"Do as I say!" : parenting and the biology of child self-regulation

Kok, R.

Author: Kok, Rianne
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The role of maternal stress during pregnancy, maternal discipline, and child COMT Val158Met genotype in the development of compliance

Rianne Kok, Marian J. Bakermans-Kranenburg, Marinus H. Van IJzendoorn, Fleur P. Velders, Mariëlle Linting, Vincent W. V. Jaddoe, Albert Hofman, Frank C. Verhulst, and Henning Tiemeier (2012). *Developmental Psychobiology.* Advance online publication.
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Abstract

Maternal discipline is an important predictor of child committed compliance. Maternal stress can affect both parenting and child development. In a large population-based cohort study ($N = 613$) we examined whether maternal discipline mediated the association between maternal stress during pregnancy and child compliance, and whether COMT or DRD4 polymorphisms moderated the association between maternal discipline and child compliance. Family-related and general stress were measured through maternal self-report and genetic material was collected through cord blood sampling at birth. Mother-child dyads were observed at 36 months in disciplinary tasks in which the child was not allowed to touch attractive toys. Maternal discipline and child compliance were observed in two different tasks and independently coded. The association between family stress during pregnancy and child committed compliance was mediated by maternal positive discipline. Children with more COMT Met alleles seemed more susceptible to maternal positive discipline than children with more COMT Val alleles.

Introduction

Committed compliance is an important milestone in the development of self-regulation (Kochanska & Aksan, 1995). Self-regulatory capacities of children can be either supported and guided (e.g., Bernier, Carlson, & Whipple, 2010) or hampered, depending on the quality of parenting (Karreman, Van Tuijl, Van Aken, & Dekovic, 2006). Parental stress has been found to influence the quality of parenting (Nelson, O'Brien, Blankson, Calkins, & Keane, 2009) and may be indirectly associated with compliance in the child (Karreman et al., 2006). However, the association between parenting and compliance might also be dependent on child characteristics, specifically their temperament (Kochanska, 1997) or genetic make-up (Kochanska, Phillibert, & Barry, 2009). In the current study we investigated whether the association between maternal stress during pregnancy and committed compliance is mediated by maternal discipline. We also investigated whether the association between maternal discipline and committed compliance is moderated by dopamine-related gene polymorphisms.

Self-regulated or *committed compliance* is a precursor of other self-regulatory capacities such as inhibition and emotion regulation (Karreman et al., 2006). Child compliance is considered self-regulated if the child is willing and eager to obey parental requests and child behavior is not merely controlled by parental pressure (Kochanska & Aksan, 2006). A meta-analysis of the association between parenting and self-regulation showed that maternal positive and negative discipline were the main predictors of child compliance (Karreman et al., 2006). *Positive discipline* is characterized by gentle but directive requests in which the parent considers the child's desires and needs (Karreman et al., 2006; LeCuyer-Maus & Houck, 2002). *Negative discipline* refers to power-assertive and intrusive controlling strategies, characterized by anger and harshness (Karreman et al., 2006). Parental discipline is an important predictor of self-regulation because young children rely on external regulation of their emotions and behavior, and only gradually internalize regulation strategies as offered by the parent (Calkins, Smith, Gill, & Johnson, 1998).

Quality of parenting can be negatively affected by stress (Nelson et al., 2009). Yet, minor and major stresses are quite common in human life, especially in the transitional period of becoming parents (Mulder et al., 2002). In this study the effect of different types of stress during pregnancy on maternal discipline and child compliance is investigated. Maternal stress during pregnancy can affect child development through intrauterine programming of the fetal brain (Van den Bergh, Mulder, Mennes, & Glover, 2005). Maternal stress during pregnancy can be a risk indicator of a genetic vulnerability of the mother which is inherited by the child (Schermerhorn et al., 2011). Another possibility is that maternal stress during pregnancy indirectly affects child development through *spillover* of maternal stress on parenting behavior in the postnatal period (e.g., Erel & Burman, 1995; Kanoy, Ulku-Steiner, Cox, & Burchinal, 2003). Though recent studies have mainly focused on intrauterine and genetic mechanisms, postnatal environmental factors may mediate the association between stress during pregnancy and child development (e.g., Velders et al., 2011). Most studies on *postnatal* parental stressors and parenting behavior have included family-related stressors (Erel & Burman, 1995; Krishnakumar & Buehler, 2000), whereas studies on the effects of *prenatal* stress mainly focus on general stress (e.g., Bergman, Sarkar, O'Connor, Modi, & Glover, 2007; Van den Bergh et al., 2005). In the current study we investigate the specificity of family-related stress and general stress during pregnancy in predicting maternal discipline. This approach also precludes reversed causality, that is, possible contamination of maternal stress measures by child characteristics.

Children might not be equally affected by environmental factors due to their genetic and/or physiological differences. The theories of *differential susceptibility* and *biological sensitivity to context* state that variation in susceptibility to environmental influences such as parenting has an evolutionary advantage (Belsky, Bakermans-Kranenburg, & Van IJzendoorn, 2007; Ellis, Boyce, Belsky, Bakermans-Kranenburg, & Van IJzendoorn, 2011). Two possible candidate polymorphisms for differential susceptibility are the COMT Val158Met polymorphism and a functional polymorphism in exon 3 of the dopamine D4 receptor gene.

