Short title: Genetic moderation of disorganized attachment

COMT Val158Met Moderates the Effect of Disorganized Attachment on Social

Development in Young Children

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Abstract

Children with histories of disorganized attachment exhibit diverse problems, possibly because disorganization takes at least 2 distinctive forms as children age: controlling-punitive and controlling-caregiving. This variation in the developmental legacy of disorganization has been attributed primarily to variations in children's rearing experiences. Here an alternative explanation of these divergent sequelae of disorganization is evaluated—one focused on genotype. Structural equation modeling was applied to data on 704 Norwegian children to test whether the *COMT* Val158Met genotype moderates the effect of disorganized attachment, which was measured dimensionally at 4 years of age using the Manchester Child Attachment Story Task, on changes in aggressive behavior and social competence from ages 4 to 6. Children who scored high on disorganization and were homozygous for the Val allele displayed significantly greater increases in aggression and decreases in self-oriented social skills (e.g., self-regulation and assertiveness) over time than their disorganized counterparts carrying the Met allele, whereas disorganized children carrying the Met allele increased their other-oriented social skill (e.g., cooperation and responsibility) scores more than Val-homozygous children. These results are consistent with the controlling-punitive and controlling-caregiving behaviors observed in disorganized children, suggesting that the children's genotype contributed to variations in the social development of disorganized children.

Keywords: disorganized attachment, social competence, aggression, COMT Val158Met, community sample

The absence of secure attachment during infancy and early childhood predicts problematic functioning, including elevated levels of anxiety (Colonnesi et al., 2011), externalizing problems (Fearon, Bakermans-Kranenburg, van Ijzendoorn, Lapsley, & Roisman, 2010; Groh, Roisman, van Ijzendoorn, Bakermans-Kranenburg, & Fearon, 2012), and internalizing symptoms (Brumariu & Kerns, 2010; Shaw, Keenan, Vondra, Delliquadri, & Giovannelli, 1997); however, it would be a mistake to exaggerate the magnitude of the attachment-security effects under consideration.

Among children who are not securely attached, disorganized ones appear to fare the worst developmentally (Carlson, 1998; Carlson & Sroufe, 1995; Fearon et al., 2010; Lyons-Ruth, 1996; Lyons-Ruth, Easterbrooks, & Cibelli, 1997; Moss & St-Laurent, 2001; van Ijzendoorn, Schuengel, & Bakermans-Kranenburg, 1999). However, there is notable and obvious variation in how the legacy of disorganization manifests itself: whereas some children show controlling-punitive behavior toward their parents/caregiver (e.g., aggression), others engage in controlling-caregiving behavior (e.g., helpfulness; Main & Cassidy, 1988; Moss, Cyr, & Dubois-Comtois, 2004; Wartner, Grossmann, Fremmerbombik, & Suess, 1994). Prevailing theory suggests, and some evidence indicates, that these distinctive forms of disorganized attachment are the result of the distinctive parental care that each disorganized subgroup has experienced and/or the severity of the disorganization (Bureau, Easlerbrooks, & Lyons-Ruth, 2009; George & Solomon, 1998; Moss et al., 2004; Solomon & George, 2006).

In the research reported herein, we consider an alternative—although not necessarily mutually exclusive—explanation of why disorganization takes different forms as children develop. Specifically, we adopt the view that the characteristics of the child may affect how disorganized attachment manifests itself (Fearon & Belsky, 2011; Fearon et al., 2010; Renken, Egeland, Marvinney, Mangelsdorf, & Sroufe, 1989), thus testing the notion that the

child's genotype may be important (Frigerio et al., 2009; Gilissen, Bakermans-Kranenburg, van Ijzendoorn, & Linting, 2008; Kochanska, Philibert, & Barry, 2009; Luijk et al., 2010; Zimmermann, Mohr, & Spangler, 2009). Using data collected from a large cohort of Norwegian children, we used a continuous, dimensional measure of attachment disorganization at age 4 derived from the Manchester Child Attachment Story Task (MCAST) (Green, Stanley, Smith, & Goldwyn, 2000) to predict changes in parent-rated social functioning over the next two years, while evaluating the moderating influence of the *COMT* Val158Met genotype.

