by-environment (GxE) interactions in the context of parenting quality, which may explain why some parents are more susceptible to early parenting quality and more likely to repeat it than others (Beaver and Belsky, 2012). Identifying interactions between early parenting quality and offspring genotype in predicting offspring own parenting quality may help to identify those individuals who are at risk for transmitting low parenting quality over generations. A majority of studies on GxE interactions has focused on the prediction of psychopathology or illness (e.g., Cicchetti et al., 2012; Samek et al., 2017); however, knowledge on GxE interactions may also be useful in predicting transmission of parenting quality.

Genes related to the oxytocin system are of special interest for research focused on parenting behavior (Mileva-Seitz et al., 2016). Oxytocin is a social hormone and neuropeptide that plays a key role in nursing, maternal care and bonding, parent-infant synchrony, and sensitive parenting (for a review, see Feldman and Bakermans-Kranenburg, 2017). Given the well-established associations between oxytocin and parenting, oxytocin receptor gene (*OXTR*) and *CD38*

gene which regulates the release of brain oxytocin are likely candidates for genetic influences on parenting quality (Jin et al., 2007; Lomanowska et al., 2015). Previous research has shown that several single-nucleotide polymorphisms (SNPs) in *OXTR* (rs1042778, rs2254298, and rs53576) were associated with sensitive parenting (Bakermans-Kranenburg and van IJzendoorn, 2008; Feldman et al., 2012), maternal warmth (Klahr et al., 2015), and positive parenting (Michalska et al., 2014). Some studies have also highlighted the role of *CD38* polymorphism (rs3796863) in sensitive parenting (e.g., Feldman et al., 2012).

Oxytocinergic genes are also promising moderators of continuity in parenting quality, given that the role of oxytocin has previously been suggested in the transmission of maternal behavior (Meaney, 2001). Female rats receiving greater maternal care in infancy (e.g., higher licking and grooming) have higher levels of oxytocin receptors in their brains and show higher maternal care towards their offspring (Meaney, 2001). In humans, Mileva-Seitz et al. (2013) found in a sample of 187 Caucasian mothers and infants that the SNPs in oxytocin peptide gene (rs2740210 and rs4813627), but not in oxytocin receptor gene (rs237885), interact with early care quality predicting the quality of mothering later in life. Mothers with C/C or G/G genotypes (for rs2740210 and rs4813627, respectively) who experienced higher care quality early in life expressed shorter duration of instrumental care (e.g., grooming, adjusting, and cleaning the infant); whereas mothers carrying the minor alleles of these SNPs and also having higher care quality in childhood had longer duration of instrumental care. Furthermore, Feldman et al. (2012) showed in an Israeli sample of 352 individuals that parents carrying A-allele on the *CD38* rs3796863 gene and having experienced warm parental care in childhood provided more sensitive parenting to their infants. The most recent study by Fujiwara et al. (2019) using a sample of 345 Japanese participants (comprising 115 family lines of grandmothers, mothers, and their infants) has shown that mothers who experienced higher overprotection in childhood showed more rejection towards their infants when carrying the G-allele of *OXTR* rs53576 (AG/GG). These three studies relied on retrospective

measures of early care quality and had relatively small sample sizes and thus can be seen to provide preliminary evidence for the moderating role of oxytocinergic genes in the context of parenting. Larger, population-based samples with prospective measures of parenting qualities in both generations are required to understand the moderating role of oxytocinergic genes in the transmission of parenting quality.

The current study examined whether the *OXTR* and *CD38* genes of offspring moderate the intergenerational transmission of parenting quality operationalized in terms of warm and accepting parent–child relationship. Data are from the prospective Young Finns cohort study, in which individuals were followed over 34 years. In addition to exploring the role of single polymorphisms in *OXTR* (rs1042778, rs2254298, and rs53576) and *CD38* (rs3796863) genes on the transmission of parenting quality, we also followed a recent recommendation to address the polygenic effects of genes by using a cumulative genetic score (Dick et al., 2015; Duncan and Keller, 2011). This score was built by combining the risk alleles of the above-mentioned genes associated with non-optimal parenting or social impairments based on previous literature (Feldman et al., 2014). Drawing on the differential-susceptibility hypothesis (Hartman and Belsky, 2016; Pluess and Belsky, 2010), parenting quality might differentially affect offspring future own parenting quality depending on the genotype of the offspring (Brüne, 2012). Individuals with so-called “plasticity alleles” may benefit the most from the warm and accepting parent–child relationship qualities but may similarly be more prone to cold and rejecting parenting, that is they may be sensitive to the environment “for better and for worse”. On the other hand, individuals without plasticity alleles will repeat the early parenting quality to a lesser degree (i.e., there might be no transmission of parent–child relationship qualities from one to the next generation). Thus, we hypothesize that offspring with plasticity alleles who experienced a warm and supportive relationship with their mothers early in life will build a positive and supportive relationship with their own children when they become parents themselves. At the same time, if the prior experience with their parents early in life has been more

negative, this group of participants is expected to be at risk for reporting a more negative quality of the parent–child relationship as compared to those without plasticity alleles.