The COMT gene in humans is located in chromosome 22q11 and contains a common functional polymorphism that results in a methionine (Met) to valine (Val) substitution in exon 4 at codon 158 (Lotta et al., 1995). This common polymorphism results in a significant change in enzymatic activity which particularly affects dopamine levels in the prefrontal cortex. The Met allele is associated with about one-fourth lower enzymatic activity resulting in higher extracellular dopamine activity than the Val allele which is associated with higher enzymatic activity and thus lower extracellular dopamine activity (Chen et al., 2004). The dopamine D4 receptor gene (DRD4) in humans is located near the telomere of chromosome 11p and contains various polymorphisms including variations in the number of 48-bp tandem repeats in exon 3. The three common variants in observed populations are 2R, 4R, and 7R (e.g., Wang et al., 2004). The evolutionary more recent variant DRD4-7R stands out because it codes for a receptor that is less sensitive to endogenous dopamine compared to the receptors coded for by the shorter repeats. Studies on the possibility that the DRD4 tandem repeat polymorphism and/or the COMT Val158Met polymorphism are involved in differential susceptibility to environmental factors have not found consistent results. Laucht and colleagues (2012) found that parental supervision affected alcohol use only for adolescents homozygous for the COMT Met allele, whereas Grigorenko and colleagues (2007) found that the effect of maternal rejection on reading comprehension skills was larger for carriers of the COMT Val allele than carriers of the COMT Met allele. Evidence for the DRD4 polymorphism as "susceptibility marker" is also mixed, but a recent meta-analysis confirmed the role of dopamine-related gene polymorphisms as moderators of the effects of supportive *and* insensitive parenting on child developmental outcomes, for better and for worse (Bakermans-Kranenburg & Van IJzendoorn, 2011).

In the current study we test a mediation model with mothers' self-reported stress during pregnancy as predictor, observed maternal discipline as mediator, and observed child committed compliance as outcome; and a moderation model with COMT and DRD4 as moderators of the association between maternal discipline and committed compliance. We expect that the association between stress during pregnancy and committed compliance is mediated by maternal discipline. We furthermore expect that the spillover of stress during pregnancy on maternal discipline is specific to family-related stressors and not found for general stress. We expect that not all children in our sample will be equally susceptible to their environment due to their genetic make up and that therefore the association between maternal discipline and child compliance is moderated by dopamine-related gene polymorphisms. The full model is presented in Figure 1.

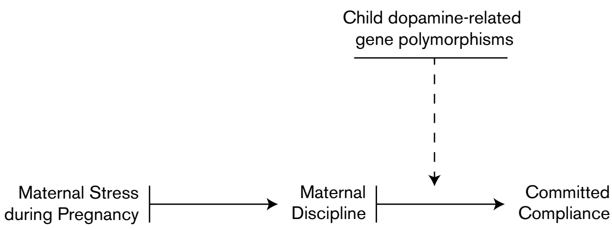

Figure 1. Design of mediation and moderation model.

Method

Setting

The current investigation is embedded within the Generation R Study, a prospective cohort study investigating growth, development, and health from fetal life onwards in Rotterdam, the Netherlands (Jaddoe et al., 2010). Detailed measurements were obtained in a subgroup of children of Dutch national origin, meaning that the children, their parents, and their grandparents were all born in the Netherlands (e.g., Luijk et al., 2010; Tharner et al., 2011). Further eligibility criteria were enrollment before a gestational age of 25 weeks and a delivery date between February 2003 and August 2005. Data were collected with questionnaires and visits to the research center for behavioral assessments. All measures were approved by the Medical Ethics Committee of the Erasmus Medical Center, Rotterdam. Written informed consent was obtained from all adult participants.

Study population

In the current study, prenatal measurements, genetic information, questionnaire data at the child's age of 2 months, and data of the lab visit at the child's age of 36 months are presented. Data were available for 852 children and their primary caregiver participating in the 36-month visit. Because the current study focuses on mother-child dyads 136 children who attended the 36-month visit with their father or grandparent were excluded. Of the 716 remaining children data on compliance was available for 694 children. We had information on the discipline style of the mother for 675 dyads. Reasons for missing data on child compliance or maternal discipline were technical or procedural difficulties during the tasks. Information on maternal family stress during pregnancy was available for 626 mothers. Within this group, 26 mothers participated in the 36-month visit twice, with twins or siblings. One half of each twin or sibling pair was randomly selected for the analyses to avoid paired data. The final sample for the mediation analyses thus consisted of 613 mother-child dyads. Nonresponse analyses on the 81 children excluded from the analyses or with missing data on maternal discipline or maternal family stress indicated that these children did not differ from the participating children on any of the background variables. A significant difference was found for the level of maternal positive discipline during the discipline task: mothers excluded from analyses used less positive discipline strategies than mothers included in the analyses, $t(682) = -2.39$, $p < .05$, and more negative discipline strategies, $t(687) = 2.46$, $p < .05$. Also, mothers excluded from the analyses reported less family stress during pregnancy than mothers included in the analyses, $t(642) = -2.07$, $p < .05$.

Information on COMT rs4680 genotype and DRD4-7 repeat polymorphism was available for 436 of the 613 children, which comprise the population for the moderator analyses. Reasons for missing data on child genotype were lack of consent for collecting genetic material, absence of a cord blood sample due to logistical difficulties (the Netherlands has Europe's highest rate of home births, > 30%), or problems with determination of genotype. Analyses on the 177 children and mothers that could not be included in the genotype analyses indicated that they did not differ from the other dyads on most background variables, family stress during pregnancy, maternal discipline style, and child compliance. Children excluded from the analyses had less often an older sibling than children included in the analyses, $t(383.27) = -2.63$, $p < .01$, and had a lower gestational age at birth, $t(233.55) = -2.91$, $p < .01$.

Information on general stress during pregnancy was missing for 13 mothers (2%) and maternal educational level was unknown for 7 mothers (1%). Information on maternal psychological problems at 2 months was missing for 79 of the 436 mothers included in the genetic analyses (18%). In total .004% of the values in the mediation model were missing and 2.1% of the values in the moderation model. Missing data on general stress during pregnancy, educational level, and maternal psychological problems at 2 months were imputed by multiple imputations. The sample consisted of 49% girls; and 61% were firstborn. The average weight at birth was 3503 g ($SD = 549$) and the average age of the child at the 36-month visit was 37.6 months ($SD = 1.6$). The mean age of mother at intake was 31.8 ($SD = 3.8$); 66% of mothers had a high level of education (at least higher vocational training or a bachelor's degree).