Types of Preschool Disorganized Attachment

Considerable change occurs in children's social behavior in the initial 4 to 6 years of life. In general, children follow a developmental path whereby aggressive behavior modestly increases during the initial 30 to 42 months of life and peaks at approximately 4 years of age before steadily declining (Cote, Vaillancourt, LeBlanc, Nagin, & Tremblay, 2006; Tremblay et al., 2004). Regarding social skills, children advance from a simple instrumental use of social responses during infancy to voluntary pro- and antisocial behaviors during preschool and early school years. Cognitively, children develop increased insight and sensitivity to social feedback and a readiness to influence others. There is thus a steady improvement in social skills (Berger, 2011; Matthews, Deary, & Whiteman, 2009). Social skills encompass a variety of competencies, but a main distinction may be generated between two dimensions: *other-oriented* skills, which emphasize the needs of others, such as prosociality, cooperation and responsibility, and *self-oriented* skills, which signify the adaptive ability to make oneself heard, to not be submissive in relationships and regulate attention and emotions that may thwart social relationships such as self-assertiveness and self-control (Groeben, Perren, Stadelmann, & von Klitzing, 2011; Rose-Krasnor, 1997).

Children with histories of disorganized attachment in infancy tend to deviate from the above-delineated normative developmental pattern but differ in the manner in which they do deviate (Moss, Bureau, St-Laurent, & Tarabulsy, 2011; Moss, Cyr, Bureau, Tarabulsy, & Dubois-Comtois, 2005; O'Connor, Bureau, McCartney, & Lyons-Ruth, 2011). During preschool or early school years, two distinctive disorganized subtypes can be distinguished (Bureau & Moss, 2010; George & Solomon, 1996, 2008; O'Connor et al., 2011). Individuals regarded as *controlling-punitive* use harsh commands, behave in threatening manners, and may exhibit physical aggression toward the parent, which explains why parents regard such children as unadaptable, moody, confrontational, hyperactive, and difficult to control (George & Solomon, 1996; Moss et al., 2011). In the present study, a behavioral pattern that reflects a controlling-punitive style is defined by increased aggression and decreased self-oriented social skills (e.g., the ability to appropriately express feelings when wronged or receive criticism well) (Bureau et al., 2009; Moss et al., 2004) from 4 to 6 years of age.

Disorganized children who manifest a *controlling-caregiving* style behave differently than controlling-punitive children. Controlling-caregiving children rarely show distress or express negative emotions when with their mothers and appear to want to prevent the parent from becoming upset; therefore, they behave in an exceptionally cheery, polite, and/or helpful manner (Moss et al., 2011). Such children are attentive to the needs of the parent and generally refrain from challenging their parents, aiming to please them instead; as a result, the children keep their parents content. The naïve observer might regard controlling-caregiving behavior as evidence of social competence; mothers, when rating child behavior, may judge their children similarly and fail to appreciate that too much, perhaps, of a good thing—being other-oriented, responsible and cooperative—may actually reflect a strategy to maintain parental satisfaction and not be psychologically healthy development. Children who manifest a controlling-caregiving style often appear socially competent, at least according to their

parents' views and may be inclined to manifest a high degree of other-oriented social skills when with their parents. Conceivably, this is a proactive method of coping with aggressive or frightening parental behavior that is presumed to foster disorganization (van Ijzendoorn et al., 1999; David & Lyons-Ruth, 2005). In fact, this style may explain why mothers of controlling-caregiving children perceive their children to be highly adaptable (Moss et al., 2011), and emphasize their children's precociousness and taking responsibility for maternal emotions (George & Solomon, 1996).

