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The role of oxytocin receptor gene (OXTR) and mother's emotional warmth in predicting adulthood sociability

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ABSTRACT

The oxytocin receptor gene (OXTR) may function as a "plasticity gene" that increases or decreases sociability in those individuals susceptible to growing up in a beneficial versus more adverse environment. This study used data from 2289 (55% female) participants from the ongoing prospective Young Finns Study. Maternal emotional warmth was assessed in 1980 when the participants were 3–18 years old. Participants' sociability temperament was measured at five follow-ups, from 1992 to 2012. Emotional warmth in childhood and OXTR genotype were not directly associated with temperamental sociability. We found a nominally significant gene–environment interaction (p = .03) suggesting that participants with a genetic profile of rs1042778 T-allele and rs2254298 A-allele are affected high versus low emotional warmth, whereas homozygotes of both G-alleles are unaffected by the same environmental influence. Our findings should be, however, interpreted as a null result as the interaction effect did not survive correction for multiple testing.

1. Introduction

Temperament traits are regarded as early emerging personality traits that have persistence later in life and are biological in origin (Buss, 1991; Buss & Plomin, 1975). A prominent theory of temperament – which describes inter-individual differences in adulthood temperament – is the Emotionality, Activity, and Sociability (EAS) theory by Buss and Plomin (1986). Emotionality is defined as distress that is accompanied by intense autonomic arousal, activity as the expenditure of physical energy, and sociability as an individual's tendency to prefer the presence of others to being alone (Buss, 1991).

In the current study, we focus on adulthood sociability, as it is a motivational trait that captures preference for social behavior. Individuals with high adulthood sociability socialize whenever possible, are willing to be responsive to others and to cooperate with them, and find it rewarding to spend time with other people (Buss, 1991). More precisely, being sociable is motivated by the intrinsic social rewards of sharing activities, attention from others, and responsivity from others (Buss, 1991). Temperamental sociability has been shown to have moderate (heterotypic) continuity (Katainen, Räikkönen, & Keltikangas-Järvinen, 1998) and the biological sensitivity associated with sociability is associated with how an individual experiences the social environment (Buss & Plomin, 1986). Finally, the study of adulthood sociability development is of clinical relevance, as (lack of) sociability does not only affect close relationships and social behavior but it is also involved in the etiology of various health problems and longevity across the life span (Elovainio et al., 2015; Yang et al., 2016).

1.1. Oxytocin receptor gene (OXTR)

As temperament is thought to be heritable to a large extent (Saudino, 2005), specific candidate genes might play a role in the development of sociability. The neuropeptide oxytocin (OT) has been found to regulate social behavior (Ebstein, Knafo, Mankuta, Chew, & Lai, 2012) and indeed higher plasma levels of the neuropeptide OT are, under most conditions, associated with enhanced social behavior in humans and non-human animals (Bartz, Zaki, Bolger, & Ochsner, 2011; Feldman et al., 2012). Unlike for other hormones, there is only one

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known receptor for OT. Since the first associations were discovered in 2005, allelic variations in the OXTR have been associated with inter-individual differences in a variety of social phenotypes (Ebstein et al., 2012; Li et al., 2015; Peltola et al., 2014; Skuse et al., 2014), yet, a recent meta-analysis of OXTR effects failed to explain a significant part of human social behavior (Bakermans-Kranenburg & van Ijzendoorn, 2014). A recent study of Feldman et al. (2012) connected these two lines of research demonstrating a link between plasma OT levels and single nucleotide polymorphisms (SNPs) in the OXTR (i.e., rs1042778 and rs2254298). A third SNP (rs53576) of the OXTR has been associated with structural alterations of the oxytocinergic regions of the hypothalamus and with amygdala activity during the processing of emotionally salient social cues (Tost et al., 2010). It is further possible that an OXTR SNP has an effect on the initial level of sociability and an effect on changes that occur in this temperament dimension as participants grow older, making it crucial to investigate whether the identified candidate genes have an influence on sociability across the life span.