Central measures

Committed compliance

Compliance was assessed at 36 months in a disciplinary context ("Don't") of 2 min in which the parent allowed the child to play with an unattractive teddy bear, but prohibited the child to touch or play with a set of attractive toys that were displayed before the child. Child behavior was coded every 20 s using a coding system based on Kochanska and Aksan (1995) and Kuczynski, Kochanska, Radke-Yarrow, and Girnius-Brown (1987). The predominant behavior of the child in the six 20 s segments was coded in five mutually exclusive categories. Committed compliance was coded if the child appeared to have embraced maternal agenda wholeheartedly, made no attempt to touch or play with the toys, and needed no prompting by the parent. Situational compliance was coded when the child needed regular prompting and/or showed difficulty in complying. Passive noncompliance was coded if the child ignored the mother's request. Resistant noncompliance was coded when a child actively resisted the mother, that is, protesting or whining. Defiant noncompliance was coded if the child reacted angrily through physical or verbal behaviors. The data were independently coded by two trained coders. Coders were unaware of other data concerning the mother-child dyad and were extensively trained and regularly supervised. Reliability of the coders was assessed directly after the training and at the end of the coding process to detect possible rater drift. The intercoder reliability (intraclass correlation coefficients, ICC) for the two coders directly after the training was .81 on average ($n = 20$) and .84 at the end of the coding process ($n = 33$), with an ICC of .87 over the total set ($n = 53$).

CATPCA (Categorical Principal Components Analysis; Meulman, Heiser, & SPSS, 2010; see also; Linting, Meulman, Groenen, & Van der Kooij, 2007) was used to investigate the correlation structure of the data. Defiant noncompliance scores were excluded from the CATPCA because only one child showed defiant noncompliance behavior. A solution with all variables on nominal scaling level was compared to a solution with all variables treated numerically (which equals the standard PCA solution) to investigate whether there was substantial nonlinearity in the relations across variables. The difference between nominal and numerical solutions was only 10% in variance accounted for, so nonlinearity did not have much influence on the solution and thus the numerical solution was selected. A one-dimensional structure explained 50% of variance. Factor scores were extracted by regression method, and were used for all further analyses. The dimension was labeled *Committed Compliance* and contrasts committed compliance with the other categories. Factor scores for Committed Compliance were log transformed to approach normality.

Maternal discipline style

The discipline style of the mother was observed at 36 months in a disciplinary context which was similar to, but independent of the task in which compliance was observed. In this task of 2 min the parent prohibited the child to touch or play with a set of attractive toys that were displayed before the child. Coding procedures were based on Kuczynski and colleagues (1987), and Van der Mark, Van IJzendoorn, and Bakermans-Kranenburg (2002). Maternal verbal and physical discipline strategies were observed and coded in different categories: Commands, Support, and Physical obstruction or interference (micro coded); and with the revised Erickson 7-point rating scale for *Supportive Presence* (macro coded; Egeland, Erickson, Clemenhagen, Hiester, & Korfmacher, 1990). Both micro- and macro coding strategies were used because they can represent two different types of parental behavior: planned or intuitive behaviors which may reflect different dimensions of the same underlying construct (Mesman, 2010). To create a more comprehensive picture of positive and negative strategies, micro- and macro codes were combined. Commanding was coded when mothers prohibited their child to touch or play with toys in an authoritarian manner. Support involved all maternal remarks that helped the child to comply, such as distracting the child from the toys and responding to what the child said. Physical obstruction or interference was coded when mothers used physical force to keep the child from touching the toys. The mother's supportiveness toward her child during the discipline task was coded with the Supportive Presence scale which refers to the amount of positive regard and emotional support the mother shows toward the child. A supportive mother is a reassuring, calm, and affectively positive secure base for the child. Support and Supportive Presence represent a maternal positive discipline style. Commands and Physical obstruction are indicators of maternal negative discipline style.

Maternal behavior was coded by five trained coders. Coders were unaware of other data concerning the mother-child dyad. Coders were extensively trained and regularly supervised. Reliability of the coders was assessed directly after the training and at the end of the coding process to detect possible rater drift. The number of times a specific behavior was coded was divided by the total number of codings to create a relative score for each behavioral category, to make the score for each category independent of the number of maternal messages. The ICC for the relative frequency of Commands was .71 directly after the training ($n = 27$) and .84 at the end of the coding process ($n = 30$), with an overall ICC of .85 ($n = 57$). The ICC for the relative frequency of Support was .80 on average directly after the training ($n = 27$) and .86 on average at the end of the coding process ($n = 30$), with an overall ICC of .85 ($n = 57$). The ICC for Physical Interference was .90 on average directly after the training ($n = 27$) and .90 at the end of the coding process ($n = 30$), overall ICC .90 ($n = 57$). The ICC for Supportive Presence was .68 on average directly after the training ($n = 27$) and .85 on average at the end of the coding process ($n = 30$), overall ICC .79 ($n = 57$). Support and Supportive Presence were positively correlated, $r(611) = .27$, $p < .01$, as were Commands and Physical discipline, $r(611) = .24$, $p < .01$. An overall maternal positive discipline score and an overall maternal negative discipline score were created by standardizing and summing the scores. Maternal positive discipline was square root transformed to normality and maternal negative discipline was log transformed to normality.

Family stress during pregnancy

Family stress during pregnancy was reported by the mothers on the subscale *General Functioning* (GF) of the McMaster Family Assessment Device (FAD, Byles, Byrne, Boyle, & Offord, 1988) at 20 weeks of pregnancy. GF is a reliable and validated self-report measure of family functioning or dysfunctioning and perceptions of how the family unit works together on essential tasks suitable for nonclinical samples (Byles et al., 1988; Kabacoff, Miller, Bishop, Epstein, & Keitner, 1990). Previous studies on the GF scale of the FAD found that this scale can be used as a single index representing the overall functioning of the family (Byles et al., 1988; Kabacoff et al., 1990; Ridenour, Daley, & Reich, 1999). Byles and colleagues (1988) found that the GF subscale is associated with marital violence or disharmony and parental separation. The GF scale consists of 12 items. One half of the items describe healthy functioning (e.g., “We can express our feelings towards each other.”) and the other half describe unhealthy functioning (e.g., "We don't get on well with each other."). Mothers rated how well the statements describe their family at that moment on a 4-point Likert scale ranging from "totally disagree" to "fully agree". The internal consistency of GF was $\alpha = .90$. Item scores (reversed when necessary) were summed and divided by the total number of items. From all mothers with valid scores at least 10 item scores were available. The distribution of scores was skewed and therefore scores were transformed inversely to approach normality and mirrored for interpretation purposes.

