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Change in Parenting, Change in Student–Teacher Relationships, and Oxytocin Receptor Gene (OXTR): Testing a Gene-×-Environment (G×E) Hypothesis in Two Samples

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Prior research suggests that parenting affects children's relationships, including those with teachers, although there is variation across individuals in such effects. Given evidence suggesting that oxytocin may be particularly important for the quality of social relationships, we tested the hypotheses (a) that change in parenting from 4 to 6 years of age influences and predicts change in the student–teacher relationship from 6 to 8 years of age and (b) that this effect is moderated by a polymorphism related to the child's oxytocin receptor gene (*OXTR*), rs53576. In 2 studies, participants included, respectively, 652 socioeconomically diverse Norwegian children from a community sample (50.8% male; mean age of 54.9 months at first assessment) and 559 such children from 8 different U.S. locales (49.0% male; approximately 54 months at the first assessment). Norwegian results showed that change in parenting predicted change in student–teacher relationships, but only in the case of children homozygous for the A allele of rs53576 and in a manner consistent with differential-susceptibility theory: for AA carriers, when parenting changed for the worse, so did children's relationship with teachers, whereas when parenting changed for the better, the teacher–child relationships improved accordingly. Such G×E findings could not be replicated in the American sample. Results are discussed in terms of 2 contrasting models of Person-×-Environment interaction (differential susceptibility and diathesis stress) and potential reasons for failure to replicate.

Keywords: diathesis stress, differential susceptibility, OXTR rs53576, parenting, student–teacher relationship

Evidence indicates that the quality of student–teacher relationships has wide-ranging implications for children's functioning and development (Hamre & Pianta, 2001), including behavior problems (Silver, Measelle, Armstrong, & Essex, 2005), school engagement and academic achievement (Ladd, Birch, & Buhs, 1999; Roorda, Koomen, Spilt, & Oort, 2011), peer relations (De Laet et al., 2014), and social competence (Skalická et al., 2015). Such findings underscore the importance of illuminating the determinants of student–child-relationship quality. Available evidence suggests that positive parent–child relations may lay the groundwork for children's positive relations with their teachers (Booth, Kelly, Spieker, & Zuckerman, 2003; DeMulder, Denham, Schmidt, & Mitchell, 2000); in the present study, we evaluated the effects of parenting in two separate samples, one Norwegian

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(Study 1) and the other from the United States (Study 2). Notably, we focused on *change* in parenting predicting *change* in teacher–child relationships because evidence of change in predictors forecasting change in outcomes is more indicative of causal processes in observational research like that which is the focus of this report than simple cross-time predictor-outcome associations. Thus, we predicted that parenting that becomes more positive over time would lead to increasingly positive change in the teacher–child relationship, whereas parenting that becomes increasingly negative would result in deterioration in teacher–child relations over time.

Given the increasing evidence that environmental effects, including those involving parenting, vary according to the child's dispositional qualities (Belsky, Bakermans-Kranenburg, & Van Ijzendoorn, 2007; Belsky & Pluess, 2009, 2013; Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van Ijzendoorn, 2011), often as a result of their genotype (Bakermans-Kranenburg & van Ijzendoorn, 2011), we investigated genetic moderation of parenting effects on teacher–child relations in the research reported herein. Based on research showing that oxytocin (Meyer-Lindenberg, Domes, Kirsch, & Heinrichs, 2011) and variations in the oxytocin receptor gene (*OXTR*) are involved in social interaction and sociality (Feldman, Monakhov, Pratt, & Ebstein, 2016; Li et al., 2015), we specifically evaluated genetic moderation via this polymorphism. More specifically, we evaluated whether effects of change in parenting from 4 to 6 years of age on change in the student–teacher relationship from 6 to 8 years of age vary as a function of *OXTR* rs53576. We also evaluated whether such genetic moderation of parenting is consistent with the differential susceptibility or diathesis stress model of Person-×-Environment interaction. Because research has repeatedly shown that children's behavior also affects parenting (e.g., Reitz, Dekovic, Meijer, & Engels, 2006), we adjusted for children's externalizing and internalizing problems and their observed behavior toward their parents.

Determinants of the Student–Teacher Relationship

Children vary considerably in their relationships with their teachers. Although a range of background factors may promote or hinder the development of rewarding student–teacher relationships, such as child gender (Jerome, Hamre, & Pianta, 2009), disabilities (Murray & Greenberg, 2001), and temperament (Rudasill, Reio, Stipanovic, & Taylor, 2010), as well as family income (Wyrick & Rudasill, 2009), these factors are not likely targets of interventions to improve this relationship. The parent–child relationship, however, is more appropriate given evidence that it affects children's relationships with teachers (Howes & Hamilton, 1992; O'Connor & McCartney, 2006) and is subject to change (Wyatt Kaminski, Valle, Filene, & Boyle, 2008).

Attachment theory (Bowlby, 1973) and social learning theory (Bandura, 1977) offer some insight into why parent–child relations may influence the student–teacher relationship.

According to attachment theory (Bowlby, 1973), repeated exposure to sensitive parenting fosters an internal working model in which others, including teachers, are benign if not benevolent and are predictable and in which student–teacher interactions are predicted to be rewarding. Insensitive or even frightening parenting, however, should promote internal working models in which others cannot be trusted and social exchanges will be unpleasant and not mutually beneficial. From the perspective of attachment theory, one would expect sensitive (and security-inducing) parenting to lay the groundwork for a positive student–teacher relationship, with the opposite true of insensitive parenting. In line with this view, securely attached children have been found to develop positive relationships with their teachers, whereas those with insecure attachments are at heightened risk of developing problematic ones (DeMulder et al., 2000; O'Connor & McCartney, 2006; Rydell, Bohlin, & Thorell, 2005). It must be acknowledged, however, that such theoretically anticipated associations have not emerged in all relevant research (Goossens & van IJzendoorn, 1990).

From the standpoint of social learning theory (Bandura, 1977), which emphasizes learning processes involving modeling and reinforcement (rather than internal working models), it is expected that children whose parents behave in supportive ways and praise positive social behavior will themselves behave in ways that promote positive teacher–child relationships. In contrast, parents who treat their children harshly or neglectfully may model aggressive or unresponsive behavior that the child learns and generalizes to other adults, thereby adversely affecting relationships with teachers. Moreover, insensitive and especially harsh parenting is expected to instigate coercive parent–child interaction processes that (inadvertently) reinforce negative child behavior, which can itself undermine other relationships (Patterson, Debaryshe, & Ramsey, 1989), including teacher–child ones. Not surprisingly, social learning-related research indicates that negative parenting (e.g., criticizing, making negative statements, and/or rejecting) is associated with child behavioral problems (Webster-Stratton & Hammond, 1999), whereas positive parenting (e.g., responsiveness, praise) promotes social skills and reduces behavioral problems (Webster-Stratton, Reid, & Hammond, 2001). Notably, there is also evidence that children with such behavioral problems develop poorer relationships with their teachers (Henricsson & Rydell, 2004; Murray & Zvoch, 2011).

Despite emphasizing different mechanisms responsible to account for why there should be an association between the quality and functioning of parent–child and teacher–student relationships, both theoretical frameworks just considered, attachment theory and social learning theory, share the view that experiences in one relationship, especially that with parents, influence experiences in other relationships, including student–teacher ones. It is for this reason that we predicted that the development of parent–child relationships, operationalized in terms of change over time from 4 to 6 years, would predict the development of teacher–child relationships from 6 to 8 years of age.

Variation in Environmental Effects

Even if the processes under consideration prove generally operative, parenting may not affect all children equally. Indeed, it has long been assumed that some children are more susceptible to the negative effects of problematic parenting or other conditions of adversity than other children because of their own personal characteristics, be they genetic, temperamental, and/or physiological in character. In fact, this assumption is central to the long-standing and widely embraced diathesis-stress model of Person-×-Environment interaction (Zuckerman, 1999).