1.2. Gene–environment (GxE) interactions

Examining genes or environments separately from each other may lead to biased findings because of GxE interactions. Due to their genotypes, some children and adolescents may be more sensitive to the effects of early life experiences—for better or worse— while for others the same environmental influences might have only a weak effect if any (Belsky & Pluess, 2009). Therefore, allelic variation in OXTR might moderate how individuals experience social relationships and situations instead of having a direct effect on sociability. It has been, for instance, argued that biologically elevated sensitivity to social cues might result in higher distress under conditions where individuals' social needs are not met (McQuaid, McInnis, Stead, Matheson, & Anisman, 2013).

Few GxE studies (e.g., Bradley et al., 2011; Hammen, Bower, & Cole, 2015; Hostinar, Cicchetti, & Rogosch, 2014; van Roekel et al., 2013) have investigated whether OXTR variant rs53576 moderates the influence of adverse childhood environments on phenotypes related to sociability (e.g., emotional dysregulation, unstable relationships with close others, loneliness, or perceived social support). Unfortunately, their results are inconclusive as both carriers of the G-allele (Bradley et al., 2011; Hostinar et al., 2014; van Roekel et al., 2013) and the A-allele (Hammen et al., 2015) of rs53576 are found to be more strongly affected by adverse early-environmental influences, dependent on the social phenotype and environmental factor studied. Furthermore, it is not certain whether social phenotypes, including sociability, are influenced by OXTR genotypes in beneficial environments. The only available study did not find significant GxE interactions between rs53576 and perceptions of positive company on loneliness (van Roekel et al., 2013). Children and adolescents might also be differentially susceptible (i.e. more or less sensitive to beneficial as well as adverse environments depending on their OXTR genotypes) to the emotional warmth experienced during childhood (Jokela et al., 2007), potentially accounting for inter-individual differences in sociability development.

Researchers must give a good reason not only for the selection of potential candidate genes, but also the choice of the right environmental factor is important and needs to be justified (Dick et al., 2015). Numerous studies have shown associations between early parental environment and children's development (for a review, see Collins, Maccoby, Steinberg, Hetherington, & Bornstein, 2000). Most theories agree that emotional warmth—sometimes also called closeness or love—is a defining characteristic of an early environment beneficial to the offspring (Clark & Ladd, 2000; MacDonald, 1992; Schaefer, 1959). Also, the EAS approach to temperament agrees that one of the more powerful social rewards is to be liked or loved, especially when offered by parents to their children (Buss, 1991). These intrinsic rewards, in turn, can strengthen the tendency to seek out for others and remain in their company and indeed the maternal warmth in childhood has been associated with children's temperament during adolescence (Katainen et al., 1998). For that reason, it is important to examine GxE interactions in this context.

1.3. The current study

Candidate gene–environment interaction studies have been criticized because it is difficult to justify which environmental and which genetic factor should be studied, and because of several statistical concerns which we tried to address in the current study (Dick et al., 2015; Keller, 2014). In summary, there has been a strong claim in the literature that OXTR variants are responsible for inter-individual differences in a variety of social behaviors. The evidence is sparse for temperament dimensions, with not a single study linking OXTR polymorphisms to the sociability dimension of the Buss–Plomin EAS temperament model (Buss, 1991; Buss & Plomin, 1975). Of the environments that could be studied, the maternal emotional warmth during childhood has been shown to influence the development of temperament (Katainen et al., 1998) and personality traits (Josefsson et al., 2013) and is probably especially important for the development of sociability. We hypothesize, however, that this is only the case if the child carries certain genotypes in the OXTR. The current study, therefore, examined whether or not combinations of the three most promising candidate genes in the OXTR (rs1042778, rs2254298, and rs53576) interact with growing up in a beneficial versus more adverse environment in predicting adulthood sociability. The study is well-powered as it is based on five repeated measurements, assessed 20 years apart in a population-based sample, and uses a well-established scale to measure adulthood sociability.

2. Methods

2.1. Participants

Data were derived from the Young Finns Study (Raitakari et al., 2008), which is a multicenter prospective study monitoring change in cardiovascular risk in representative Finnish birth cohorts, conducted across five university cities with medical schools and their rural surroundings. The initial sample consisted of 3596 children and adolescents (Caucasians), who were 3, 6, 9, 12, 15, and 18 years at the study baseline in 1980 (T0). After the baseline, several follow-up waves have been conducted. Those subjects were excluded for whom no information on their genes or the environmental factor was available and those who had no data from any of the follow-ups, in which our dependent variable was fielded (Fig. 1). The final sample included 2289 participants (1026 male; 1263 female). Participants gave written informed consent, and local ethics committees approved the study. Moreover, the study procedure of each study phase was in accordance with the Helsinki Declaration.