Stress during pregnancy

General stress during pregnancy was reported by mother on the Dutch version of the long-lasting difficulties (LLD) list (Hendriks, Ormel, & Van Willige, 1990) at 20 weeks of pregnancy. This list contains 12 items on difficulties in the preceding year and mothers rate the occurrence and severity of these difficulties on a 4-point Likert scale ranging from "no" to "serious". The items concerned for example difficulties at work or school, financial and housing problems, and difficulties with friends or family. Item scores were summed and divided by the total number of items. For all mothers at least 10 item scores were available. The overall distribution was skewed and scores were square root transformed to approach normality. The internal consistency of the LLD in this sample was $\alpha = .57$. This alpha is quite low but this is expected because the list contains a broad range of difficulties that do not necessarily co-occur (Hendriks et al., 1990).

DRD4 48 bp VNTR and COMT Val158Met (rs4680)[1]

DNA was collected from cord blood samples at birth. To check for potential contamination with maternal blood, gender was determined in male participants. Gender mismatch was detected in 0.5% of cases, resulting in an expected contamination of 1% of cases. Cases with gender mismatch were not genotyped. Genotyping of polymorphism COMT was performed using Taqman allelic discrimination assay (Applied Biosystems, Foster City, CA) and Abgene QPCR ROX mix (Abgene, Hamburg, Germany). The genotyping reaction was amplified using the GeneAmp® PCR system 9600 (95 °C [15 min], then 40 cycles of 94 °C [15 s] and 60 °C [1 min]). The fluorescence was detected on the 7900HT Fast Real-Time PCR System (Applied Biosystems) and individual genotypes were determined using SDS software (version 2.3, Applied Biosystems). Genotyping was successful in 97-99% of the samples. To confirm the accuracy of the genotyping results 276 randomly selected samples were genotyped for a second time with the same method. The error rate was less than 1% for all genotypes. The allele frequency of the Met allele was 52%. Frequency distribution conformed to Hardy-Weinberg equilibrium (HWE), $\chi^2(1) = 0.44$, $p = .51$. COMT

[1] No other polymorphisms or other genetic markers were tested.

genotype was coded as 0 when the child had no Val alleles and two Met alleles, as 1 when the child had one Val allele and one Met allele, and genotype was coded as 2 when the child had two Val alleles and no Met alleles.

Genotyping of the DRD4 48 bp VNTR was amplified using primers D4-F-GCGACTACGTGGTCTACTCG and D4-R-AGGACCCTCATGGCCTTG. Reactions were performed in a 384-wells format in a total reaction volume of 10 ul containing 10 ng DNA, 1 pmol/ul of each primer, 0.4 mM dNTPs, 1 M betaine, 1x GC buffer I (Takara Bio Inc., Otsu, Japan) and 0.5 U/ul LA Taq (Takara Bio Inc.). PCR cycling consisted of initial denaturation of 1 min at 94 °C, and 34 cycles with denaturation of 30 s at 95 °C, annealing of 30 s at 58 °C and extension of 1 min at 72 °C. PCR fragments were size-separated on the Labchip GX (Caliper Life sciences, Hopkinton, MA) using a HT DNA 5K chip (Caliper Life sciences). The number of DRD4 repeats was determined using the size of the PCR fragments. To assure genotyping accuracy 225 random samples were genotyped for a second time. Three samples (1.3%) gave different genotypes. These discrepancies were specific for the repeats longer than 7. The HT DNA 5K chip was unable to accurately distinguish the 7, 8, 9, and 10 repeat. As the frequency of the 8, 9, and 10 repeat is low; all samples with a 7 repeat or longer were analyzed as one group. The allele frequency of the long repeat (7 or longer) was 20%. Frequency distribution conformed to HWE, $\chi^2(1) = 0.01$, $p = .92$. DRD4-7 R polymorphisms were entered in the analyses as two groups: no 7 or longer repeats (code 0) and one or two 7 or more repeats (code 1).

Covariates

Gender, age of mother, educational level, and maternal psychological problems

Gender of the child will be taken into account because it has been reported that the ability to inhibit responses and to comply may differ between boys and girls (e.g., Kochanska et al., 2010; Silverman, 2003). Information on gender was obtained from community midwife and hospital registries at birth. The age of the mother and her educational level were reported at the intake of the Generation R Study. Educational level was dichotomized as “high” (at least higher vocational training or a bachelor’s degree, $n = 402$) and “low/medium” ($n = 211$). Maternal psychological problems at 2 months were assessed with the Dutch version (De Beurs, 2004) of the Brief Symptom Inventory (BSI, Derogatis, 1993; Derogatis & Melisaratos, 1983). The BSI is a validated self-report questionnaire of 53 items rated on 5-point Likert scales ranging from “not at all” to “extremely”, resulting in scores on nine subscales and a global index for severity of psychological problems. The internal consistency of this index in the current study was $\alpha = .94$. Scores were transformed inversely to approach a normal distribution and mirrored for interpretation purposes.

Statistical analyses

Due to missing data on general stress during pregnancy (2%), maternal educational level (1%), and maternal psychological problems (18%) we generated five imputed data sets for the mediation analyses and 15 imputed data sets for the moderation analyses. Missing data are not uncommon in longitudinal studies, and multiple imputations are frequently used to estimate 20-40% missing data per variable (e.g., Pluess & Belsky, 2010). Missing data were imputed with the predictive mean matching method in IBM SPSS Statistics, version 19.0.1 for Windows (Meulman et al., 2010). Data were analyzed in separate data sets and subsequently pooled to obtain an overall result based on 5 or 15 imputations. Analyses conducted with the imputed data sets ($N = 613$, $N = 436$) yielded similar (significant) results compared to analyses with the complete data sets ($N = 593$, $N = 357$). Results of the imputed data sets are presented unless otherwise indicated.