The alternative and more recently introduced differential-susceptibility model extends thinking about variation in response to environmental conditions by stipulating that the very children most likely to be adversely affected by problematic parenting will be most likely to benefit from supportive care (Belsky, 2005; Belsky et al., 2007; Belsky & Pluess, 2009, 2013; Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2011). According to this evolutionary inspired perspective, children with certain personal attributes that make them especially sensitive to environmental conditions should develop both better and worse teacher–child relationships, depending on the quality of their parenting experience, than children whose personal attributes make them less sensitive to such experiences and exposures. In the present report, we evaluated whether the diathesis stress or differential susceptibility model better accounts for variation in teacher–child relationships as a function of parenting—in two separate samples. To this end, we focused on one particular genetic polymorphism that has been found to be influential in research on relationships and the relational process (Carter, 2014), *OXTR* rs53576.

Oxytocin Receptor Gene

Oxytocin (OXT) has been related to a variety of socioemotional behaviors, including anxiety, aggression, and social recognition (Lee, Macbeth, Pagani, & Young, 2009). A review of relevant evidence by Meyer-Lindenberg and associates (2011) revealed that OXT affects how individuals interpret social cues, thereby influencing social cognition and behavior, including attachment, social recognition, and social exploration.

OXT functions as a hormone and a neurotransmitter, expressing its actions via the OXTR (Carter, 2014). The genetically polymorphic *OXTR* is located on chromosome 3p25, and one of these polymorphisms (rs53576) can influence social behavior (Krueger et al., 2012). The single nucleotide polymorphism (SNP) rs53576 is an intronic variation, caused by a guanine (G) to adenine (A) replacement (G and A allele). Although our knowledge regarding the specific functionality of this variation is limited, the rs53576 genotype has been shown to impact brain structure and functionality such as hypothalamus gray matter and amygdala volume. When exposed to emotionally salient cues, individuals homozygous for the G allele showed heightened task-related amygdala activation. Carriers of the A allele evinced the lowest activation and increased coupling of the hypothalamus and amygdala, in which the connectivity between the two was mirrored by the dose of the minor allele (Tost et al., 2010).

Even though little is known about the specific function of *OXTR* SNP rs53576, it has been the subject of numerous genotype-phenotype association studies, some of which might link it, indirectly, to student–teacher relationships, including support seeking (Chen et al., 2011), trust (Krueger et al., 2012), and even parental sensitivity (Bakermans-Kranenburg & van Ijzendoorn, 2008). More specifically, some findings indicate that carriers of the A allele (i.e., AA or AG) are, relative to G homozygotes, less empathic and more reactive to stress (Rodrigues, Saslow, Garcia, John, & Keltner, 2009), exhibit lower trust-related behaviors (Krueger et al., 2012), and prove to be less sensitive parents (Bakermans-Kranenburg & van Ijzendoorn, 2008; Klahr, Klump, & Burt, 2015). Moreover, at least one of two meta-analyses has documented associations between rs53576 and sociality (e.g., extraversion, social skills, and prosocial behavior). Specifically, Li et al. (2015) observed that although G homozygotes did not differ from A carriers with regard to the quality of their close relationships, G homozygotes did score higher on general sociality—a result that Bakermans-Kranenburg and van IJzendoorn's (2014) meta-analysis did not discern. Such inconsistency across investigations, including even meta-analyses, is not unusual in research on genotype-phenotype associations.

Gene-×-Environment Interaction

Indeed, evidence such as that reviewed above highlighting inconsistency in research on the main effects of parenting and of candidate genes stimulated Caspi et al.'s (2002, 2003) pioneering research on Gene-×-Environment (G×E) interactions. Over the past decade, numerous reports have appeared documenting such G×E interplay (e.g., Babineau et al., 2015; Bresin, Sima Finy, & Verona, 2013; Brown et al., 2013; Hygen et al., 2015; Hygen, Guzey, Belsky, Berg-Nielsen, & Wichstrøm, 2014); however, the G×E field has been subjected to controversy and critique (e.g., Duncan & Keller, 2011). Nevertheless, prior research indicates that the *OXTR* SNP rs53576 interacts with various environmental factors in predicting diverse behavioral and psychological phenotypes. Most relevant to the present inquiry is research showing that rs53576 moderates the effect of maltreatment on regulatory behavior and disorganized attachment (Bradley et al., 2011), perception of social support (Hostinar, Cicchetti, & Rogosch, 2014), and borderline personality features (Cicchetti, Rogosch, Hecht, Crick, & Hetzel, 2014). Moreover, rs53576 has been found to moderate the effect of unsupportive parenting on children's coping styles (McInnis, McQuaid, Matheson, & Anisman, 2015) and the effect of maternal depression on youths' depressive symptoms (Thompson, Hammen, Starr, & Najman, 2014). Such G×E findings involving both parenting and rs53576 motivated the current investigation of the interaction of these two predictors in forecasting change in the student–teacher relationship.

As it turns out, the just-cited G×E studies involving rs53576 do not consistently indicate which allelic subgroup or subgroups prove more and less sensitive to environmental effects. In some studies it is A carriers who emerge as most vulnerable to the negative effects of adversity (Thompson et al., 2014), whereas in others it is G carriers who prove to be at environmental risk (Bradley et al., 2011; Hostinar et al., 2014). Moreover, some research indicates that the rs53576 moderation of environmental effects varies by gender, with GG boys and A-carrier girls proving more susceptible to the anticipated negative effects of adversity (Cicchetti et al., 2014). This inconsistency may be the result of the diverse predictors and outcomes examined in different studies or other methodological factors that vary across inquiries. Nevertheless, the fact that no allelic subgroup stands out as consistently susceptible or vulnerable directly informs our approach to statistical analysis, given our concern for alternative models of G×E interaction.

When prior evidence indicates that particular allelic subgroups proves more or less susceptible to environmental effects in a more, rather than less, consistent manner (e.g., short allele carriers of the *5-HTTLPR* polymorphism), it is appropriate to use Widaman et al.'s (2012; Belsky, Pluess, & Widaman, 2013) competitive model-fitting approach when seeking to determine whether a differential-susceptibility or diathesis-stress framework best fits the data. This approach involves foregoing traditional exploratory tests of G×E interaction using regression models and moving directly to model fitting. However, in situations such as the present in which prior research does not provide a strong basis for predicting which allelic subgroup will prove most environmentally sensitive, exclusive reliance on competitive model fitting is not appropriate. Thus, in the current inquiry, we first used the traditional regression approach to identify which allelic subgroups; if any, prove more and less sensitive to the effects of change in parenting on change in the student–teacher relationship before using model fitting to evaluate whether any detected G×E interaction proves more consistent with differential susceptibility or diathesis stress thinking.

Recent years have witnessed an outpouring of concern regarding the replicability of scientific findings (Jasny, Chin, Chong, & Vignieri, 2011; Ryan, 2011). Perhaps nowhere has this issue emerged so forcefully in the human behavioral sciences as in research involving measured genes. Much of this concern originated in this disappointment that arose when initial and significant genotype-phenotype associations could not be detected in subsequent studies (Hamer, 2002; Insel & Collins, 2003). When attention turned to G×E interaction, following the publication of pioneering work in this area by Caspi and associates (Caspi et al., 2002, 2003), it was not long before issues of replication arose here as well. The situation no doubt became especially confusing when different meta-analyses of the supposedly same G×E interaction yielded radically different conclusions. Whereas Risch et al. (2009) claimed that the interaction between the serotonin transporter, *5-HTTLPR*, and stressful life events did not reliably predict depression in women, Karg and collegues (2011) drew the opposite conclusion in their meta-analyses, so did Uher and McGuffin (2008, 2010) in a review of human G×E findings reported over the first decade of such work (see also Kaufman, Gelernter, Kaffman, Caspi, & Moffitt, 2010; Rutter, 2010). In so doing, the latter scholars highlighted the need to pay special attention to the issue of measurement (see also Caspi, Hariri, Holmes, Uher, & Moffitt, 2010). More recently, Duncan and Keller (2011) concluded that most findings were likely to be false positive (see also Moore & Thoemmes, 2016).

In light of the concerns raised and observations made about G×E findings in particular, we conducted a second study using data from 8 of 10 sites (that collected genetic data) involved in a large scale, American study, National Institute of Child Health and Human Development (NICHD). NICHD Study of Early Child Care and Youth Development (NICHD Early Child Care Research Network, 2005), to determine whether it was possible to replicate the G×E finding which emerged in Study 1 conducted in Norway. Important to appreciate is that measurement across the two studies were not identical, even if highly similar, and that policies and practices of schools in the two countries cannot be presumed to be the same.