2.2. Measures

2.2.1. Adulthood sociability

The sociability dimension of the Buss–Plomin EAS temperament model (Buss, 1991) was used to measure sociability. Adulthood temperament was assessed in 1992 (T1), 1997 (T2), 2001 (T3), 2007 (T4), and 2012 (T5) with five items, such as, “I like to be with people”. They were rated on a 5-point Likert scale (1, totally disagree; 5, totally agree). Higher scores indicate higher sociability. Cronbach's alpha was generally high, ranging from .78 at T3 to .80 at T5. Note that participants belonging to the youngest age cohort were at T1 still in their adolescence (i.e. 15 years old).

2.2.2. Maternal emotional warmth

Mothers reported their perceptions of the early emotional environment, i.e. the emotional warmth between mother and child with four

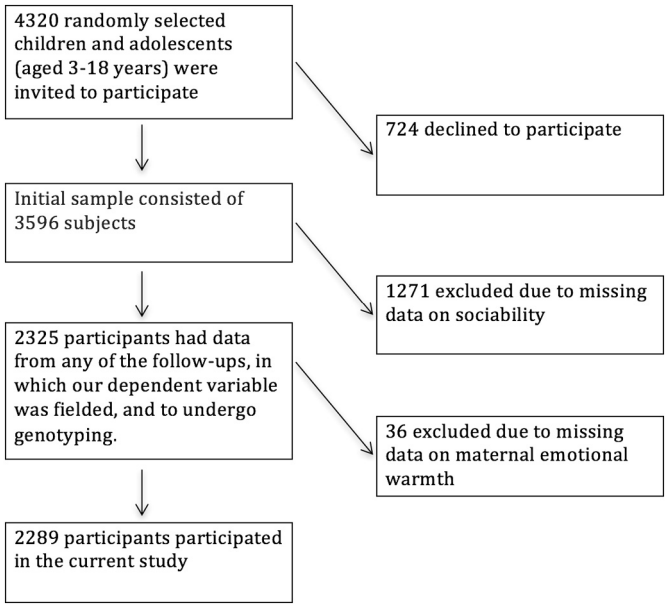

Fig. 1. Population diagram.

items, e.g. "My child is emotionally important to me" (Makkonen et al., 1981) on 5-point fully-labeled Likert scales (e.g., 1, low importance; 5, high importance). Most mothers answered the scale in 1980 (Cronbach's alpha = .64). The assessment was repeated after three years; being measurement invariant across gender and over time (Katainen et al., 1998). The second assessment was used only for those 52 mothers who did not participate at T0. Only 254 mothers reported a more adverse parenting environment (score < 4). Thus, cubic root transformation was used. To avoid potential bias in the maternal reports due to differences in the age of the child (e.g., mothers reporting being warmer with young children than adolescents), we further standardized the environmental factor within the six birth cohorts (mean = 0.02; *SD* = 0.96).

2.2.3. Parental socio-economic status (SES)

At baseline, SES was assessed with two indices: The years of education of the mother and the father (averaged) and the family's annual income. These two indices were first transformed into *Z*-scores and then averaged to form a single variable.

2.2.4. Genotyping

The oxytocin receptor gene (OXTR) is located on chromosome 3. We used three candidate SNPs of the OXTR: rs1042778 (G to T), rs2254298 (G to A), and rs53576 (G to A). Rs1042778 and rs53576 were directly genotyped using an Illumina 670k genotyping array (see Smith et al., 2010, for details) and rs2254298 was imputed using the IMPUTE2 software and the 1000 Genomes Project March 2012 haplotypes as a reference with an excellent imputation quality (info ~ 0.99). As complex phenotypes are controlled by many genes of small effect, Belsky and Israel (2014) advocate for using genetic risk or plasticity scores to assess cumulative effects of genes on a given phenotype. Therefore, four genetic profiles were developed that count the number of potential markers of plasticity namely, the G/G genotypes on rs1042778, rs2254298, and rs53576 (see Table 1). Genetic profiles A, B, and C are taking the values 0, 1, and 2. On profile D, an individual can have between zero and three G/G genotypes. We counted individuals' G/G genotype as genetic predisposition of plasticity, as the A- and T-alleles of these OXTR SNPs have repeatedly been shown to be associated with social deficits and impairments (Bakermans-Kranenburg & van Ijzendoorn, 2014; Feldman et al., 2012; Li et al., 2015; Tost et al., 2010).