The associations among covariates, family and general stress, maternal discipline style, committed compliance, DRD4-7 repeat alleles, and COMT rs4680 genotype were determined. A mediation model testing whether maternal discipline mediated the association between stress during pregnancy and child compliance was conducted according to the four criteria as described by Baron and Kenny (1986) for maternal positive discipline and maternal negative discipline separately. In the first step the association between family stress and maternal discipline style was investigated. The second step concerned the association between family stress and committed compliance. In the third step the association between maternal discipline style and committed compliance was investigated, and in step 4 a hierarchical regression analysis was conducted in which the association between family stress and committed compliance was investigated, controlling for maternal discipline style. If the four criteria were met, a Sobel test for mediation was performed as a significance test for the indirect effect of family stress on committed compliance via maternal discipline style (Baron & Kenny, 1986). The mediation model was repeated with general stress instead of family stress as the predictor to investigate the specificity of the association between family-related stressors, maternal discipline style, and child compliance.

A hierarchical regression analysis was performed to investigate possible interaction effects between maternal discipline, COMT rs4680 genotype, and DRD4 polymorphism on committed compliance. In the regression equation we included gender, maternal age, educational level, and psychological problems in the first step, followed by child genotypes, followed by maternal discipline, the interactions between child genotypes and maternal discipline, between child COMT rs4680 genotype and DRD4-7R polymorphism, and the three-way interactions between COMT, DRD4, and maternal discipline. Interaction terms between maternal discipline style and child genotype were computed after centering of the constituent variables. If interaction effects were significant, the sample was stratified by genotype to investigate the associations between maternal discipline style and committed compliance per genotype group. Furthermore, if interaction effects were significant regions of significance were estimated to further examine the differential susceptibility hypothesis (Hayes & Matthes, 2009).

Results

Distribution of main variables

Children had an average compliance score of 0.01 (range -3.31–0.84, $SD = 1.00$; transformed: $M = 0.75$, $SD = 0.19$). Mothers had an average score of 0.04 (range = -4.91–3.55, $SD = 1.54$; transformed: $M = 1.80$, $SD = 0.35$) on maternal positive discipline and an average score of -0.03 (range = -2.25–8.63, $SD = 1.46$; transformed: $M = 0.57$, $SD = 0.15$) on maternal negative discipline. The mean score for maternal family stress during pregnancy was 1.41 (range 1.00–3.50, $SD = 0.40$; transformed: $M = 1.24$, $SD = 0.18$), and the mean score for general stress was 0.14 (range 0.00–1.17, $SD = 0.18$; transformed: $M = 0.27$, $SD = 0.26$), indicating that the majority of mothers reported relatively low levels of general and family stress during pregnancy. The average global severity of maternal psychological problems was 7.70 (range 0.00–77.00, $SD = 9.58$; transformed: $M = 1.68$, $SD = 0.32$).

Bivariate associations with background variables[2]

Girls were more compliant ($M = 0.78$, $SD = 0.18$) during the discipline task than boys ($M = 0.72$, $SD = 0.20$), $p < .01$. Mothers used fewer negative discipline strategies toward girls ($M = 0.54$, $SD = 0.14$) than toward boys ($M = 0.60$, $SD = 0.15$), $p < .01$, and more positive discipline strategies toward girls ($M = 1.85$, $SD = 0.35$) than toward boys ($M = 1.75$, $SD = 0.33$), $p < .01$. Younger mothers reported more general stress during pregnancy than older mothers, $r(611) = -.08$, $p < .05$. Highly educated mothers reported less family stress during pregnancy ($M = 1.23$, $SD = 0.18$) than mothers with a lower educational level ($M = 1.27$, $SD = 0.18$), $p < .01$. Highly educated mothers also used fewer negative discipline strategies ($M = 0.56$, $SD = 0.15$) during the discipline task than mothers with a lower educational level ($M = 0.59$, $SD = 0.14$), $p < .05$, and more positive discipline strategies ($M = 1.82$, $SD = 0.35$) than mothers with a lower educational level ($M = 1.76$, $SD = 0.34$), $p < .05$. Higher levels of family stress and general stress during pregnancy were correlated with higher levels of maternal psychological problems at 2 months after birth, $r(434) = .14$, $p < .01$ and $r(426) = .25$, $p < .01$.

[2] Means and standard deviations are reported of the transformed data.

Bivariate correlations among main variables

The bivariate correlations among the main variables are presented in Table 1. Child COMT rs4680 genotype (additive: 0, 1, or 2 valine alleles) was correlated with committed compliance; children with more Val alleles were more compliant than children with more Met alleles. Family stress and general stress as reported by the mother during pregnancy were positively correlated. Higher levels of family stress also predicted less positive discipline at 36 months. Children of mothers with a higher level of family stress during pregnancy were less compliant during the discipline task at 36 months of age. Maternal positive discipline was negatively correlated with maternal negative discipline. Maternal positive discipline was correlated with a higher level of committed compliance, and maternal negative discipline was correlated with a lower level of committed compliance (observed in different settings). General stress during pregnancy was not related to parenting style or committed compliance at 36 months.

Table 1. *Correlations between child compliance and predictor variables.*

	General Stress	Family Stress	Positive Discipline	Negative Discipline	Committed compliance
COMT rs4680	-.01	-.09	.08	-.08	.11*
General Stress		.24**	.01	.01	.03
Family Stress			-.12**	.07	-.10*
Positive Discipline				-.69**	.36**
Negative Discipline					-.43**
Committed Compliance					

* $p < .05$, ** $p < .01$.

Family stress, discipline, and committed compliance: Mediation?