Study 1

Method

Participants and recruitment. The Trondheim Early Secure Study (TESS) is a prospective study conducted in the city of Trondheim, Norway. The study population comprised the 2003 and 2004 birth cohorts and their parents. Parents and their child(ren) were invited to participate in the study through an invitation letter sent to their home. The letter also included the Strengths and Difficulties Questionnaire (SDQ) version 4–16 (Crone, Vogels, Hoekstra, Treffers, & Reijneveld, 2008), which was used for screening. Completed SDQs were returned by 3,358 of 3,456, families (97.2%) at the Well Child Clinics (when the child attended a routine health check for 4-year-olds). Only parents with adequate proficiency in Norwegian were included in the study. Eligible parents (n = 3,016) acquired information of the study through procedures approved by the Regional Committee for Medical and Health Research Ethics. Parents of 2,475 children provided written consent to participate.

Variability, and thus statistical power, was increased by oversampling children with mental health problems. To accomplish this task, the SDQ total scores were divided into four strata (0–4, 5–8, 9–11, and 12–40), and defined proportions of children in each stratum (.37, .48, .70, and .89, respectively) were selected to participate using a random number generator. The selection probabilities increased with increasing SDQ scores. Of the 1,250 parents drawn to participate, we tested 936 (74.9%). Data were collected at the Norwegian University of Science and Technology, where the children met together with one parent, usually the mother (84.4%). Trained personnel performed all interviews and observations. Altogether, 762 children participated in the follow-up assessment 2 years later (T2), whereas 699 children participated 2 years after that (T3). The day-care teacher (at age 4) who knew the child best was instructed to fill in a questionnaire measuring the student–teacher relationship, and 989 teachers completed the scheme at age 4, whereas 788 and 607 teachers completed the scheme in 1st and 3rd grade, respectively. At age 4, the day-care teachers had known the child for an average of 1.7 years (SD = .9). At first grade (age 6), the teacher had known the child for .7 years (SD = .4) and for 2.1 years (SD = 1.4) in third grade. Among these children, 652 were successfully genotyped for the *OXTR* rs53576 polymorphism and thus formed the basis of the analysis sample.

There were 332 (49.2%) females in the present sample; most lived with their biological parents, most of whom were married (see Table 1). Those who had a poor teacher–child relationship at Time 1 were less likely to be genotyped (T1; Odds ratio [OR] = 0.98, 95% confidence interval [CI] = 0.96–1.00, p = .03). Positive parenting at Time 1 made it less likely to drop out at Time 2 (OR = 0.98, [0.96–1.00], p = .03) and Time 3 (OR = .95, [.91–1.00], p = .03). Hence, because of the initial values of the outcome variable being predictive of attrition, we suspect that data were missing not at random (MNAR), and we performed the analyses accordingly—see Statistical Analysis.

Measures.

Student–teacher relationship. The student–teacher relationship was measured using the Student–Teacher Relationship Scale (STRS; Pianta, 2001) at 4, 6, and 8 years of age applying a 5-point Likert-type scale ranging from 1 = *definitely does not apply* to 5 = *definitely applies*. The total scale consists of 28 items and provides three dimensions measuring teacher-perceived closeness (11 items), dependency (5 items), and conflict (12 items) with the child. Sample items include "I share an affectionate, warm relationship with this child" (closeness), "This child is overly dependent on me" (dependency), and "This child easily becomes angry with me" (conflict). The STRS is a widely used instrument of preschool- and elementary-aged children (e.g., Birch & Ladd, 1997; Howes & Ritchie, 1999; Skalická et al., 2015). Because we had no hypothesis regarding which aspect of the student–teacher relationship would be (differentially) affected by the parent–child

Table 1
Sample Characteristics (n = 652)

Variable	*M*	*SD*	Minimum	Maximum	*N*
Demographics					
Child age at T1 (months)	54.87	2.98	48.23	67.81	610
Male children (%)	50.8%				332
Age of parent at clinic (in years)	35.02	4.75	21.00	57.00	620
Women brought child to clinic (%)	84.4%				523
Relation to the child					
Biological parents (%)	98.2%				609
Adoptive parents (%)	1.1%				7
Stepparents (%)	.2%				1
Foster parents	.5%				3
Marital status					
Married (%)	55.7%				343
Lives together, >6 months (%)	34.3%				211
Lives together, <6 months (%)	1.1%				7
Divorced (%)	6.2%				38
Separated (%)	1.5%				9
Never lived together (%)	1.0%				6
Widow (%)	.3%				2
Ethnicity					
Ethnicity male parent (%) Norwegian	94.4				587
Ethnicity female parent (%) Norwegian	96.3%				599
Genotype					*n* = 652
Genotype A/A (%)	11.8				77
Genotype A/G (%)	46.8				305
Genotype G/G (%)	41.4				270

relationship, we applied the STRS total score. Cronbach's αs were .81, .84, and .83 at T1 through T3, respectively.

Parenting. Parenting was measured using the Dyadic Parent–Child Interaction System (DPICS; Eyberg, Nelson, Duke, & Boggs, 2005), which is an observation measure designed to capture the quality of parent–child interactions. The DPICS is used to assess progress in Parent–Child Interaction Therapy (PCIT; Brinkmeyer & Eyberg, 2003), a parent-training program commonly used to address behavioral problems in children (Bjørseth & Wichstrøm, 2016; Nixon, Sweeney, Erickson, & Touyz, 2003) but applied to internalizing problems as well, such as notably depression (modified version; Lenze, Pautsch, & Luby, 2011) and anxiety (Choate, Pincus, Eyberg, & Barlow, 2005). To tap parent–child interaction under diverse conditions the DPICS codes the interaction in three standardized 5-min sessions with very different demands on the parent (and the child). First, in Child-led play, the parent is instructed to let the child lead the interaction, which might facility sensitivity and behavioral descriptions, following the child's lead. In the second situation, Parent-led play, the parent is instructed to lead the play and make the child follow, facilitating demands, instructions, and more controlling behavior from the parent. Third, in Clean-up, the parent is instructed to have the child clean up the material used by herself or himself. Thus, in this situation parents are requested to enforce a rule and handle conflict id the child does not behave according to the instruction. Correlations between parent behavior in the three situations ranged from modest (r = .13) to moderate (r = .43). A sumscore of parenting in the three situations was created. Each session is videotaped, and the recordings were coded by observers naive to the study hypotheses and any information about the family. Before coding, the observers underwent substantial training, and reliability checks (80% agreement required to proceed) were conducted after every 25th video coding throughout the process.

According to the DPICS coding manual, each utterance from the parent and child is assigned a code, and there are 27 parent codes capturing positive, neutral, and various forms of alleged negative parenting. Because our aim was to contrast differential susceptibility with diathesis stress, we opted for a measure of parenting that ranged from positive to negative, and not merely the absence of positivity or negativity. Researchers have grouped the DPICS codes in various ways, but one of the most common ways is to assign positive communication to "Do-skills" (that are promoted in PCIT) consisting of labeled (e.g., *you did know the right answer*) and unlabeled praises (e.g., *much better!*), behavioral descriptions (e.g., *you are singing a song*), and reflections (e.g., child: *My doll has blue eyes*, parent: *She does have blue eyes*). Arguably, questions and commands from parents do not necessarily represent negative communication in all circumstances. Therefore, to avoid such ambiguity, we used only the negative talk (e.g., *you are being naughty*) and negative touch (e.g., hitting, kicking, grabbing, or shaking the child) categories. We henceforth created a communication composite that consisted of the ratio of positive communication to negative communication. A low score indicated parental communication dominated by negative communication, a score of 1 indicated as many positive as negative utterances, and a score >1 indicated communication dominated by positive communication. The coders were blind to all of the information about the family and the same coder coded the three sessions. The blinded coders recoded tapes from 106 families, yielding an intraclass correlation coefficient (ICC) of .80 for our communication measure across multiple pairs of coders.