Method

Participants

The participants were from the population-based Young Finns Study (YFS). At the baseline of the study in 1980, the sample comprised 3596 Finnish children and adolescents in six age cohorts of 3, 6, 9, 12, 15, and 18 years and their parents. They were enrolled from five geographical areas representing all parts of Finland using random sampling from the population register of the Social Insurance Institution. Eight follow-ups have been conducted 3-5 years apart. The detailed description of the YFS design and sample selection are given elsewhere (Raitakari et al., 2008).

Written informed consent was received from all participants who were at least twelve years old and from the parents of younger participants. The YFS was approved by the local committees of the five participating universities (the medical schools of Helsinki, Kuopio, Oulu, Tampere, and Turku) and conducted in accordance with the Helsinki declaration.

Procedure

The mothers of the original YFS participants are referred to in this study as the first generation (G1), the YFS participants as the second generation (G2), and their children as the third generation (G3). Two previous studies on the transmission of parent–child relationship qualities have been conducted in the YFS. In one of them, the study design comprised measures for G1 parent–child relationship qualities from 1980, and for G2 parent–child relationship qualities from 2008 (Savelieva et al., 2017a); in another study, G1 parent–child relationship qualities were also reported in 1980, and G2 parent–child relationship qualities were reported in 2008 and 2012 (Savelieva et al., 2017b). The current study design comprised the measures of G1 parent–child relationship qualities towards G2 in 1980, G2 parent–child relationship qualities towards G3 in

2008, 2012, and 2014, and genetic data on G2 oxytocinergic genes. At the study baseline in 1980, G1 mothers (mean age = 38) reported self-perceived qualities of the parent–child relationship towards the child (G2; mean age = 11). After 28 years in 2008, when G2 participants (mean age = 39; 62% female) have become parents themselves, they reported self-perceived qualities of the parent–child relationship with the G3 children (mean age = 11.6; 50.3% female). These qualities have been reported towards all the children in the family together in 2008 and 2012, whereas in 2014, G2 parents reported their relationship qualities towards each of the G3 children in the family separately. To be consistent across all measurement points, we averaged reports of parent–child relationship qualities in 2014 across several children and used the mean estimates in the analyses. G1 and G2 reported on their parent–child relationship qualities using the same measures, and the assessments were conducted independently of each other since G2 were unaware how G1 had rated themselves.

At the baseline of the study, 3412 G1 mothers reported their parent–child relationship qualities towards G2. Of those, 2319 G2 participants underwent genotyping. Of these, 1198 participants had rated their own parent–child relationship qualities in 2008, 1088 participants in 2012, and 861 participants in 2014. Altogether, 622 participants had full data on parent–child relationship qualities from the three measurement points.

Measures

Qualities of the parent–child relationship. Qualities of the parent–child relationship were based on parental self-perceptions of the relationship with the child, measured via a questionnaire comprising two scales: 1) emotional warmth and 2) acceptance of the child behavior, both derived from the Operation Family Study (Makkonen et al., 1981). The emotional warmth scale comprised four items (“My child is important to me”, “I am important to my child”, “I enjoy spending time with my child”, and “My child enables me to self-actualize myself”). The acceptance scale consisted of three items (“I often become irritated with my child “, “In difficult situations, my child

is a burden”, and “My child takes too much of my time”). These scales measure the parental perception of their relationship with children and reflect the degree to which there is a warm and loving or cold and rejecting feeling in the parent–child relationship (Schaefer, 1959). They tap into the general emotional tone of a parent–child dyad, which define the overall emotional atmosphere within a family and thereby reflect parenting qualities, rather than parenting behaviors or practices (even though some questions include behavioral elements) (Dix, 1991). All the items were scored on a 5-point Likert-type scale. The acceptance scale was reversed coded so that a high score reflects high levels of emotional warmth and acceptance. Four items for emotional warmth and three items for acceptance were averaged to form two manifest variables that were used in all analyses, respectively. Both parent–child relationship qualities scales were negatively skewed in both generations and were therefore corrected by a cubic root transformation. The Cronbach’s α reliability coefficients of emotional warmth were 0.68 for G1 in 1980; for G2, 0.71 in 2008, 0.69 in 2012, and 0.75 in 2014. The corresponding coefficients for acceptance were 0.67 in 1980; for G2, 0.68 in 2008, 0.70 in 2012, and in 2014. The results of the confirmatory factor analyses conducted previously supported the construct validity of these scales (Savelieva et al., 2017a). Previous research also shows moderate continuity in the emotional warmth and acceptance scales over different developmental periods (Merjonen et al., 2011) and that the scales measure stable characteristics of the parents (Katainen et al., 1997). These scales have been also shown to predict several offspring outcomes in adolescence and adulthood, including dispositional compassion, perceived social support, self-esteem, and depressive tendencies (Dobewall et al., 2018a; Heinonen et al., 2003; Hintsanen et al., 2019; Jokela et al., 2007).