We tested whether the relation between family stress during pregnancy and child committed compliance at 36 months was mediated by positive or negative maternal discipline strategies. As shown in Table 1, family stress during pregnancy indeed predicted less positive maternal discipline at 36 months (step 1). The level of family stress during pregnancy also predicted committed compliance at 36 months (step 2), and maternal positive discipline was positively associated with committed compliance at 36 months (step 3). To test the fourth criterion of Baron and Kenny (1986) a hierarchical regression analysis was performed in which family stress during pregnancy was entered first and maternal positive discipline was entered second. The standardized regression weight of the association between family stress during pregnancy and committed compliance decreased from $\beta = -10$, $p < .05$ to $\beta = -.05$, $p = .17$. This suggests that the association between family stress during pregnancy and committed compliance at 36 months was mediated by maternal positive discipline. Sobel's test of the indirect effect of family stress via maternal positive discipline was significant, $z = -2.94$, $p < .01$. The mediation model is presented in Figure 2.

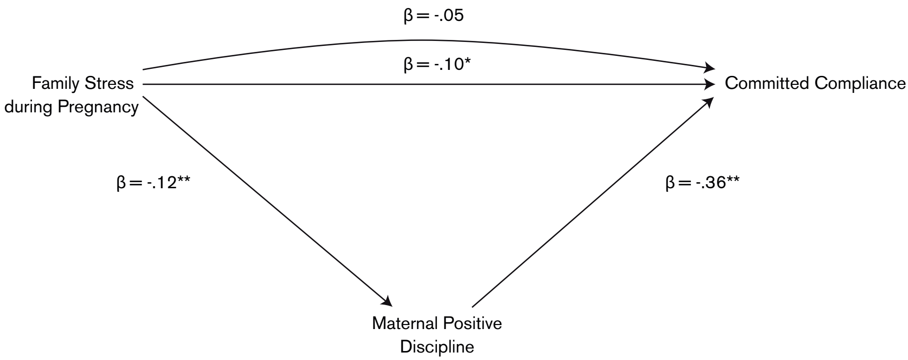

Figure 2. Maternal positive discipline mediates the association between family stress during pregnancy and child committed compliance.

The specificity of family stress as a predictor in this mediation model was supported by the fact that maternal *general* stress during pregnancy was neither associated with maternal discipline style at 36 months, nor with committed compliance at 36 months. The difference in correlations of maternal positive discipline with family stress ($r[611] = -.12$, $p < .01$) and with general stress ($r[611] = .01$, $p = .89$) was significant, $z = 1.93$, $p < .05$. The specificity of maternal positive discipline as the mediator appeared confirmed by the fact that family stress during pregnancy did not significantly predict maternal *negative* discipline at 36 months (see Table 1). However, the difference in correlations of family stress during pregnancy with maternal negative discipline ($r[611] = .07$, $p = .09$) and with maternal positive discipline ($r[611] = -.12$, $p < .01$) was not significant, $z = -0.88$, $p = .19$.

Maternal discipline and committed compliance: moderation by DRD4 or COMT?

To investigate whether DRD4 polymorphism or COMT genotype moderated the association of maternal positive and negative discipline with committed compliance a hierarchical regression analysis was performed in which we controlled for the covariates child gender, maternal age, educational level, and psychological problems. Two-way interaction effects and three-way interaction effects remained in the analysis if significant. The results of the final regression model based on the imputed datasets are presented in Table 2.

Table 2. *Predictors of child committed compliance (N = 436).*

	Committed Compliance						
	B	*SE*	β[a]	*t*	*p*	R^{2a}	R^2*change*[a]
Step 1						.03	.03
Gender	.02	.02	.05	1.16	.25		
Educational level	-.01	.02	-.03	-.64	.52		
Age mother	.00	.00	.04	.98	.33		
Mat. psych. problems	.00	.03	.00	.05	.96		
Step 2						.04	.02
DRD 4	.02	.01	.09	1.97	<.05		
COMT rs4680	.02	.01	.06	1.40	.16		
Step 3							
Pos. Disc.	.05	.03	.09	1.44	.15	.20	.16
Neg. Disc.	-.43	.08	-.33	-5.53	<.01		
Step 4						.21	.01
COMT x Pos. Disc.	-.09	.04	-.11	-2.46	<.05		

Note. Betas are taken from the final models.
[a] Averages taken from the final regression models of the 15 imputed datasets.

There was a significant association between DRD4 and committed compliance, β = .09, $p < .05$, indicating that children with one or more 7-repeat alleles were more compliant than children with no 7-repeat allele. There was no significant association between COMT rs4680 genotype and committed compliance, β = .06, $p = .16$. After controlling for child genotype and maternal negative discipline, higher levels of maternal positive discipline were no longer associated with child compliance at 36 months, β = .09, $p = .15$. Higher levels of maternal negative discipline were associated with less committed compliance at 36 months, β = -.33, $p < .01$. The three-way interactions for DRD4, COMT, and maternal positive and maternal negative discipline were not significant and therefore excluded from the analysis. The two-way interaction terms for DRD4 and maternal positive discipline and DRD4 and negative discipline, and the two-way interaction term for COMT genotype and negative discipline were also not significant and excluded from the analysis. The two-way interaction effect of COMT rs4680 and positive discipline on committed compliance was however significant. COMT rs4680 genotype moderated the association between maternal positive discipline and child compliance, β = -.11, $p < .05$, R^2change = .01. Results were similar when we controlled for maternal anxiety or maternal depression instead of global severity of psychological problems.

Analyses of the association between maternal positive discipline and committed compliance per genotype indicated that the association was stronger for the Met/Met carriers ($r[106] = .51$, $p < .01$) than for the Val/Met carriers ($r[223] = .29$, $p < .01$) or the Val/Val carriers, ($r[101] = .16$, $p = .10$). The slope of the Met/Met carriers differed significantly from the slope of the Val/Met carriers, $z = 2.23$, $p < .05$, and from the slope of the Val/Val carriers, $z = 2.87$, $p < .01$. We estimated regions of significance to further test the interaction effect of COMT rs4680 genotype and maternal positive discipline on committed compliance. The lower and upper bounds of the regions of significance were 0.00 and 0.98, respectively. This indicates that the interaction effect was significant for both the lower end of maternal positive discipline and the higher end of maternal positive discipline. The unadjusted associations between maternal positive discipline and committed compliance per genotype, with the regions of significance as shaded areas, are displayed in Figure 3.