Genotype. Genotyping of *OXTR* rs53576 was performed using KASP assays by LGC Genomics (http://www.lgcgroup.com/kasp), which are based on competitive allele-specific PCR and enable high-throughput genotyping of specific SNPs. The KASP genotyping reaction consists of three components: the sample DNA, KASP Assay mix and KASP Master mix. The SNP-specific KASP Assay mix and the universal KASP Master mix are added to DNA samples, and a thermal cycling reaction is performed followed by an endpoint fluorescent read that enables detection of the specific allele/s present in a DNA sample for the chosen SNP. The KASP Master mix contains the two universal FRET reporter cassettes, which are labeled with FAM and HEX. The KASP Master mix also contains ROX passive reference dye, Taq polymerase, free nucleotides and MgCl2 in an optimized buffer solution. The KASP Assay mix is specific to the target polymorphism and comprises two competitive, allele-specific forward primers and one common reverse primer. Each forward primer incorporates an additional tail sequence that corresponds to one of two universal FRET cassettes present in the KASP master mix. During thermal cycling of the reaction, the target polymorphism is amplified and fluorescent labels are incorporated via successive rounds of PCR. Once the KASP reaction is complete, the resulting fluorescence is measured on a BMG PHERAstar plate reader. The raw data are analyzed and scored on a Cartesian plot, also known as a cluster plot, to assign a genotype to each DNA sample using LGCs proprietary Kraken software.

Covariates. At ages 4 and 6 years, child internalizing (α = .83, α = .82, respectively) and externalizing problems (α = .89, α = .86) were measured by parental ratings on the Child Behavior Check List (CBCL; Achenbach, 1991); the 1.5–5 years version was used at age 4 and the 6–18 year version at age 6. Children's behavior toward their parents were observed while interacting with their parents in the Child led play, Parent led play, and Clean-up situations described above and assessed using the DPICS. A ratio of positive (Positive touch, Laughter, and Prosocial behavior) to negative behavior (Negative talk, Commands, Whining, Yelling, and Negative touch) was computed at age 4 and 6, respectively (ICC = .60).

Statistical analysis. To assess the effect of level and change in parent communication from 4 to 6 years of age on level and change in the student–teacher relationship from 4 to 8 years, we used piecewise growth modeling within a structural equation framework using Mplus 7.31 (1998–2012). The piecewise growth model yields three growth factor-related outcomes, the intercept, which was set at age 4, the first period of growth in the student–teacher relationship from age 4 to 6, and the second period of growth in the student–teacher relationship from age 6 to 8. Likewise, as predictors, we modeled the level (set at age 4) and change (from age 4 to 6) in parent communication. To model growth, the residuals of the STRS and parent communication at each time point were set to zero. The two periods of growth in the student–teacher relationship were regressed on the intercept (age 4) of parenting, and the second growth in the student–teacher-relationship was regressed on the growth in parent communication (from 4 to 6 years) as well. The intercept of the student–teacher relationship and parent communication indices were allowed to correlate. To adjust for expected regression toward the mean effects, the growth in the student–teacher relationship and parent communication was regressed on the respective intercepts.

The second stage of analysis proceeded, as outlined at the end of the introduction, in two steps because of the failure of prior G×E work to highlight which allelic subgroups were more or less sensitive to environmental effects. Thus, we first conducted an exploratory G×E test using piecewise regression analyses from 4 to 6 years and from 6 to 8 years to determine whether G×E was operative and which allelic group(s) appeared most developmentally malleable. If a significant G×E effect emerged, we proceeded to the second step involving the competitive, model-fitting approach developed by Widaman and associates (2012; Belsky et al., 2013) to evaluate the relative fit of two competing G×E accounts, diathesis stress versus differential susceptibility. To examine whether the child's behavior toward the parent and child's degree of internalizing and externalizing problems confounded the results, the child's initial values of these potential confounders at age 4 as well as the change from age 4 to 6 years were entered as covariates in three separate models, one for each potential confounder. Three separate models were conducted because entering all covariates in one model was not applicable because there were more parameters than the sample size allowed for; thus, such a model could not be identified.

Under diathesis-stress theorizing, the predicted interaction should be ordinal in form. Consider a biallelic polymorphism with three possible genotypes, containing 0, 1, or 2 putative "risk" alleles. According to diathesis-stress, a regression model with a Linear G × Linear E interaction should reveal four outcomes: (a) a small or zero effect of the environment for the ("resilient") group with 0 risk alleles, (b) a stronger, significant effect of the environment for the "vulnerability" group with 2 risk alleles, (c) a middling outcome by the group with 1 risk allele, and (d) a crossover point of the linear functions at or near the most positive value for the environment.

Differential susceptibility leads to a contrasting prediction regarding the form of the G×E interaction. The alternate alleles under differential susceptibility are recast as "plasticity" and "nonplasticity" alleles, rather than risk and resilience alleles, respectively. The predicted interaction would still have a small (or nil) effect of the environment for the least-plastic group, a stronger, significant effect of the environment for the plastic group, and a moderate effect for the moderately plastic group. However, the crossover point of these three linear functions would be near the middle of the distribution of scores on the environmental variable, thus revealing a "for better and for worse" pattern (Belsky et al., 2007), with "better" outcomes (i.e., more positive student–teacher relationship) predicted for the most-plastic group under more favorable environmental conditions (i.e., greater positive change in parenting) and "worse" outcomes (i.e., poorer student–teacher relationship) for the most-plastic group under less favorable conditions (i.e., less positive/more negative change in parenting).

The location of the crossover point for the predicted outcomes is, therefore, the crucial parameter that distinguishes predictions for the G×E interaction for the competing diathesis-stress and differential-susceptibility positions. Widaman et al. (2012) proposed a reparameterized regression model that makes the crossover point one of the parameters to be estimated. One major benefit of the reparameterization is that the point estimate of the crossover point is accompanied by a *SE*, so that an interval estimate can be calculated. Among other things, the reparameterized model allows model fit under differential-susceptibility and diathesis-stress conditions to be statistically contrasted, with the better fitting model offered as the optimal representation of the data.

Widaman et al. (2012; Belsky et al., 2013) distinguished four reparameterized models that can provide tests of key parameters consistent with (a) weak and (b) strong differential-susceptibility and (c) weak and (d) strong diathesis-stress predictions. In the case of weak models, all of the subgroups show significant associations between predictor and outcome, but it proves stronger for some groups than others. In strong models, the degree to which there is a predictor-outcome association also varies as a function of allelic condition, but the association is nonsignificant for at least one subgroup. Thus, whereas strong models presume that some individuals are not susceptible to environmental effects (i.e., no association between predictor and outcome), weak models presume that all individuals are susceptible, while some individuals are presumed to be more susceptible than others.

Therefore, to determine whether an interaction effect reflects diathesis-stress or differential susceptibility, we evaluated whether the regression slopes for the A homozygotes and the G carriers crossed within the range of available data of parent communication using the competitive model-testing procedures of Widaman et al. (2012) and Belsky et al. (2013). Recall that there is not sufficient available evidence to single out AA, AG, or GG carriers as a priori plastic or resilient or grouping hetero or homozygotes. Treating all G carriers as members of a single group was therefore based on preliminary analyses revealing that the effects of parenting on STRS did not vary across hetero-and homozygote G carriers (see Table 3).

A robust maximum likelihood estimator was applied. The analyses were performed on cases that were genotyped and had information on the dependent variable, that is, STRS, and missing data on the independent variables were handled according to a full information maximum likelihood procedure (FIML). The attrition analyses indicated that data were missing not at random (MNAR). FIML uses all available information and arrives at less biased estimates than complete case analysis in the present MNAR situation (Schafer & Graham, 2002). To examine whether G×E was present, we tested the difference in pairs of regression slopes from parent communication to the student–teacher relationship in the various allelic groups by comparing the model fit of a model in which the slopes were fixed to be equal with the model fit when they were freely estimated, using a Wald test.

With a screen-stratified sample, all parameters were weighted with a factor corresponding to the number of subjects in the population in a particular stratum divided by the number of participants in that stratum (i.e., low-screen scorers were "weighted up," and high scorers were weighted down). Two-sided *p* values <0.05 were regarded as statistically significant, and 95% CIs are reported when relevant.