Genotyping. The genome-wide single nucleotide polymorphism analyses for the YFS participants were performed in 2009 by using the 670K Illumina platform. Variation over 670 000 known SNPs was measured in total from 2442 participants. Imputation up to 2.5 million SNPs was performed using information on HapMap 2 by using MACH (the genomic build 26). In the present

study, we selected three SNPs of the *OXTR* (rs1042778 (G to T), rs2254298 (A to G), and rs53576 (A to G)) and the *CD38* SNP rs3796863 (A to C) because they have been related to positive parenting, parental sensitivity, and parent-infant gaze synchrony previously (for a review, see Mileva-Seitz et al., 2016). Given that complex behaviors, such as parenting, are controlled by many genes, it was suggested using a genetic risk score or a plasticity score, an index computed combining several SNPs in a gene, to assess cumulative effects of genes on a certain phenotype (Belsky and Israel, 2014). Therefore, a cumulative genetic score was computed by summing up the previously identified genetic variants associated with non-optimal parenting or social impairments. These include the *OXTR* rs1042778 TT, rs2254298 GG, rs53576 A allele (AA or AG), and *CD38* rs3796863 CC (Bakermans-Kranenburg and van IJzendoorn, 2008; Feldman et al., 2014, 2012). Cumulative genetic score ranged from 0 (no risk alleles) to 4 (all risk alleles).

Control variables. The transmission of parenting quality is recommended to be studied under similar contextual conditions in both generations (Conger et al., 2009). Therefore, we controlled for age (G1, G2, and G3), G2 gender, partnership status (G1 and G2), socioeconomic status (SES; G1 and G2), G1 mental health problems, and G2 depressive symptoms. We used mean estimates of G3 age of all children in the family, because G2 parents reported parent-child relationship qualities towards all G3 children in the family together, not towards each child separately. In the analyses, we used the G3 mean age at the time of rating of parent-child relationship qualities (i.e., 2008, 2012, and 2014). Partnership status was coded as a dichotomous variable (0 = not living with the partner, 1 = married/cohabiting). SES was indicated by years of education and family annual income in 1980 for G1 and in 2012 for G2. The years of education and income variables were first transformed into Z-scores and then averaged to form a single variable. G1 medication use for mental health problems was self-reported in 1980. G2 depressive symptoms were measured using the Beck Depression Inventory-II in 2008 ($\alpha = .92$) (Beck et al., 1996).

Statistical Analysis

Main analyses. G1 qualities of parent–child relationships were mean centered prior to analyses to facilitate the interpretation of the results. We tested the moderating role of a) separate SNPs of *OXTR* and *CD38* genes and b) cumulative genetic score on intergenerational transmission of parent–child relationship qualities using linear regression modeling. The main analyses were conducted using a pooled estimate of three-time points for G2 qualities of the parent–child relationship using multilevel modeling (n=1208). Three models were constructed: Model 1 examined the direct effects of G1 emotional warmth and of acceptance on G2 emotional warmth and acceptance; Model 2 tested the direct effects of G2 *OXTR* and *CD38* genes on G2 emotional warmth and acceptance; and Model 3 examined interactions between G2 genes and G1 emotional warmth and acceptance on G2 emotional warmth and acceptance. Emotional warmth and acceptance were analyzed in separate models. We reported the regression coefficients in a stepwise manner: the variables in Model 2 and 3 were adjusted for the variables in the preceding models. Cumulative genetic score and each SNPs were analyzed separately. All the analyses were adjusted for G1, G2, and G3 age, G2 gender, G1 and G2 partnership status, G1 and G2 SES, G1 mental health problems, and G2 depressive symptoms.

Because of the multiple testing, we conducted the Benjamini-Hochberg test to control the false discovery rate (Benjamini and Hochberg, 1995). All p-values from the three models for emotional warmth and from the three models for acceptance were ordered from smallest to largest and ranked. We then compared each individual p-value to its Benjamini-Hochberg critical value. The largest individual p-value that was smaller than its Benjamini-Hochberg critical value was considered statistically significant, and all individual p-values smaller than that were also significant. We used the false discovery rate of 0.10 and 0.25 for the Benjamini-Hochberg critical values.

Additional analyses. Given that the intergenerational transmission of parent–child relationship qualities may differ in mother-son and mother-daughter dyads (Savelieva et al., 2017a), we tested the moderating role of G2 gender in all models, as well as repeated the main analyses separately for boys and girls in G2.

To investigate the moderating effects of age on the transmission of parent–child relationship qualities, we first categorized G1 and G3 age into categories with 5-year interval, and then tested the moderating role of G1 age, G2 age, G3 age, as well as both G1 and G2 age, and G2 and G3 age in the transmission of emotional warmth and acceptance.

Finally, we repeated all the analyses using data for G2 qualities of the parent–child relationship from three measurement points separately (i.e., from 2008, 2012, and 2014). All analyses were conducted using Stata 13.1 and Stata 15 statistical software (StataCorp, 2017, 2013).

Results

Descriptive statistics

Table 1 presents the characteristics of the sample. G2 participants were 11 years old on average when G1 mothers reported qualities of their relationship towards them; and 38 years on average when they first reported their own qualities of parent–child relationship in 2008. As it has been previously shown in the same sample (Savelieva et al., 2017a, 2017b), G2 participants reported lower acceptance towards G3 than their mothers had reported towards them (3.6 vs. 4, $p < 0.001$), but G2 were more emotionally warm towards G3 than G1 mothers towards them (4.56 vs. 4.48, $p < 0.001$). *OXTR* rs1042778, rs2254298, and rs53576 and the *CD38* SNP rs3796863 were in Hardy-Weinberg equilibrium, indicating that the genotype frequencies of these SNPs in the study population were stable (all $ps > 0.181$).