Table 1
No. of participants' with zero, one, two, and three G/G genotypes in four genetic profiles.

Genetic profiles	N			
	0	1	2	3
A (rs1042778 and rs22542778)	169	1580	694	–
B (rs1042778 and rs53576)	877	1386	180	–
C (rs22542778 and rs53576)	289	1442	712	–
D (rs1042778, rs22542778, and rs53576)	100	1035	1169	139

2.3. Statistical analysis

Latent Growth Curve Modeling (LGCM) was used to analyze inter-individual differences in the initial levels, i.e., intercept, of sociability and the rate of change, i.e., slope, of sociability over time. LGCM is a powerful tool to search for direct effects of allelic variations in genes as well as potential GxE interactions (Van Roekel, Scholte, Verhagen, Goossens, & Engels, 2010). To limit the influence of measurement error on our estimates, we applied multiple indicators LGCM (Bishop, Geiser, & Cole, 2015). Statistical programming software "R" (version 3.1.2 (2014-10-31)) was used to conduct the analyses.

For model evaluations, we report Chi-Square (X^2) estimates and a combination of two global fit indices. A model is commonly judged as having a good fit by a CFI value ≥ .95 and an RMSEA value ≤ .05 and an acceptable fit by CFI ≥ .90 and RMSEA ≤ .08.

After establishing measurement invariance (please see, Appendix S1), we tested a sequence of developmental models in which the five measurements of sociability (latent) reflected the growth curves. In Model 1 was the unconditional developmental model. In the model that followed, the latent intercept and slope were regressed on the potential confounders age, SES, and a dummy variable to account for gender differences (Model 2). Then, the direct effect of mother's emotional warmth was added (Model 3). Model 4 searched for direct effects of the genetic profiles on latent growth in sociability. Model 5 examined interaction between OXTR and the environmental factor on sociability. We followed the common practice in genetic association studies that use latent growth curve models (see e.g., Van Roekel et al., 2010) and reported the regression coefficients in a stepwise manner: The variables included in Model 1 were reported without adjusting for the variables in the models that followed, whereas the variables in the Models 2 to 5 were adjusted for the variables in the preceding models, respectively. Note that each cumulative genetic score and each interaction were analyzed separately (Models 4 and 5).

To be able to probe genetic profile–environment interactions and to interpret them correctly also age was standardized before entering into the equations (Hayes, 2013). As age was centered at T1, the intercept should be interpreted as the expected level of sociability for a participant at the sample mean age (22.4 years) at this wave (cf. Mehta & West, 2000). Regions of significance were estimated with the Johnson-Neyman method (Johnson & Neyman, 1936). We handled missing data by conducting all analyses with full information maximum likelihood (FIML) estimator because in comparable settings FIML was proven to have advantages over available imputation strategies (Allison, 2012).

3. Results

3.1. Preliminary analyses

We tested whether subjects who participated (N = 2289) differed from those who were excluded from the current analysis (N = 1307). Non-participants were more likely to be male (difference 11% points; X^2 = 46.03) and less sociable in the 2001 (mean difference (ΔM) = −0.14; p < .01) and 2007 (ΔM = −0.09; p = .04) measurements. They also had lower family SES at baseline (ΔM = −0.08; p < .01).

There was no evidence of deviation from Hardy-Weinberg

Table 2
Descriptive statistics of the study variables.

Variable	No. of cases	Mean (%)	SD
Age in 1980	2289	10.44	5.04
Gender (male = 1; female = 0)	2289	(0.45)	
SES	2275	0.02	0.66
Emotionally warm environment	2285	4.46	0.51
rs1042778			
T/T	343	(0.15)	
G/T	1084	(0.47)	
G/G	862	(0.38)	
rs2254298			
A-allele	375	(0.16)	
G/G	1914	(0.84)	
rs53576			
A/A	438	(0.19)	
A/G	1075	(0.47)	
G/G	776	(0.34)	
Sociability			
T1	1774	3.86	0.73
T2	1596	3.48	0.75
T3	1729	3.42	0.73
T4	1715	3.29	0.71
T5	1446	3.26	0.71

Note. Sociability was calculated as a mean of five items.