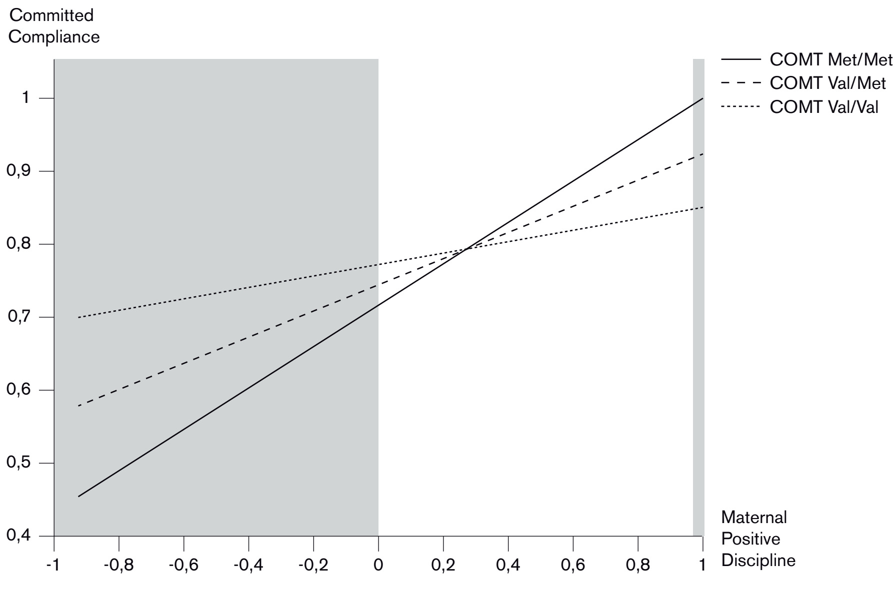

Figure 3. Interaction between COMT rs4680 and maternal positive discipline predicting child committed compliance. The shaded areas represent regions of significance.

Discussion

In our prospective cohort study, starting from fetal life, family stress during pregnancy predicted lower levels of committed compliance at 36 months of age, through lower levels of maternal *positive* discipline in toddlerhood. The positive association between maternal positive discipline and committed compliance was moderated by COMT rs4680 genotype, in that the association was stronger in children with the Met/Met genotype than for children with other COMT genotypes.

The results indicate that maternal family stress during pregnancy is associated with child self-regulation through its negative association with maternal discipline. These findings are in accordance with the spillover hypothesis (Erel & Burman, 1995) which states that parents with a positive and supportive marital relationship will be better able to sensitively respond to their children's needs, whereas parents with a stressful marital relationship may have fewer resources to provide a sensitive environment for their child. Because family stress was measured prenatally in our study and 61% of children were firstborn, this measure mostly represented stress related to the partner relationship. In 39% of cases other siblings could have influenced the measure of family stress. However, several empirical studies and meta-analyses have confirmed that not only marital discord but also other family stressors (e.g., home chaos or job-role dissatisfaction) can negatively affect parent-child interaction (Erel & Burman, 1995; Kanoy et al., 2003; Krishnakumar & Buehler, 2000; Nelson et al., 2009).

The mediation pathway through parenting complements the literature focusing on effects of prenatal stress on child development through prenatal programming effects (e.g., Bergman et al., 2007; Huizink, Robles de Medina, Mulder, Visser, & Buitelaar, 2003; O'Donnell, O'Connor, & Glover, 2009). Although in our study we cannot rule out any intrauterine effects of family stress on the fetus, at least part of the effect on child development seems to be through the postnatal rearing environment. A recent study with a prenatal cross-fostering design in pregnancies through in vitro fertilization disentangled inherited and environmental influences on child health outcomes and also found a mediation pathway from maternal stress during pregnancy through postnatal environmental factors to child psychopathology (Rice et al., 2010). Other studies found protective effects of maternal sensitivity and attachment security in the association between maternal stress during pregnancy and child development (Bergman, Sarkar, Glover, & O'Connor, 2010; Grant, McMahon, Reilly, & Austin, 2010). Our findings emphasize the importance of the influence of parenting on the child, in addition to biological and genetic effects, for the association between maternal stress during pregnancy and child development.

Our study population represented a homogeneous, socio-economically advantaged group that experienced relatively low levels of prenatal family stress and general stress. We should therefore be cautious in generalizing our findings to less advantaged populations. On statistical grounds the influence of prenatal stress on child compliance through parenting will rather be an underestimation than an overestimation of the effect in the whole population.

The effect of stress during pregnancy on maternal discipline and committed compliance was specific for family-related stress and not found for general stress. Family stress may be more severe and therefore exert a more pronounced effect on parenting and child development. Previous studies by Bergman and colleagues (2007) and Stott (1973) also found that the effects of stress during pregnancy on parenting and child behavior are mainly accounted for by family-related stressors. However, because our measure of general stress concerned the whole preceding year the stressful events did not necessarily occur during pregnancy. This might explain why the association between family stress with maternal discipline and child compliance was stronger than for our measure of general stress. However, the content of the questionnaire did refer to long-lasting difficulties, which implies that they will not often be resolved within a short period. Because even the relatively low levels of family stress that mothers in our sample experienced during pregnancy affected maternal discipline and child compliance, this study offers important knowledge on the mechanisms underlying the spillover effect of family stress during pregnancy on parenting.

The effect of family stress on committed compliance was mediated by maternal positive discipline but not by negative discipline. Although the association between the two discipline strategies appeared to be rather strong, positive discipline and negative discipline seem not to represent the ends of one continuum. The specificity of the effect could however also be explained by the fact that our sample was relatively homogeneous, consisting of Native Dutch and middle class participants. We could not investigate the effect on more harsh types of maternal discipline, because mothers in our sample hardly showed any harsh discipline strategies. Perhaps only very severe family stress is associated with a more extreme level of maternal negative discipline style. Maternal negative discipline did appear to be a stronger predictor of child committed compliance than maternal positive discipline. We investigated the specific effect of maternal family stress *during pregnancy* on maternal discipline. Because mothers reported family stress prenatally this measure was independent of child behavior after birth and this measure could therefore not be confounded by child compliance, temperament, or other child factors.