This analysis leads us to predict that controlling-caregiving children will show increased other-oriented social skills toward parents and, to a lesser degree, display increases in self-oriented social skills from 4 to 6 years of age. We acknowledge that a high level of other-oriented social skills and low level of self-oriented social skills may not be ideal indicators of excessive caregiving. Nevertheless, it appears reasonable to presume that this behavior style captures the essential aspects of controlling-caregiving behavior. If our analysis reveals that disorganization has different effects on children depending on their genetics, in a manner consistent with our specific predictions (see the following subsection), then this result will suggest that our controlling-caregiving indicators are reasonable proxies for this developmental construct. Because disorganization, by definition, refers to the nature of a relationship that a child has with his or her caregiver, we expect that the developmental sequelae of disorganization examined in this study will be evident when parents, and not teachers, serve as informants regarding child behavior.

The Genetic Moderation of Attachment Effects

Although behavior—and not molecular—genetic studies indicate that attachment security is not heritable (Bokhorst et al., 2003; Roisman & Fraley, 2008), some molecular-genetic studies reveal relationships between particular attachment classifications and genotypes. For example, research by Lakatos and colleagues (2000) observed that children

classified as disorganized were more likely to carry the 7-repeat allele of the *DRD4* gene polymorphism. Some evidence reveals that gene-environment interactions influence attachment security and disorganization (Bakermans-Kranenburg & van Ijzendoorn, 2007; Cicchetti, Rogosch, & Toth, 2011; Spangler, Johann, Ronai, & Zimmermann, 2009). However, critically important recent efforts to replicate such molecular genetic correlates produced from small studies have failed when examining large, representative samples and this result occurs whether the focus is on genotype-phenotype associations or gene-environment interactions (Luijk et al., 2011; Mesquita et al., 2013; Roisman, Booth-LaForce, Belsky, Burt, & Groh, 2013).

However, we address a different molecular-genetic question about attachment in this study: namely, whether particular polymorphisms moderate attachment effects on social behavior. Four recent studies have addressed this matter. The results indicate that the effects of early attachment security on later child functioning appear to be moderated by the child's genotype. The results of three investigations show that insecurely attached children carrying short alleles in the 5-HTTLPR region underperform those carrying long alleles on measures of regulatory control (Kochanska et al., 2009), autonomy (Zimmermann et al., 2009), and stress response (Frigerio et al., 2009; Gilissen et al., 2008). Insecurely attached children have also been observed to respond in more stressful manners than secure infants when carrying the CC allele of the GABRA6 genotype or the Val/Val variant of the *COMT* gene (Frigerio et al., 2009).

In addition to these investigations of the genetic moderation of effects of attachment security versus insecurity, one molecular genetic study of attachment has examined whether genotype moderates the effect of disorganization on future child functioning. That study failed to detect evidence of such a gene-X-attachment interaction (Luijk et al., 2010). The acceptance of null results is risky because the absence of evidence is not evidence of absence,

and it appears appropriate to continue to empirically address the possibility of a genetic moderation of the effects of disorganized attachment, as we do here. Thus, we evaluated such gene-X-disorganization interaction effects and relied on a measure of disorganization obtained at a different point in development than Luijk and colleagues (2010). Whereas the prior investigation was based on the Strange-Situation disorganization classification measured in infancy, we relied on a dimensional measure derived from a story-stem task (i.e., MCAST) administered at age 4. Moreover, rather than using an earlier measure of disorganization to predict later measurements of children's functioning, we used an index of disorganization to predict *change* in social functioning from 4 to 6 years of age. This approach not only preserved the temporal ordering of the predictors and outcomes examined but also emphasized *development*.