Table 2 presents the bivariate correlations between qualities of the parent–child relationship and offspring genotype. As it has been previously reported in the same sample (Savelieva et al., 2017a, 2017b), higher G1 acceptance correlated with higher G2 acceptance in all three follow-ups;

and higher G1 emotional warmth correlated with higher G2 emotional warmth. No correlations between G1 emotional warmth or G1 acceptance and offspring genotype were found. This reduces the likelihood that gene-environment correlations have confounded the associations reported below (Dick et al., 2015; Dobewall et al., 2018b; Klahr and Burt, 2014). G2 acceptance in 2014 correlated with G2 *OXTR* rs2254298 GG genotype ($r = 0.09$, $p = 0.008$). G2 emotional warmth in 2012 correlated with *CD38* rs3796863 CC ($r = 0.06$, $p = 0.036$) and cumulative genetic score ($r = 0.07$, $p = 0.018$).

G2 genotype as a moderator of the intergenerational transmission of parent–child relationship qualities

Table 3 shows that G1 emotional warmth predicted G2 emotional warmth adjusting for all covariates ($B = 0.11$, $p < 0.001$). There also were marginal main effects of G2 cumulative genetic score ($B = 0.003$, $p = 0.053$) on G2 emotional warmth and *OXTR* rs1042778 ($B = 0.01$, $p = 0.038$) on G2 emotional warmth. These main effects remained significant after controlling the false discovery rate of 0.25 but became nonsignificant with the false discovery rate of 0.10 (Table A.1). There was no interaction effect between G1 emotional warmth and G2 cumulative genetic score on G2 emotional warmth ($p = 0.815$). Table 4 shows that G1 acceptance predicted G2 acceptance after adjusting for all control variables ($B = 0.06$, $p = 0.031$). There were neither main effects of G2 cumulative genetic on G2 acceptance nor interaction effect between G1 acceptance and G2 cumulative genetic score on G2 acceptance (all p -values > 0.188). The estimates for all control variables are shown in Table A.2 and A.3 in Appendices.

The analysis with separate SNPs revealed a statistically significant interaction between G1 emotional warmth and *OXTR* rs53576 on G2 emotional warmth adjusting for all covariates ($p = 0.010$; Table 3). G1 maternal emotional warmth was associated with higher G2 emotional warmth among those participants with the AA/AG genotype ($B = 0.010$, 95 CI [0.006, 0.013], $p < 0.001$) but not among those with the GG genotype ($B = 0.002$, 95 CI [-0.003, 0.007], $p = 0.419$) (Figure 1).

The interaction effect remained significant after controlling the false discovery rate of 0.25 but became nonsignificant with the false discovery rate of 0.10 (Table A.1).

Regarding acceptance, a statistically significant interaction effect of *OXTR* rs1042778 on the transmission of acceptance was found after adjusting for all covariates ($p = 0.024$, Table 4). G1 maternal acceptance was associated with higher G2 acceptance among those participants with the GG/GT genotype ($B = 0.008$, 95 CI [0.002, 0.013], $p = 0.005$) but not among those with the TT genotype ($B = -0.009$, 95 CI [-0.023, 0.005], $p = 0.195$) (Figure 2). This interaction effect remained significant after controlling the false discovery rate of 0.25 but became nonsignificant with the false discovery rate of 0.10 (Table A.1).

Results from additional analyses

The main results conducted separately for G2 boys and girls are presented in Table A.4 and Table A.5, but there were mainly no statistically significant interactions indicating no moderating role of G2 gender in the transmission of parent–child relationship qualities. Only one three-way interaction was statistically significant between G1 acceptance and *OXTR* rs53576 and G2 gender on G2 acceptance ($p = 0.031$), suggesting that there might be an interaction effect of *OXTR* rs53576 on the transmission of acceptance only among G2 boys, but not girls.

No moderating role of G1 age, G2 age, and G3 age, as well as both G1 and G2 age, and G2 and G3 age was found in the transmission of emotional warmth and acceptance, indicating that the continuity of parent–child relationship qualities was not significantly different across various parental and offspring age groups in both generations (data not shown). These results are in line with our previous findings conducted in the same sample but using different study design (Savelieva et al., 2017b).

Table A.6 and Table A.7 show the main effects of G1 emotional warmth and acceptance and of G2 genes, as well as interactions between G1 emotional warmth and acceptance and G2 cumulative genetic score on G2 emotional warmth and acceptance using three measurement points

separately. The findings with separate time points were largely in line with those presented in Table 3 and Table 4.

Discussion

The current study examined whether oxytocin receptor gene polymorphisms and *CD38* gene moderate the transmission of parent–child relationship qualities across generations. We found that G1 maternal emotional warmth was related to higher G2 emotional warmth among those G2 participants with the *OXTR* rs53576 AA/AG genotype, but not among those with the GG genotype. We also found that G1 acceptance was associated with higher G2 acceptance among those G2 participants with the *OXTR* rs1042778 GG/GT genotype, but not among those with the TT genotype. In other words, individuals with the A-allele of *OXTR* rs53576 were more likely to have higher emotional warmth towards their children when they had experienced higher emotional warmth in childhood from their mothers. Similarly, participants with the A-allele and lower emotional warmth in childhood reported colder relationship quality with their children becoming parents themselves. Likewise, the participants with the G-allele of *OXTR* rs1042778 were more likely to repeat the same levels of acceptance they had experienced in childhood. These findings are in line with the differential-susceptibility hypothesis (Pluess and Belsky, 2010), suggesting that some individuals are more susceptible to positive or negative conditions of their early environment. Although our results remained significant after correcting for multiple testing, they should be confirmed in future studies (Dick et al., 2015). Therefore, our study provides the first evidence for a moderating role of oxytocinergic genes in the transmission of parent–child relationship qualities.