Results

Preliminary descriptive analyses. Table 2 displays the descriptive statistics of and correlations among all variables included in the primary piecewise growth analysis. Measures of parenting and the student–teacher relationship were moderately skewed. However, and more important to our inquiry, the distribution of the change in parenting and in student–teacher relationship were not skewed, $S_{parenting} = -.47$, $S_{STRS12} = -.06$, and $S_{STRS23} = .03$. There was a decline in student–teacher relationship scores from day-care (age 4) to Grade 1 (age 6) as seen in the mean value of the yearly change score, $M = -1.23$, $p < .001$, but not from age 6 to 8, $M = .09$, $p = .62$. A slight drop in parenting scores from age 4 to 6 was also seen, $M = -.48$, $p = .015$.

Furthermore, parenting at age 4 was not correlated with STRS at age 4, but a small correlation emerged between positive parenting at age 4 and 6 and better STRS scores at ages 6 and 8—indicating that it is not until children start school that parenting is predictive of student–teacher relationships. Moreover, day care teachers reported better relationships with children homozygous for the A allele (i.e., AA) at age 4, whereas teachers reported better relationships with GG homozygotes at age 8; the GGs also received more positive communication from parents at age 4 than the other allelic groups. As shown in Table 2, the latter association emerged in the context of AG heterozygotes receiving less positive communication.

Primary prediction analyses. Table 3 presents the results of the piecewise regression analyses. Recall that these analyses evaluated whether rs53576 moderated (1) the effect of level of positive parenting at age 4 on (a) student–teacher-relationships level at age 4 of and on (b) change in the student–teacher relationship from age 4 to 6 and (c) from age 6 to 8, and also whether this polymorphism moderated (2) the effect change in positive parenting from age 4 to 6 on change in a positive student–teacher relationship from age 6 to 8. The results revealed that in the case of AA homozygotes, a higher *level* of positive parenting at age 4 was associated with better student–teacher relationships at age 4 and predicted improved student–teacher relationships from age 4 to 6 ($p = .03$) and from age 6 to 8 ($p = .06$). Although these significant (or near-

Table 2
Descriptions of and Correlations Between Study Variables (TESS)

Study variables	*M* or %	*SD*	Skewness	1	2	3	4	5	6	7
1. Parenting–4 years	7.30	8.88	1.74							
2. Parenting–6 years	6.35	7.65	1.84	.29***						
3. Student–teacher relationship–4 years	118.08	7.45	−1.22	.07	.04					
4. Student–teacher relationship–6 years	115.56	8.18	−1.45	.08*	.09*	.23***				
5. Student–teacher relationship–8 years	116.09	9.73	−1.57	.08*	.11**	.27***	.55***			
6. OXTR–AA	11.8%			.02	.00	.07*	.01	−.07		
7. OXTR–AG	46.8%			−.12**	.00	−.07	−.02	−.05	−.33***	
8. OXTR–GG	41.4%			.11*	.00	.02	.01	.09*	−.31***	−.80***

Note. TESS = Trondheim Early Secure Study; OXTR = oxytocin receptor gene.
* $p < .05$. ** $p < .01$. *** $p < .001$.

Table 3

Effect of Level (At Age 4 Years) on Level of (At Age 4) and Change in Positive Parenting From Age 4 To 6 Years and Age 6 To 8 Years and the Effect of Change in Positive Parenting From Age 4 to 6 Years on Change in the Student–Teacher Relationship From 6 To 8 Years According to Variations in the Rs53576 Genotype (TESS)

Predictors and outcome	AA (n = 77) β	AA 95% CI	AA p-value	AG (n = 305) β	AG 95% CI	AG p-value	GG (n = 270) β	GG 95% CI	GG p-value	Pairwise comparisons between genotypes: AA vs. AG Wald (p-value)	AA vs. GG Wald (p-value)	AG vs. GG Wald (p-value)
Level of student–teacher relationship at 4 years[a]												
Level of parenting at 4 years[b]	.21	[.04, .38]	.016	.08	[−.01, .18]	.09	−.01	[−.17, .16]	.94	.96 (.33)	2.15 (.14)	.73 (.39)
Change from 4 to 6 years in student–teacher relationship[a]												
Level of parenting at 4 years[b]	.19	[.02, .36]	.031	.04	[−.02, .10]	.21	.03	[−.07, .13]	.58	1.35 (.24)	1.74 (.18)	.09 (.76)
Change from 6 to 8 years in student–teacher relationship[a]												
Level of parenting at 4 years[b]	.34	[−.02, .70]	.06	.02	[−.18, .22]	.83	.07	[−.10, .23]	.43	1.51 (.22)	1.44 (.23)	.06 (.81)
Change in parenting from 4 to 6 years[b]	.58	[.18, .97]	.004	.07	[−.10, .25]	.41	.03	[−.13, .18]	.74	5.11 (.024)	7.23 (.007)	.19 (.66)

Note. TESS = Trondheim Early Secure Study; CI = confidence interval.
[a] outcome. [b] predictor.

significant) effects did not emerge in the case of AG and GG carriers, the differences in effects between AA carriers and the other genotypes were not significant; that is, there was no (statistically significant) genetic moderation.

Notably, however, the effect of *change* in parent communication from 4 to 6 years on change in teacher–student relationships from age 6 to 8 proved to be genetically moderated, with the parenting effect on teacher–student relationships among AA carriers being significantly stronger than that among AG and GG carriers. Given that AA carriers differed from both AG and GG carriers and that the latter two allelic subgroups did not differ from each other, in the next stage of analysis, A homozygotes were contrasted with G carriers.

To adjust for potential confounders (internalizing behavior, externalizing behavior, and child behavior toward parent) we entered the level of the respective potential confounder at age 4 as well as change in the potential confounder from age 4 to 6 in our model.

Important to appreciate before moving on to the next stage of analysis is that adjustment for potential confounders made no substantial impact on the documented effects of parenting on later student–teacher relationship or the genetic moderation of this effect. More specifically, when child behavior toward the parent was controlled, the difference in the effect of change in parenting from age 4 to 6 on change in student–teacher relationship from age 6 to 8 remained between the AA and GG groups, Wald = 5.77, df = 1, p = .02 as well as between the AA and AG groups, Wald = 4.15, df = 1, p = .04. This was also the case when controlling for externalizing problems, AA and GG groups: Wald = 6.65, df = 1, p = .01; AA and AG groups: Wald = 4.23, df = 1, p = .04, and mostly so when controlling for internalizing problems, AA and GG groups: Wald = 64.49, df = 1, p = .03; AA and AG groups: Wald = 2.59, df = 1, p = .11. As regards the latter difference between the AA and AG groups, this difference in regression coefficients with adjustment of .27 (95% CI [−.058, .59]) compared with a difference in regression coefficients of .40 with no adjustment for internalizing problems. Hence, because the latter difference falls within the CI of the first difference, this change in the effect of change in parenting on change in the student–teacher relationship when adjustment for internalizing problems was implemented was not significant.

Given the possibility that evocative GE correlations (rGE) might explain G×E findings (Plomin, DeFries, McClearn, & McGuffin, 2008), and that one cross-sectional study indicated that OXTR might influence child behavior, which in turn affect parenting (Kryski et al., 2014) and considering that OXTR evidenced some weak main effects with predictors and outcome (see Table 2) we examined whether our main finding regarding the AA carriers could be attributed to rGE. If this was the case there should be an indirect effect from AA-status to parenting (either intercept or change) and from parenting to student–teacher relationship. We found no indication of such rGE involving level of parenting at age 4 (indirect effect = .02, p = .76) or change in parenting from age 4 to 6 (indirect effect = .00, p = .94).

To determine whether the detected G×E interaction proved to be more consistent with the diathesis stress or the differential susceptibility framework, we evaluated whether the cross-over point of the regression lines for the effect of change in positive parenting from age 4 to 6 on change in the student–teacher relationship from 6 to 8 years among AA and G carriers differed from the highest and lowest observed values of change in positive parenting from 4 to 6 years. Thus, the cross-over point was first fixed to the lowest observed change value using the model constraint procedure in Mplus. Then, in a new analysis, the cross-over point was fixed to the highest observed change value. The results of these analyses proved that the cross-over-point was clearly higher than the lowest observed value, $C_{min} = 43.40$ [33.39; 53.42], $p < .001$, and lower than the highest value, $C_{max} = -21.53$ [−31.54; −11.51], $p < .001$. The detected G×E interaction proved more consistent with that differential-susceptibility than diathesis-stress framework.