Committed compliance and maternal discipline style were measured at the same age, thus bidirectional effects cannot be ruled out. Previous studies have stressed the importance of investigating the bidirectional nature of mother-child interaction (Combs-Ronto, Olson, Lunkenheimer, & Sameroff, 2009; Smith, Calkins, Keane, Anastopoulos, & Shelton, 2004). However, studies by Calkins (2002) and Del Vecchio and Rhoades (2010) indicate that the influence of maternal discipline on child behavior is larger than vice versa.

Unexpectedly, children with 7-repeat alleles were more compliant at 36 months than children with no 7-repeat alleles ($\beta = .09$). This seems to contrast with studies on associations between the 7-repeat allele of DRD4 and negative developmental outcomes, for example Attention Deficit Hyperactivity Disorder (for a meta-analysis see Faraone, Doyle, Mick, & Biederman, 2001). It has, however, also been found that children with a 7-repeat allele were more timid in response to new stimuli and showed low levels of excitation compared to children without 7-repeat alleles (De Luca et al., 2003). Furthermore, Auerbach, Faroy, and Ebstein (2001) found that children with the long variant of the DRD4 genotype showed less active resistance and fewer struggles in response to arm restraint. Timidity and lower levels of excitation in the disciplinary task in our study could explain our observation of little resistance and higher levels of compliance in children with 7-repeat alleles.

DRD4 did not moderate the association between maternal discipline and committed compliance ($\beta = .06$), though previous studies reported interaction effects of DRD4 and parenting on various aspects of child development. Some studies found that the children with one or more 7-repeat alleles were more susceptible to parenting (e.g., Bakermans-Kranenburg & Van IJzendoorn, 2011; Knafo, Israel, & Ebstein, 2011) others found that children without 7-repeat alleles were more affected by parenting (e.g., Gervai et al., 2007; the African-American subsample of Propper, Willoughby, Halpern, Carbone, & Cox, 2007). The difference between our findings and the findings of the above-mentioned studies might be an indicator that differential susceptibility is domain-specific instead of domain-general (Ellis et al., 2011). Because our parenting measure and our child outcome were different from these studies, we cannot confirm nor disprove the possibility of DRD4 to moderate the relation between parenting and child behavior. To our knowledge the current study is the first to investigate the moderating role of DRD4 and COMT in the association between maternal positive discipline and committed compliance. The current findings should be further investigated and replicated in future studies.

The COMT Met homozygous children were more hampered in the development of committed compliance by low levels of maternal positive discipline but they also appeared to be more positively affected by a higher level of maternal positive discipline. Though the interaction between COMT genotype and maternal discipline was only significant at the extremes, the pattern is indicative of differential susceptibility. These findings correspond to Dreher, Kohn, Kolachana, Weinberg, and Bermann (2009)' findings on differences in responses to reward related to COMT genotype. They found that Met carriers showed higher levels of activation in the orbitofrontal cortex than Val carriers when receiving a reward, which might reflect higher saliency of reward value in Met carriers. Similarly, Wichers and colleagues (2008) found that the ability to experience rewards, operationalized as the effect of minor daily event appraisals (neutral, pleasant, or very pleasant) on the level of positive affect, was higher for participants with more Met alleles. This effect was even more pronounced for pleasant events. An increased susceptibility of children with the Met/Met genotype to rewarding cues might be due to larger increases in dopamine levels in prefrontal, orbitofrontal, and limbic regions as a result of these cues (e.g., Drabant et al., 2006; Dreher et al., 2009). Effects of parental supervision on alcohol use were also found to be larger in Met/Met carriers than in Val carriers (Laucht et al., 2012).

The interaction effect of child COMT genotype with maternal positive discipline accounted for only 1% of explained variance of the total of 21% for the whole model. This is a small effect, but even moderator effects that explain only 1% of the variance should be considered important because with this magnitude of explained variance the chances are small that incorrect conclusions are drawn or that interactions are observed when none exist (Evans, 1985). COMT and DRD4-7R were the only polymorphisms that were tested for main effects on child committed compliance and moderation of the relationship between maternal discipline and child committed compliance. Future studies should replicate our findings, also in less advantaged populations and in other ethnic groups. It would be important to involve fathers' self-reported family stress together with paternal discipline style in future models to further ground the effects of family stress on child development through postnatal rearing environment. To separate the contributions of the effects of stress during pregnancy through prenatal programming from effects on postnatal rearing environment both models should be tested simultaneously in one study with observations of environmental factors.

It should be noted that the Val allele was the minor allele in our study. In European-Caucasian populations the Met allele is often the minor allele (e.g., Perroud et al., 2010; Smolka et al., 2007), though a number of studies report a higher prevalence of the Met allele (compared to the Val allele) in European descent populations (e.g, Collip et al., 2011; Van IJzendoorn, Bakermans-Kranenburg, & Mesman, 2008; Wishart et al., 2011).

Non-response analyses on the mothers and children that had to be excluded due to missing data indicated that mothers used less positive discipline and more negative discipline, and that they experienced less family stress during pregnancy. These differences imply that the excluded mothers were less able to use sensitive discipline strategies when disciplining their child which might have resulted in a restricted range of maternal behavior in the current sample. Maternal psychological problems at 2 months were not associated with maternal discipline, child COMT rs4680 genotype, or committed compliance. Because COMT rs4680 genotype has often been associated with maternal psychopathology, the absence of a relation between psychological problems and parenting or committed compliance indicates that the gene-environment interaction we found is unlikely to be due to a gene-environment correlation.

The current study provides evidence for a spillover effect of maternal family stress during pregnancy on maternal discipline during toddlerhood, which is associated with a less optimal level of self-regulation in children. The magnitude of the influence of maternal positive discipline appeared to depend on the child's susceptibility to discipline that turned out to be associated with the dopamine-related COMT genotype. These findings underline the importance of including gene-environment interactions when investigating the development of self-regulation.

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