Previous studies, which were conducted in Caucasian samples, have identified the A-allele of rs53576 as a “risk allele” which is associated with less emotionally warm and sensitive parenting quality (Bakermans-Kranenburg and van IJzendoorn, 2008; Klahr et al., 2015). One study has, however, found that the A-allele of rs53576 is associated with higher levels of positive parenting (Michalska et al., 2014). Our results may explain these contradictory findings by suggesting that the

A-allele of rs53576 may be regarded as a “plasticity allele” given that participants carrying this allele were the most susceptible to either warm or cold qualities of the parent–child relationship they had experienced early in life.

Furthermore, the recent study (Fujiwara et al., 2019) conducted in Japanese sample has shown that the intergenerational transmission of parenting is evident among mothers with the G-allele of *OXTR* rs53576 (AG/GG); whereas our results coming from Finnish sample show that the transmission is evident only among parents with the A-allele of *OXTR* rs53576 (AG/AA). The discrepancy in results of Fujiwara et al. study and ours may support the suggestion that the effects of *OXTR* allelic variations on human affiliation may be culture dependent and differ in Caucasian and non-Caucasian populations (for review, see Feldman et al., 2016). For example, parenting is operationalized in our study in terms of emotional warmth (also known as closeness and connectedness), which is considered to vary within and between cultures (MacDonald, 1992); whereas Fujiwara and colleagues have focused on overprotection. Overprotection is considered a specific feature of parenting in Asian cultures, being a common practice and being accepted as a social norm in Japan (Fujiwara et al., 2019). Therefore, it might be possible that this culture-specific pattern of parenting may confound the link between parenting and oxytocinergic genes. It should be noted, however, that in Fujiwara et al. study the genotype frequency of *OXTR* rs53576 was not in Hardy-Weinberg equilibrium among grandmothers, suggesting that the selection of grandmothers might be biased. Further studies from different cultures are needed to examine the role of broader social and cultural context in the intergenerational transmission of parenting and oxytocin functioning.

Less research has been done on investigating the role of *OXTR* rs1042778 SNP in the context of parenting quality. One study has found that parents with the TT genotype touched their children less frequently than parents with the GG/GT genotype (Feldman et al., 2012); whereas another study suggested that mothers with the TT/GT genotype displayed greater positive parenting

towards their children, although the findings were less consistent (Michalska et al., 2014). Our results add to the growing body of literature suggesting that the transmission of acceptance was observed among the individuals with the GG/GT genotype, but not among those with the TT genotype. Further research is needed to investigate the role of *OXTR* rs1042778 SNP in parenting behavior.

In contrast to previous studies (Bakermans-Kranenburg and van IJzendoorn, 2008; Feldman et al., 2012; Klahr et al., 2015; Michalska et al., 2014), we found no main effects of G2 *OXTR* rs2254298, *OXTR* rs53576, and *CD38* rs3796863 on G2 emotional warmth or acceptance. However, we found a small and nominally significant main effect of *OXTR* rs1042778 on G2 emotional warmth, which corresponds to results from Feldman et al. (2012) and Michalska et al. (2014) studies. Moreover, the main effect of the cumulative genetic score on parent–child relationship qualities was close to zero and nominally significant. We also found no moderating role of the cumulative genetic score on the transmission of parent–child relationship qualities. One potential difference between our findings and the previous one is that participants in the present study reported the perception of the parent–child relationship qualities, whereas the previous studies assessed positive or sensitive parenting behaviors (Bakermans-Kranenburg and van IJzendoorn, 2008; Feldman et al., 2012; Klahr et al., 2015; Michalska et al., 2014). Furthermore, it is possible that different SNPs affect sensitivity to parenting differently in different populations.

Strengths and limitations

Several limitations should be taken into account while interpreting the findings. First, the qualities of the parent–child relationship were measured on non-standardized scales. Although both the reliability and the construct validity of this measure have been shown to be relatively good (Katainen et al., 1997; Savelieva et al., 2017a), these findings should be replicated with standardized measures of parenting quality. Second, our measures of the parent–child relationship qualities relied on parents’ self-reports, not on observations by a third party. Although direct

observations may provide a more accurate picture, it is nevertheless a costly method and not always practicable in long-term, large-scale population-based studies spanning decades. Third, our measures of parent-child relationship qualities reflect only parental perception of the relationship with children, whereas measures of children's perception of the relationship with parents were not provided. Parental perception of their relationship with children may or may not correlate with the actual behavior of parents, of which there also were no measures in the Young Finns Study. Fourth, qualities of the parent-child relationship were reported by mothers and not fathers in the first generation, because mothers were typically the primary caregivers at the time of the first data collection in 1980. However, having information from both mothers and fathers in the first generation would have provided better possibilities to test for GxE interactions in the transmission of the parent-child relationship qualities. Fifth, even though we used the pooled estimate across three measurement points, the multiple statistical comparisons may increase the risk of false positive findings, and the findings need to be replicated in another population. Finally, the YFS sample was mainly White Caucasian, which may limit the generalizability of our findings to a more ethnically diverse population.