To test whether a strong versus weak version of differential susceptibility fit the data best, we compared one model in which the change in student–teacher relationship did not vary as a function of change in parenting among G carriers but only among A homozygotes (i.e., strong differential susceptibility) to a second model in which the change in student–teacher relationship did vary as a function of change in parenting in both genotypic groups even if to a differing degree (i.e., weak differential susceptibility). The strong differential susceptibility model fit the data well, $\chi^2 = 3.46$, $df = 3$, $p = .33$, as did a weak differential susceptibility model, $\chi^2 = 2.71$, $df = 2$, $p = .26$. Because the two models were not different when compared using Satorra's method (Satorra, 2000), $\Delta\chi^2 = .58$, $df = 1$, $p = .44$, the strong differential susceptibility model was preferred for reasons of parsimony. As shown in Figure 1, G carriers did not benefit from increased positive parenting, nor did they succumb to the potential negative effects of decreased positive or increased negative parenting. A homozygotes, in contrast, benefitted from increased positive parenting and suffered from declines in positive parenting. Thus, under increased positive parenting, the children's prospective relations with their teachers improved, whereas under declines in positive parenting, their future relations deteriorated.

Discussion

Given evidence that positive and supportive student–teacher relationships benefit children, the primary purposes of the research reported herein were to determine whether parenting, and change in parenting, predicted the development of this other influential relationship in interaction with child genotype *OXTR* rs53576, given the latter's repeated association with multiple aspects of social functioning, and whether any detected G×E interaction proved more consistent with diathesis-stress or differential susceptibility models of Person-×-Environment interaction.

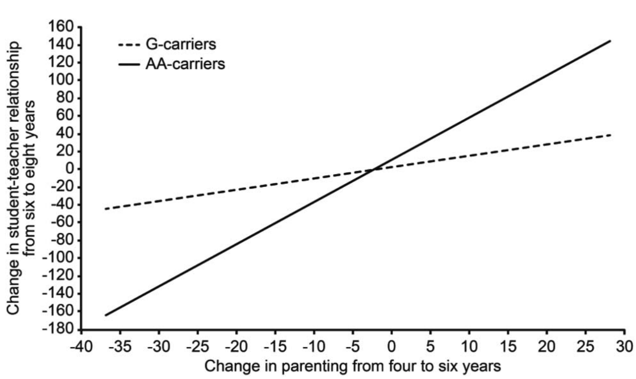

Figure 1. Change in parenting from 4 to 6 years predicting change in student–teacher relationship from 6 to 8 years in Study 1.

The results revealed that (a) although there was no evidence of genetic moderation of effects of parenting at age 4 on age-4 student–teacher relationships or (b) on change in the student–teacher relationships from age 4 to 6, (c) such genetic moderation proved evident when change in parenting from age 4 to 6 was used to predict change in student–teacher relationships from age 6 to 8. Notably, the latter finding proved consistent with the differential susceptibility rather than diathesis stress model of Person-×-Environment interaction (Belsky et al., 2007, 2013; Belsky & Pluess, 2009, 2013; Ellis et al., 2011). Recall in this regard that in the case of AA homozygotes only, greater improvement in parenting from age 4 to 6 predicted increases in the quality of student–teacher relationships from age 6 to 8, although, at the same time, smaller increases or greater declines in parenting predicted more deterioration of the student–teacher relationship.

Among G-carrying children, there were no effects of parenting at any age on student–teacher relationship, which is why the results were more consistent with the strong than weak version of differential susceptibility. Recall that the weak version requires significant predictor-outcome associations for multiple subgroups, with these associations simply being stronger in some subgroups than in others (Belsky et al., 2013; Widaman et al., 2012). G-Carrying children, then, appear much less developmentally plastic or malleable in response to environmental conditions, at least the environmental condition identified in this report, change in parenting. Whether the same would prove to be the case with regard to other oxytocin pathway genes, environmental conditions, or developmental outcomes, including those associated with relationships, and/or at other times of measurement—both earlier and later in development—remains to be determined.

Although there were grounds for predicting a G×E interaction involving *OXTR* rs53576 in the current inquiry, it was not anticipated that evidence of such would emerge only when change in parenting from age 4 to 6 was used to predict change in student–teacher relationships from age 6 to 8. We are forced to wonder why a similar G×E interaction did not emerge when parenting at age 4 was used to predict change in teacher–student relationships from age 4 to 6. Because this latter association was significant only for AA carriers and not for G carriers, although the difference was not strong enough to generate a significant G×E interaction, it would be a mistake to conclude that the two sets of results were completely inconsistent. Indeed, the fact that the significant G×E effect involved parenting change whereas the insignificant one involved only parenting measured at a single point in time raises the possibility that it may be relational stability—or lack thereof—that AA carriers are most responsive to.

Also to be considered is that the parenting change that proved sensitive to genetic moderation occurred across a major developmental transition, from preschool to school. In Norway, students are scheduled to have one—and the same—teacher in most, if not all subjects, during Grades 1 to 3. In contrast, the change from day care (age 4) to 1st grade (age 6) always involves a change of teacher. Hence, whereas the change from age 6 to 8 in the student–teacher relationship captures the change within a specific relationship, the change from age 4 to 6 also involves a change of persons within that relationship. Moreover, in first grade, the teachers had known the student for only approximately half a year. Together, these factors may make the change in student–teacher relationship from day-care to school a less sensitive measure of changes in relationship quality than within school, from age 6 to 8. Whether these considerations explain the variation in findings reported here will need to be determined by future research.

We acknowledge that little is known about the functioning of *OXTR* rs53576. However, recent studies using animal models and brain region-specific manipulations of oxytocin activity are beginning to highlight the complex effects of oxytocin (Maroun & Wagner, 2016). The many impacts of oxytocin on social behavior are suggested to partly be due its local effects on amygdala. It is also reported that AA carriers of rs53576 demonstrate increased coupling of the hypothalamus and amygdala (Tost et al., 2010). This is significant in the present context because hypothalamus is involved in the regulation of the autonomic nervous system (ANS) and thereby regulating the physiological part of emotional responses. Moreover, amygdala and hypothalamus are both involved in emotional processing (Allen, 2009). Additionally, the A allele is found to confer higher physiological and dispositional stress reactivity (Rodrigues et al., 2009).Taken together, we speculate that the amygdala-hypothalamus-Oxytocin connection and the stress reactivity findings may explain some of the present findings; AA children's brains might be more reactive to environmental stimuli such as parenting. However, further experimental research is necessary to achieve greater understanding of the biological mechanisms involved. In fact, given concerns regarding replicability of all scientific findings, there is a need to determine if those which emerged from Study 1 can be replicated, the issue addressed in Study 2.

Study 2

Method

Participants. Participants were recruited during the first 11 month of 1991 in 24 hospitals from 10 data collection locations in the United States (Charlottesville, VA; Irvine, CA; Lawrence, KS; Little Rock, AR; Madison, WI; Morganton, NC; Philadelphia, PA; Pittsburgh, PA; Seattle, WA; and Wellesley, MA). In total, 8,986 women who gave birth in selected 24-hr interval were screened for eligibility and 1,364 families with healthy newborns completed a home interview when the infant was 1 month, becoming research participants. More details about recruitment and selection procedure can be found in NICHD ECCRN (2005).

The analysis sample for Study 2 included all White children on whom DNA was obtained and for whom the OXTR haplotype rs53576 was successfully assayed. This subsample included 562 children. DNA was not available if parents or children did not agree to provide sample or the quality of the sample was compromised or proved too limited to assay. Furthermore, three children were excluded from the sample because of missing data on variables central to this inquiry (i.e., parenting and student–teacher relationship), resulting in a final analysis sample of 559 children-(n_{boys} = 274). Whereas measurements of parenting were made in Study 1 at ages 4 and 6 years and of the and student–teacher relationship at ages 4, 6, and 8 years, related measurements in Study 2 of parenting were obtained at 54 months and in 1st Grade (approximately 6 years of age) and, for the teacher–child relationship, at 54 months, 1st grade, and 3rd grade (about 8 years of age).