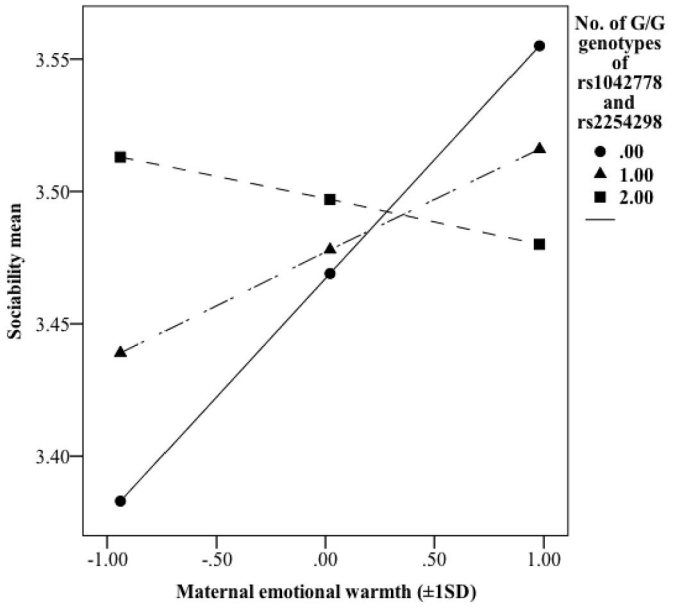

Fig. 2. The interaction between the cumulative genetic score (genetic profile A) and maternal emotional warmth in predicting the mean of sociability across time: Carriers of zero G/G genotypes in rs1042778 and rs2254298 = 0; carriers of one G/G genotype = 1; carriers of two G/G genotypes = 2.

Equilibrium in any of the three SNPs (Table 2).

The means of the five sociability items showed moderately high test-retest reliabilities across waves, ranging from r = .37 between T1 and T5 to r = .72 between T4 and T5.

3.2. Multiple indicator latent growth curve models

Across Models 1–5 the global fit indices indicated that a linear trajectory describes the data well (Table 3). While RMSEAs suggested a good fit (≤ .05), CFIs indicated at least acceptable fit (≥ .93).

The initial developmental model indicated that latent sociability, b = 3.56 (SE = 0.02) for the intercept, decreased over time, b = − 0.18 (SE = 0.01) for the slope (Model 1). Variance estimates were significant for both the initial level and the rate of change of sociability (not shown).

Also Model 2 indicated that sociability decreases with age, as sociability was lower in those who entered the study in older age. The regression coefficients of the intercept on gender indicated further that men had lower initial levels of sociability than women. Additionally, the latent slope was altered by the control variables. In older participants, sociability changed more slowly and also in those with higher SES, sociability decreased somewhat slower.

Model 3 did not indicate any direct association between maternal emotional warmth and adulthood sociability.

We also did not find any significant association between the cumulative genetic scores and sociability growth curves (Model 4).

Out of the four cumulative genetic scores, only the genetic profile "A", which combines rs1042778 and rs2254298, moderated the effect of maternal emotional warmth on the initial level of sociability (p = .03) (Model 5). Fig. 2 illustrates the nature of this genetic profile–environment interaction. More sensitive individuals—those carrying

Table 3
Sociability growth curves.