The main strength of this study is its intergenerational design that fulfils the key criteria for an intergenerational study presented by Thornberry (2016). These criteria include: 1) having prospective data of the parent-child relationship qualities from two generations; 2) having independent measures of the parent-child relationship qualities, based on different informants (i.e., G1 mothers and G2 offspring), thus excluding the possibility of common informant bias; 3) having comparable measures of qualities of the parent-child relationship in two generations, which were collected at approximately the same ages in G1 and G2 during the assessment phases. In addition, the three repeated measurements of the parent-child relationship qualities in G2 were applied to use all the available data of G2 relationship qualities in the analysis and to conduct a pooled estimate of these measurement points.

Conclusion

In conclusion, our findings add to the growing body of research supporting a link between oxytocin functioning and parenting quality. Our study suggests the moderating role of *OXTR* rs53576 and rs1042778 on the transmission of parent–child relationship qualities across generations. Further research is needed to replicate these findings, as well as understand the role of a cumulative genetic score of oxytocinergic genes in the transmission of parenting quality.

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Table 1. Descriptive statistics (n=1198)

Variable	Mean (SD)	n (%)	Range
G1 age (1980)	38 (7.59)		21 to 66
G2 age (1980)	11.3 (4.79)		3 to 18
G2 age (2008)	39.3 (4.79)		31 to 46
G3 mean age (2008)	9.8 (5.41)		1 to 25
G1 gender (female)		1198 (100%)	
G2 gender (female)		737 (62%)	
G1 partnership status		1051 (88%)	
G2 partnership status		1051 (88%)	
G1 socioeconomic status	-0.01 (0.59)		-1.40 to 2.74
G2 socioeconomic status	-0.01 (0.82)		-1.93 to 3.03
G1 mental health problems (yes)		35 (1.5%)	
G2 depressive symptoms	5.23 (6.36)		0 to 43
G1 acceptance (1980)	4.02 (0.63)		1.67 to 5
G2 acceptance (2008)	3.56 (0.70)		1 to 5
G1 emotional warmth (1980)	4.48 (0.49)		1.25 to 5
G2 emotional warmth (2008)	4.56 (0.44)		2.25 to 5
G2 <i>OXTR</i> rs1042778			
TT		175 (14.6%)	
GT		562 (46.9%)	
GG		462 (38.5%)	
G2 <i>OXTR</i> rs2254298			
AA		11 (0.9%)	
AG		181 (15.1%)	

GG	1007 (84%)
<i>G2 OXTR rs53576</i>	
GG	401 (33.4%)
AG	565 (47.1%)
AA	233 (19.4%)
<i>G2 CD38 rs3796863</i>	
AA	165 (14%)
AC	549 (46%)
CC	485 (40%)
<i>G2 cumulative genetic score</i>	
0	39 (3.3%)
1	251 (21%)
2	543 (45.2%)
3	336 (28%)
4	30 (2.5%)

Note. G1 = Generation1, G2 = Generation2, G3 = Generation 3.

Partnership status was coded as a dichotomous variable: 1 = married/cohabiting, 0=not living with a partner. Socioeconomic status is a standardized composite variable consisting of years of education and annual income. G1 medication use for mental health problems was self-reported (no/yes). G2 depressive symptoms were measured using the Beck Depression Inventory-II.

Table 2. Bivariate correlation between G1 and G2 parent–child relationship qualities and G2 genotype

Variable	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.
1. G1 acceptance (1980)	1												
2. G2 acceptance (2008)	.08	1											
3. G2 acceptance (2012)	.07	.60	1										
4. G2 acceptance (2014)	.11	.44	.57	1									
5. G1 emotional warmth (1980)	.31	.02	-.01	-.01	1								
6. G2 emotional warmth (2008)	.03	.28	.23	.17	.12	1							
7. G2 emotional warmth (2012)	.03	.30	.34	.23	.11	.62	1						
8. G2 emotional warmth (2014)	.01	.19	.25	.28	.08	.51	.63	1					
9. G2 <i>OXTR</i> rs1042778	-.00	.01	.00	.02	.00	.03	.04	.05	1				
10. G2 <i>OXTR</i> rs2254298	.01	.01	.01	.09	.02	.03	.04	.02	.16	1			
11. G2 <i>OXTR</i> rs53576	-.01	.01	.00	-.05	.02	-.01	.00	-.05	-.22	-.07	1		
12. G2 <i>CD38</i> rs3796863	-.00	.00	.02	.06	.02	.03	.06	.03	.02	.00	.03	1	
13. G2 cumulative genetic score	-.01	.01	.02	.05	.03	.04	.07	.02	.38	.48	.46	.62	1

Note. Absolute value $|r|$ of correlation .06 or higher is statistically significant.

G1 = Generation1, G2 = Generation2.