Measures.

Student–teacher relationship. Children's 1st and 3rd grade teachers were asked to rate their perceptions about their relationship with the study child using the Student–Teacher Relationship Scale, Short form (STRS; Pianta, 2001). This form consisted of 15 items (of the 28 items used in Study 1) scored on a 5-point Likert scale that ranged from 1 = *definitely does not apply* to 5 = *definitely applies*. The scale measured two dimensions of teacher–child relationship: teacher–child conflict (7 items; e.g., "The child easily becomes angry at me") and teacher–child closeness (8 items, e.g., "I share an affectionate, warm relationship with the child"). As in Study 1, subscale scores were combined to create a STRS total score (α = .83, .86 *and* .89 for 54 months, Grade 1 and Grade 3, respectively). This was done to reduce number of statistical tests and because there were no distinguishing hypotheses for the two dimensions of the student–teacher relationship that were measured.

Parenting. Parenting was measured when children were 54 months of age and, again, in 1st grade. Mother–child interaction was videotaped in free-play for 15 min; videotapes from all research sites were shipped to a central location and coded by highly trained and reliable evaluators blind to any and all information about the family. The response categories ranged from 1 = *very low* to 7 = *very high* on each of the six scales reflecting the mothers' behavior, including mothers' supportive presence, respect for the child's autonomy, stimulation of cognitive development, quality of child assistance, hostility toward the child, and mothers' confidence. As in Study 1, we created the positive or negative parenting ratio by dividing the sum of three positive parenting scales (i.e., supportive presence, respect for the child's autonomy, and quality of child assistance) by the maternal hostility rating. Therefore, a score of 3 indicated positive and negative parenting behavior occur to the same extent proportionally, whereas a score $>$3 indicated mother–child interaction dominated by positive parenting.

Genotyping. Genetic data were collected by buccal swabs when children were 15 years of age. DNA extraction and genotyping for the NICHD Study of Early Child Care and Youth Development (SECCYD) was performed at the Genome Core Facility in the Huck Institutes for Life Sciences at Penn State University under the direction of Deborah S. Grove, Director for Genetic Analysis. Taqman SNP Genotyping Assays were performed using an Allelic Discrimination Assay (Applied Biosystems, Foster City, CA) protocol. Forty nanograms of DNA were combined in a volume of 5 μl with 2X Universal PCR Mix (Applied Biosystems) and 1/20 the volume of the Taqman SNP assay in a 384 well plate. A Pre-Read was performed and then PCR as follows: a 10 min hold at 95 °C, followed by 40 to 45 cycles of 15 secs at 92 °C and then 1 min at 60 °C in a 7900HT PCR System. After amplification, a Post-Read was performed to analyze. Automatic and manual calls were made. Frequency distributions for the OXTR rs53576 SNP did not depart significantly from the Hardy-Weinberg equilibrium, n (GG) = 233, n (AG) = 260, n (AA) = 66, $\chi^2 = 0.26$, $p > .05$. The analysis sample coded GG as "3," AG as "2," and AA as "1."

Statistical analysis. Analyses in Study 2 followed the exact same procedures used in Study 1. Specifically, we assessed the effects of level and change in parenting behavior from 54 months to 1st grade on level and change in student–teacher relationship from 54 months to 3rd grade using piecewise growth modeling within a structural equation framework in Mplus 7.3 (Muthén & Muthén, 1998–2012). The piecewise growth model yields three growth-factor-related outcomes, the intercept, which was set at 54 months, the first period of growth in the student–teacher relationship from 54 months to 1st grade, and the second period of growth in this relationship from 1st grade to 3rd grade. Likewise, as predictors, we again modeled the level (set at 54 months) and change (from 54 months to 1st grade) in parenting. To model growth, the residuals of the STRS and parenting at each time point were set to zero. As in Study 1, the two periods of growth in the student–teacher relationship were regressed on the intercept (54 months) of parenting, with the second period of growth in the student–teacher-relationship regressed on growth in parenting from 54 months to grade one. The intercept of the student–teacher relationship and parenting indices were allowed to correlate. To adjust for expected effects of regression toward the mean, growth in the student–teacher relationship and in parenting were regressed on their respective intercepts.

Results

Preliminary descriptive analyses. Table 4 displays the descriptive statistics of and correlations among all variables included in the primary piecewise growth analysis. Measures of parenting and the student–teacher relationship were again moderately skewed, even though parenting measures were skewed to a lower extent. However, the distribution of changes in parenting and in student–teacher relationships were again not skewed, $S_{parenting} = -.10$, $S_{STRS12} = -.24$, and $S_{STRS23} = .11$. Mean comparisons revealed that there was a small decline—across the entire sample—in student–teacher relationship score from 1st grade to 3rd grade as seen in the mean value of the yearly change score, $M = -0.52$, $p = .005$. No overall change emerged in terms of STRS score from 54 months to 1st grade ($M = 0.36$, $p = .12$) and parenting scores from 54 months to 1st grade ($M = .01$, $p = .96$; unstandardized change scores reported). Furthermore, parenting at 54 months was only significantly and positively correlated with student–teacher relationships at 54 months, not later time points (i.e., 1st and 3rd grade), despite trends in the same direction. Parenting measured at 1st grade, however, was significantly and positively associated with student–teacher relationships at 1st grade, but not 3rd grade. Finally, *OXTR* genotype was not significantly associated with student–teacher relationship at any measurement occasion.

Primary prediction analyses. Table 5 presents the results of the piecewise regression analyses. Recall that these analyses evaluated whether rs53576 moderated (1) the effect of *level* of positive parenting at 54 months on (a) student–teacher-relationship level at 54 months and on (b) change in the student–teacher relationship from 54 months to 1st grade and (c) from 1st grade to 3rd grade; and also whether this polymorphism moderated (2) the effect *change* in positive parenting from 54 months to 1st grade on change in positive student–teacher relationship from 1st grade to 3rd grade. Results revealed that in the case of GG homozygotes, a higher level of positive parenting at 54 months was associated with better student–teacher relationship at 54 months ($p = .02$). Even though this significant effect did not emerge in the case of AA and AG carriers, the differences in effects between GG and other genotypes were not significant, that is, there was no (statistically significant) genetic moderation. Furthermore, none of the other associations between parenting and student–teacher relationship, level or change, turned out significant in any of the allelic group, and none of the associations were moderated by the OXTR rs53576 genotype.

General Discussion

Recall that results of Study 1 involving a representative community sample (after back-weighting) of Norwegian children revealed a G×E interaction consistent with the (strong) differential-susceptibility model of Person × Environment interaction. Thus, for AA homozygotes (only) of the *OXTR* rs53576 polymorphism, positive and negative changes in parenting from age 4 to 6 forecast, respectively, positive and negative changes in the student–teacher relationship from age 6 to age 8. Given widespread contemporary concerns about the replicability of many scientific findings, perhaps most especially those involving measured genes and involving G×E interactions, we sought to replicate the Norwegian findings by taking advantage of somewhat similar data collected as part of a large scale U.S. study. Clearly, this replication effort failed, as the G×E interaction detected in Study 1 and involving the same polymorphism and change in parenting failed to predict change in the student–teacher relationship in Study 2. Why might that have been the case?

The most obvious reason is that, consistent with previously cited critiques of G×E findings, those discerned in Study 1 simply

Table 4
Descriptions of and Correlations Between Study Variables in the NICHD Study (N = 559)

Study variables	*M* or %	*SD*	Skewness	1	2	3	4	5	6	7
1. Parenting–54 months	14.14	5.11	−.82	—						
2. Parenting–Grade 1	14.15	5.37	−.71	.33***	—					
3. Student–teacher relationship–54 months	65.11	7.70	−1.11	.13*	.14*	—				
4. Student–teacher relationship–Grade 1	65.82	7.73	−1.12	.06	.08*	.31***	—			
5. Student–teacher relationship–Grade 3	64.79	8.13	−1.04	.10†	.04	.35***	.46***	—		
6. OXTR–AA	11.8%			.06	.02	−.02	.06	.04	—	
7. OXTR–AG	46.5%			−.06	.01	−.04	−.08†	−.07†	−.34***	—
8. OXTR–GG	41.7%			.02	−.01	.06	.04	.05	−.31***	−.79***

Note. NICHD = National Institute of Child Health and Human Development.
† $p < .10$. * $p < .05$. *** $p < .001$.