Model	Predictor	Intercept (b)	(SE)	p	Slope (b)	(SE)	p	X^2	(df)	RMSEA	CFI
Model 1	Developmental model							1300.118	(227)	.05	.94
	Point estimates	3.556	(0.021)	< .001	− 0.177	(0.014)	< .001				
Model 2	Adding covariates							1499.209	(296)	.04	.94
	Gender (male = 1; female = 0)	− 0.218	(0.029)	< .001	0.027	(0.019)	.149				
	Age	− 0.057	(0.014)	< .001	0.022	(0.009)	.015				
	SES	− 0.001	(0.021)	.950	0.029	(0.014)	.041				
Model 3	Adding direct effect of early environment							1543.301	(319)	.04	.93
	Maternal emotional warmth (EW)	0.016	(0.015)	.276	0.015	(0.010)	.114				
Model 4	Adding separately direct effects of four genetic profiles										
	A (no. of G/G genotypes of rs1042778 and rs22542778)	0.031	(0.026)	.222	− 0.018	(0.016)	.267	1926.068	(342)	.04	.93
	B (no. of G/G genotypes of rs1042778 and rs53576)	0.008	(0.024)	.729	− 0.011	(0.015)	.459	1929.251	(342)	.04	.93
	C (no. of G/G genotypes of rs22542778 and rs53576)	0.001	(0.023)	.977	0.001	(0.015)	.928	1931.054	(342)	.04	.93
	D (no. of G/G genotypes of rs1042778, rs22542778, and rs53576)	0.014	(0.021)	.499	− 0.010	(0.014)	.454	1927.523	(342)	.04	.93
Model 5	Adding separately four genetic profile–environment interactions										
	Maternal emotional warmth (EW)*A	− 0.068	(0.031)	.030	0.027	(0.021)	.198	1941.607	(365)	.04	.93
	EW*B	− 0.017	(0.026)	.520	0.015	(0.017)	.368	1946.925	(365)	.04	.93
	EW*C	− 0.008	(0.022)	.707	0.010	(0.015)	.495	1958.072	(365)	.04	.93
	EW*D	− 0.032	(0.024)	.187	0.020	(0.016)	.203	1940.838	(365)	.04	.93

Note. Maternal emotional warmth was cubic transformed and standardized within birth cohorts. The cumulative genetic scores count the number of G/G genotypes on rs1042778, rs2254298, and rs53576. b = unstandardized coefficient. The models were added in a stepwise manner so that variables included in Model 1 are reported without adjusting for the variables in the other models, whereas e.g. the variables in the Model 5 have been adjusted for the variables in all preceding models. In Models 4 and 5, each genetic score and each interaction were analyzed separately.

minor alleles of OXTR rs1042778 and rs2254298—tend to be more affected by growing up in a warm versus more distant environment. This effect decreased near linearly with the number of G/G genotypes, so that those who carry G/G genotype for both SNPs were unaffected by the environmental influence. The GxE interaction was, however, only nominally significant as it did not survive correction for multiple testing (Bonferroni corrected p-value ≤ .013). Regions of significance included maternal emotional warmth (transformed and standardized) values below −1.045 (corresponding to a raw score of approximately 3.70), representing 11.6% of the cases. A Chi-Square test (ANOVA) showed that the difference between Model 4 and Model 5 (genetic profile "A") was not statistically significant (p = .87).

4. Discussion

Current results show that maternal emotional warmth in childhood and OXTR genotype were not directly associated with temperamental sociability. However, we found a nominally significant GxE interaction (p < .05) suggesting that participants might be differentially susceptible to maternal emotional warmth depending on their OXTR genotype when the effects of rs1042778 T-allele and rs2254298 A-allele were combined to a cumulative genetic score. However, this genetic profile–environment interaction should be interpreted as a null result because it became non-significant after Bonferroni correction and because adding the nominally significant interaction did not significantly improve the prediction.

It has been suggested that the social rewards offered by parents to their children are especially important for the development of sociability (Buss, 1991). However, the results of the current study do not allow concluding that maternal emotional warmth in childhood plays a direct role in inter-individual differences in adulthood sociability. Our data also do not provide support for the idea that participants' levels of sociability vary along with the number of "plasticity-alleles" they carry in the OXTR (see Belsky & Pluess, 2009) as the identified GxE interaction was not statistically significant. We assessed variation in normal parenting (i.e., not abuse or neglect), and it is possible that our measure might not represent a harsh enough environment where we could find robust evidence for genetic moderation. However, also previous GxE studies that have investigated the moderating role of polymorphism in the OXTR have been inconclusive (Bradley et al., 2011; Hammen et al., 2015; Hostinar et al., 2014; van Roekel et al., 2013). More research is needed to clarify whether OXTR polymorphisms interact with the beneficial versus adverse early environment rendering some individuals more or less susceptible to the development of sociability temperament or other social phenotypes.