Table 3. Direct and moderating effects of G2 *OXTR* and *CD38* genes in the transmission of emotional warmth (n=1167)

		G2 emotional warmth		
		B (SE)	95% CI	p
Model 1	Direct effect of early environment			
	G1 emotional warmth	0.11 (0.021)	0.066, 0.149	<0.001
Model 2	Adding separately direct effect of G2 genes			
	G2 <i>OXTR</i> rs1042778 TT	0.01 (0.004)	0.000, 0.015	0.038
	G2 <i>OXTR</i> rs2254298 GG	0.00 (0.004)	-0.005, 0.009	0.582
	G2 <i>OXTR</i> rs53576 (AA/AG)	-0.00 (0.003)	-0.006, 0.005	0.996
	G2 <i>CD38</i> rs3796863 CC	0.004 (0.003)	-0.001, 0.009	0.154
	G2 cumulative genetic score	0.003 (0.002)	-0.000, 0.006	0.053
Model 3	Adding separately GxE interactions			
	G1 emotional warmth*G2 <i>OXTR</i> rs1042778 TT	-0.09 (0.064)	-0.214, 0.036	0.164
	G1 emotional warmth*G2 <i>OXTR</i> rs2254298 GG	-0.02 (0.049)	-0.119, 0.075	0.657
	G1 emotional warmth*G2 <i>OXTR</i> rs53576 (AA/AG)	0.12 (0.045)	0.028, 0.203	0.010
	G1 emotional warmth*G2 <i>CD38</i> rs3796863 CC	-0.02 (0.042)	-0.115, 0.050	0.440

G1 emotional warmth*G2 cumulative genetic score	0.01 (0.026)	-0.045, 0.057	0.815
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Note. Models are adjusted for G1, G2, and G3 age, G2 gender, G1 and G2 SES, G1 and G2 partnership status, G1 mental health problems, and G2 depressive symptoms. Model 2 and model 3 include five separate regression models.

B = unstandardized regression coefficient, SE = standard error, CI = confidence interval, G1 = Generation1, G2 = Generation2.

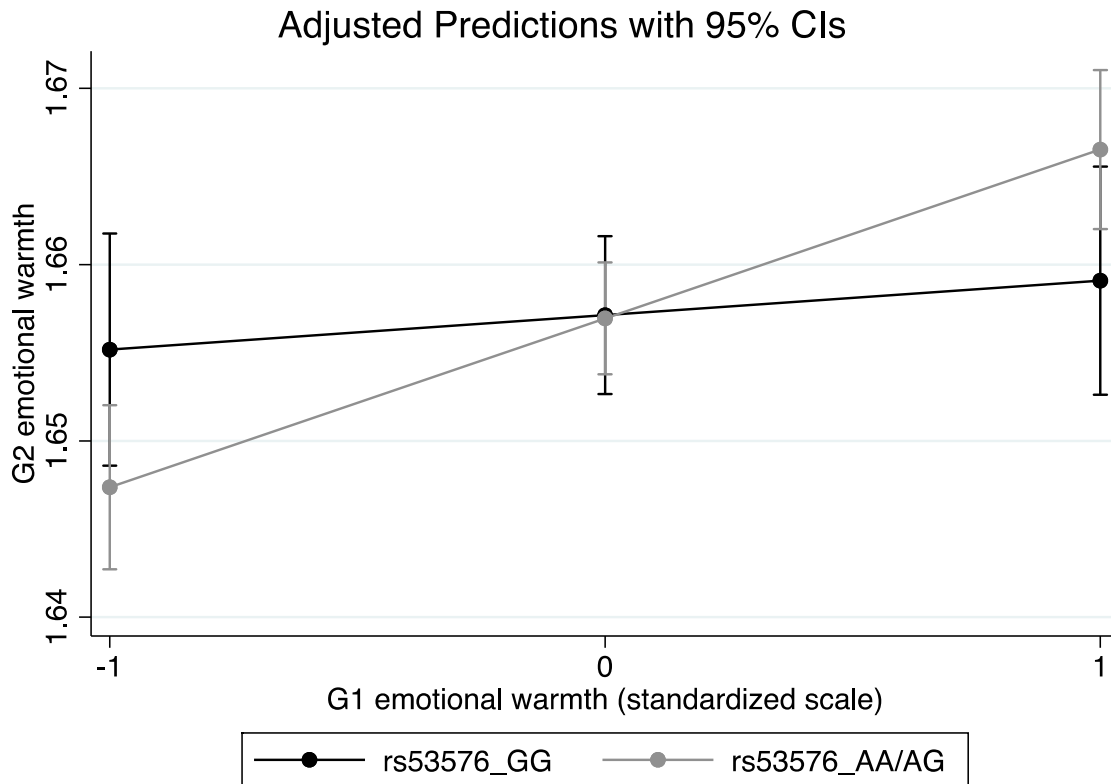
Table 4. Direct and moderating effects of G2 *OXTR* and *CD38* genes in the transmission of acceptance (n=1167)