Table 5

Effect of Level (At 54 Months) on Level of (At 54 Months) and Change in Positive Parenting From Age 54 Months to 1st Grade and 1st Grade to 3rd Grade and the Effect of Change in Positive Parenting From 54 Months to 1st Grade on Change in the Student–Teacher Relationship From 1st Grade to 3rd Grade According to Variations in the rs53576 Genotype (NICHD)

	AA (n = 66)			AG (n = 260)			GG (n = 233)			Pairwise comparisons between genotypes		
Predictors and outcome	β	95% CI	p-value	β	95% CI	p-value	β	95% CI	p-value	AA vs. AG Wald (p-value)	AA vs. GG Wald (p-value)	AG vs. GG Wald (p-value)
Level of student–teacher relationship at 54 months[a]												
Level of parenting at 54 months[b]	.05	[−.38, .47]	.83	.09	[−.08, .26]	.28	.20	[.03, .36]	.02	.02 (.89)	.19 (.66)	.48 (.49)
Change from 54 months to grade 1 in student–teacher relationship[a]												
Level of parenting at 54 months[b]	.02	[−.11, .16]	.73	.02	[−.09, .14]	.69	−.01	[−.12, .10]	.83	.00 (.99)	.17 (.68)	.20 (.65)
Change from grade 1 to grade 3 in student–teacher relationship[a]												
Level of parenting at 54 months[b]	.06	[−.22, .33]	.68	.02	[−.13, .18]	.75	−.01	[−.17, .16]	.92	.01 (.91)	.15 (.71)	.09 (.76)
Change in parenting from 54 months to grade one[b]	−.03	[−.30, .24]	.82	−.02	[−.15, .11]	.73	−.05	[−.19, .10]	.54	.00 (.98)	.01 (.93)	.02 (.88)

Note. NICHD = National Institute of Child Health and Human Development; CI = confidence interval.
[a] outcome. [b] predictor.

reflected a false positive finding. Although this very real and perhaps most likely possibility cannot—and should not—be dismissed, it is worth considering differences across the two studies that might have contributed to the apparent failure to replicate. We say "apparent" because if the differences to be highlighted actually played a role in accounting for why Study 1 results did not reemerge in Study 2, it would imply that failure to replicate would be an inaccurate characterization of how best to conceptualize the relation between the results of the two studies.

Recall from the discussion of Study 1 results that Norwegian children usually remain with the *same* teacher across Grades 1, 2, and 3. That is strikingly different from school practices in the United States, as children there typically change teachers each and every academic year. Thus, the measure of change in the student–teacher relationship was based on ratings made by *different* teachers in the U.S. sample but by the very *same* teachers in Norway. It seems quite likely, then, that Norwegian teachers who rated their third graders knew them much better than did the American third grade teachers, having spent three times as much time with them. It also seems possible that, as a result, the quality of student–teacher relationships might be different across the two countries. Conceivably, even if uncertainly, such differences across countries could have played a role in our failure to replicate Study 1 results in Study 2.

One also needs to consider the fact that school quality and teacher skills likely vary much more in the United States than in Norway, because of the funding for schools being determined by local property taxes, not by the federal or even state governments, as is the case in Norway. Such a difference stems, no doubt, from more fundamental differences between the two countries (Andreβ & Heien, 2001). Because Norway is a social democratic society in which the state funds and governs the schools, there is likely much greater heterogeneity in the quality of teachers and teaching in the United States than in Norway. Moreover, the OECD PISA study (Organisation for Economic Co-operation and Development [OECD], 2016)–The *P*rogramme for *I*nternational *S*tudent *A*ssessment: a triennial international survey—indicated that, compared with Norway, American students were a lot more prone to absenteeism and more students viewed their teachers as too strict. These differences, too, could have played a role in our failure to replicate Study 1 findings in Study 2.

Related to its social-democratic nature, it also needs to be appreciated that the social welfare system in Norway is far more supportive of families than is the American system. Thus American children from the poorest backgrounds have fewer resources—at home, at child care and at school—than they would if they lived in Norway. Not inconsistent with this observation is evidence from the OECD PISA study (OECD, 2012) showing that lower socioeconomic status in America influenced student performance and led to a negative disciplinary climate in schools.

From the standpoint of family policy it is also important to appreciate that in Norway parents are financially compensated for staying home with their newborn during the entirety of the child's first year, whereas there is no federal policy of paid leave in the United States, even if a few states and some private enterprises do offer some kind of compensation. To our knowledge, however, none are as generous as what is available to *all* families raising an infant in Norway. Furthermore, *all* Norwegian children have free access to free health care until the age of 18 and younger children have regularly scheduled examinations at free health clinics that all children are expected to attend (and which TESS used to enroll participants). This means that sampling in the NICHD Study was probably far less representative of each of the 10 locales from which families were recruited, including the eight which comprised the sample of this report because of their collection of child DNA, than was the case of TESS.

Beyond the societal differences already outlined that may have contributed to the replication "failure" under consideration, there are also methodological differences across studies that merit consideration.

Most worthy of attention is the fact that while TESS used the same measures of parent–child interaction, of teacher–student relationships and of child social functioning whenever measurements included in this report were repeated, such assessments varied across time in the NICHD Study. This meant, of course, that they also differed at times from those used in TESS, even if the general constructs being assessed were more similar than different across inquiries. Like societal differences already considered, then, these methodological differences meant that Study 2 could not be considered, even at the measurement level, an exact replication of Study 1. Once again, all this is not to say that the failure to replicate should not be taken seriously, only that there would seem to be enough uncertainty as to its cause to raise questions as to whether the contrasting findings of Study 1 and 2 truly reflect such a failure. Moreover, by examining the correlation tables for the two studies, there are apparent differences. Most significant is that in TESS, parenting at age 4 is significantly correlated with student–teacher relationship at age 6 and age 8 (school age), the same finding emerged for age 6 parenting, namely that it is significantly correlated with student–teacher relationship at ages 6 and 8. In the NICHD study parenting at age 4 is only significantly correlated with student–teacher relationship at age 4, whereas age 6 parenting is correlated with age 4 and 6 student–teacher relationship, not at age 8. No association between parenting at age 6 and student–teacher relationship at age 8 may explain why the Norwegian study found an association, whereas the American study did not.

Strengths and Limitations

Whether or not one considers this report as evidence of failure to replicate, it is important to highlight both strengths and limitations of the work presented herein. With regard to strengths, it is notable that both Study 1 and 2 included large, community-based samples—though only Study 1 could be considered representative of the community from which it was drawn (after backweighting)—independent ratings of exposures (observed parent–child interaction) and outcome (teacher ratings), adjustment for covariates, and a longitudinal design. Worth noting, in addition, was our focus on change predicting change using temporally ordered predictors and outcomes, thereby providing a stronger basis for inferring cause and effect than nonchange-oriented longitudinal studies.

Despite these evident strengths, the work was not without limitations. Perhaps most important was our focus on a single *OXTR* SNP. Thus, future studies should include more SNPs in this gene to better understand gene-environment interplay involving *OXTR*. To be appreciated, however, is that understanding of the functionality of other SNPs related to *OXTR* is presently even more limited than that of rs53576, which is the most-researched *OXTR* SNP and the reason why we focused on the allelic variation that we did. Another limitation involves the focus on (mostly) mothers, raising issues of whether the effect of change in paternal behavior would also be genetically moderated in the manner detected in Study 1—in either a Norwegian or American sample. Finally and most obviously, this report was limited by its very strength—inclusion of samples from different countries, thereby making it somewhat difficult, as we have noted, to draw conclusions about the meaning of the apparent the "failure" to replicate. The same, of course, is true of the absence of exactly the same measurements across studies These differences in particular highlight the need for additional research seeking to replicate the G×E findings discerned in Study 1 in other Norwegian communities or even perhaps the failure to replicate in other American communities.

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