We did not identify any significant main effects for OXTR cumulative genetic scores for adulthood sociability. As mentioned above, it is commonly assumed that the T-allele of rs1042778 and the A-allele of rs2254298 and rs53576 are the risk alleles for social deficits and impairments as compared to the G-allele, with many studies supporting this assumption (see Feldman et al., 2012; Tost et al., 2010). However, a recent meta-analytical review, examining a broad range of social phenotypes under the umbrella term sociability, resulted in a combined effect sizes of no more than r < .05 (p > .05) for OXTR variants rs53576 and rs2254298, when combining 48/34 studies (Bakermans-Kranenburg & van Ijzendoorn, 2014). Many of the association studies have included closely related but functionally distinct constructs, e.g. sociality and behaviors in close relationships, which may not be comparable and thus inflate the findings (Li et al., 2015). When restricting their meta-analysis to studies that investigated general 'sociality' (e.g., extraversion, empathy, and loneliness), Li et al. (2015) showed a clear association between OXTR rs53576 polymorphism and these social phenotypes (Cohen's d = .11, p = .02). In contradiction with this result, we did not find an association for genetic variation in the OXTR genotype (including rs53576, see Appendix S2) despite of assessing sociability temperament, which reflects individuals' preference for others company expressed in extended networks rather than their need for intimate relationships and closeness in families (Buss & Plomin, 1975).

It is possible that OXTR genes are associated with our environmental factor as children behave in a certain way (sociability temperament) because of their genetic make-up, which in turn elicits certain responses from their environment (maternal emotional warmth), a phenomenon called (evocative) gene-environment correlations (rGE; Avinun & Knafo, 2014). To show that there are no rGEs present we performed two-sample t-tests on the difference in means of maternal emotional warmth among carriers and non-carriers of the "plasticity-alleles". There was no significant difference between minor allele carriers and G/G genotype carriers regarding parenting. We further tested for the possibility that the effects of the covariates spuriously produced the GxE interaction in the genetic score combining the minor alleles of OXTR rs1042778 and rs2254298 (see Keller, 2014). The inclusion of the two-way interactions of gender, age, and SES with emotional warmth and OXTR did not change the results notably (b = −0.07; p-value decreased to .028). A three-way interaction, testing whether the genetic profile–environment interaction effect was moderated by participants' age, also did not change the results. We also tested for differences between men and women, yet, gender did not moderate the interaction between OXTR profiles and maternal emotional warmth (multigroup analyses available from the first author upon request). The results were further robust to different transformations of the environmental factor (raw answers, cubic root transformed, within birth cohort standardized). Thus, we followed those recommendations of Dick et al. (2015) relevant to the current study.

4.1. Limitations and strengths

The current study has some limitations. First, we did not use an objective measure of the early environment, such as observations of parenting behaviors. However, previous work has used our maternal emotional warmth measure to show that the effect of the early environment is often conditional depending on genes (see Jokela et al., 2007). Second, YFS is an ethnically homogenous sample, which limits the generalizability of the obtained results. On the other hand, this kind of sample may be helpful in examining genetic effects, as confounding related to varying ethnic groups is minimal. Finally, the participants were from several birth cohorts and thus their age ranged from 3 to 18 years at the baseline. However, analyzing the birth cohorts separately, like suggested by Mehta and West (2000), would have crucially reduced the statistical power to detect GxE interactions. As the mother-reports might have rather different meanings with children aged 18 years compared to aged 3 years, we standardized the environmental factor within birth cohort and established measurement invariance of sociability across the six age groups.

The main strengths of the current study are longitudinal comparatively large population-based data with five repeated measurements of sociability that increased our chances to detect robust associations, while many previous GxE interaction studies have lacked statistical power (Dick et al., 2015). Another strength is that the results are not confounded by common method variance as emotional warmth was reported by mothers, and adulthood sociability was reported by the participants.

4.2. Conclusions

We did not find direct effects of OXTR variants and maternal emotional warmth in childhood on adulthood sociability. The observed OXTR-emotional warmth interaction did not survive correction for multiple testing. Further work is needed to better understand the interactive role of candidate genes and early environmental influences in the development of social phenotypes.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.paid.2017.12.030.

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