		G2 acceptance		
		B (SE)	95% CI	p
Model 1	Direct effect of early environment			
	G1 acceptance	0.06 (0.028)	0.006, 0.116	0.031
Model 2	Adding separately direct effect of G2 genes			
	G2 <i>OXTR</i> rs1042778 TT	0.00 (0.007)	-0.012, 0.013	0.922
	G2 <i>OXTR</i> rs2254298 GG	0.01 (0.006)	-0.008, 0.017	0.469
	G2 <i>OXTR</i> rs53576 (AA/AG)	-0.00 (0.005)	-0.013, 0.007	0.549
	G2 <i>CD38</i> rs3796863 CC	0.00 (0.005)	-0.006, 0.013	0.488
	G2 cumulative genetic score	0.00 (0.003)	-0.004, 0.007	0.671
Model 3	Adding separately GxE interactions			
	G1 acceptance*G2 <i>OXTR</i> rs1042778 TT	-0.18 (0.081)	-0.342, -0.024	0.024
	G1 acceptance*G2 <i>OXTR</i> rs2254298 GG	-0.02 (0.065)	-0.147, 0.107	0.760
	G1 acceptance*G2 <i>OXTR</i> rs53576 (AA/AG)	-0.04 (0.057)	-0.148, 0.076	0.528

G1 acceptance*G2 <i>CD38</i> rs3796863 CC	-0.02 (0.054)	-0.122, 0.089	0.760
G1 acceptance*G2 cumulative genetic score	-0.05 (0.031)	-0.109, 0.012	0.188

Note. Models are adjusted for G1, G2, and G3 age, G2 gender, G1 and G2 SES, G1 and G2 partnership status, G1 mental health problems, and G2 depressive symptoms. Model 2 and model 3 include five separate regression models.

B = unstandardized regression coefficient, SE = standard error, CI = confidence interval, G1 = Generation1, G2 = Generation2.



Figure

1. The moderating role of *OXTR* rs53576 in the association between G1 emotional warmth and G2 emotional warmth. G1 emotional warmth was standardized with mean of 0 and ± 1 SD. G1 parental emotional warmth was associated with higher G2 emotional warmth among those participants with the AA/AG genotype ($B = 0.010$, $p < 0.001$) but not among those with the GG genotype ($B = 0.002$, $p = 0.419$).

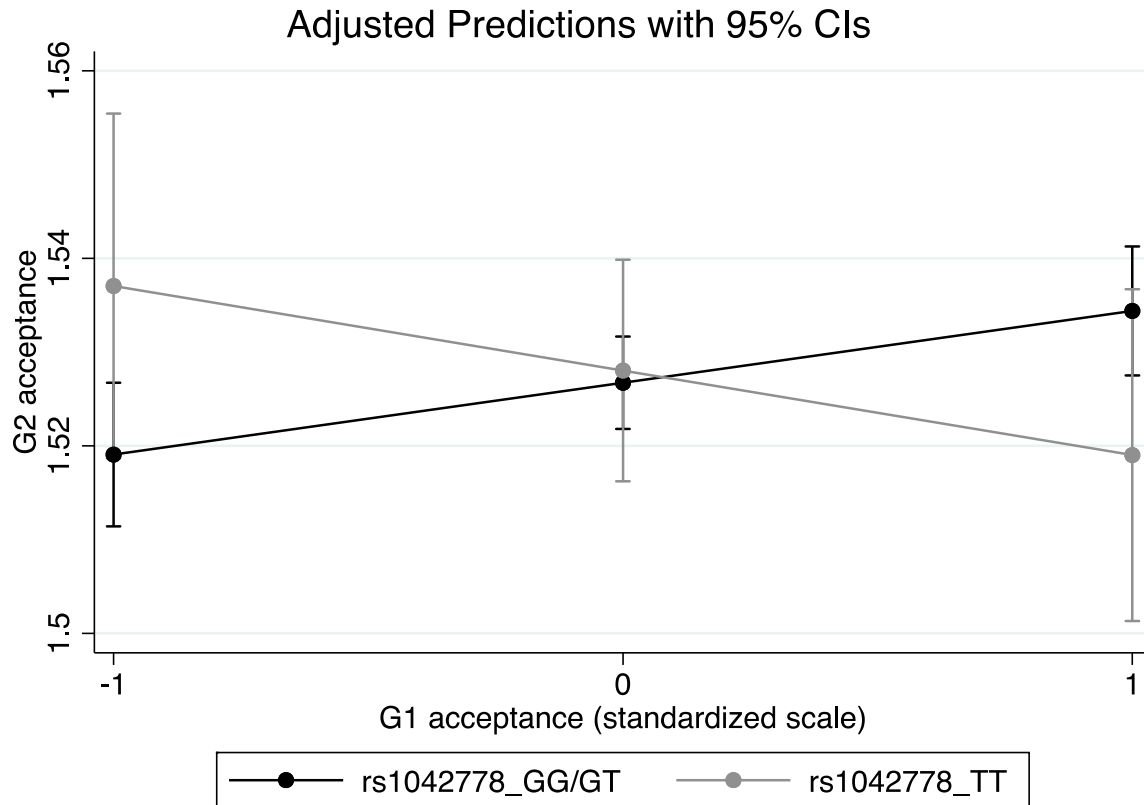


Figure 2. The moderating role of *OXTR* rs1042778 in the association between G1 acceptance and G2 acceptance. G1 acceptance was standardized with mean of 0 and ± 1 SD. G1 parental acceptance was associated with higher G2 acceptance among those participants with the GG/GT genotype ($B = 0.008$, $p = 0.005$) but not among those with the TT genotype ($B = -0.009$, $p = 0.195$).