The Molecular Genetics of Social Behavior

Several genes involved in the dopaminergic and serotonergic systems have been linked to aggression, which was a core result of this study, and correlated with disorganization, including monoamine oxidase-A (MAOA) (Frazzetto et al., 2007; Weder et al., 2009), catechol-O-methyltransferase (*COMT* Val158Met) (Albaugh et al., 2010; Baud et al., 2007; Kulikova et al., 2008), the dopamine transporter (DAT1), dopamine receptor (DRD2) (Guo, Roettger, & Shih, 2007), serotonin receptor (5HTR2A), and serotonin transporter (5HTT) (Beitchman et al., 2006; Haberstick, Smolen, & Hewitt, 2006; Zalsman et al., 2011). Although each of these genes are reasonable candidates for investigating the genetic moderation of the effects of disorganized attachment on children's social functioning, our focus was restricted to the *COMT* gene because it was the only one available in our data. Obviously, future research should expand the focus of gene-X-disorganization interaction beyond what is reported herein.

The *COMT* gene carries a single nucleotide polymorphism (SNP) located at codon 158 (Val158Met) that alters a single amino acid in the enzyme and replaces the amino acid Valine with Methionine (Lachman, Papolos et al., 1996). *COMT* instructs the production of the enzyme catechol-O-methyltransferase, which breaks down dopamine, epinephrine, and norepinephrine in the prefrontal cortex (PFC). The PFC is involved in complex human behavior, including the modulation of emotional reactions, empathy, self-awareness (Benton, 1991), judgment, foresight, planning, and working (short-term) memory (Fuster, 2011). The PFC also contributes to the assessment and control of social behavior (Allen, 2009; Yang & Raine, 2009). COMT accounts for more than 60% of dopamine degradation in the PFC but less than 15% of dopamine degradation in the striatum (Karoum, Chrapusta, & Egan, 1994). Consequently, genetic variations within the *COMT* gene would be expected to have more dramatic effects on PFC functions than on the functions of other brain regions. An individual with the Val/Val genotype (homozygous for the Val allele) will have a four-fold higher COMT activity in the PFC compared to homozygous Met allele carriers (Met/Met). Heterozygotes (Val/Met) will demonstrate intermediate activity (Weinshilboum, Otterness, & Szumlanski, 1999). Because a variation in COMT activity influences dopamine levels, particularly in the PFC, we assume that children homozygous for the Val allele will have lower levels of dopamine than Met carrying children. This expectation was central to our specific predictions regarding when disorganization will be related to behavioral change that is reflective of controlling-punitive or caregiving styles of functioning.

Val alleles in combination with adversity, such as childhood sexual abuse (Perroud et al., 2010), or present problems, such as ADHD (Caspi et al., 2008), predict elevated levels of aggression. Therefore, we anticipated that *COMT* would moderate the effect of disorganization on aggressive behavior. *COMT* in combination with ADHD has also been associated with impaired social understanding (Langley, Heron, O'Donovan, Owen, &

Thapar, 2010), which motivated the evaluation of whether *COMT* also moderated the effect of disorganization on various forms of social competence. We specifically hypothesize that a *high level of disorganization in preschool children homozygous for Val will predict changes in behavior that are reflective of a controlling-punitive style:* Val-Val carriers with histories of disorganization will show increased aggression and decreased self-oriented skills relative to their Met-carrying disorganized counterparts. We further hypothesize that *high levels of disorganization in children carrying the Met allele will predict changes in behavior consistent with the emergence of a controlling-caregiver style*: Met-carriers with histories of disorganization will show increased other-oriented social skills toward parents but will not necessarily show different changes in self-oriented social skills compared to less disorganized Met-carriers or disorganized Val homozygotes. We hypothesize that the above-described behavioral patterns will be specific to the parent-child relationship and do not expect the identical results when teachers rate the identical behaviors.

A preliminary step was performed before testing these hypotheses: as a component of the main analysis, we controlled for child gender and intelligence. The former decision was based on evidence (a) that school-age boys manifest distinctly higher levels of externalizing behavior than girls (Broidy et al., 2003; Cairns, Cairns, Neckerman, Ferguson, & Gariepy, 1989), whereas girls are more cooperative (Kochanska, Coy, & Murray, 2001); and (b) that gender may moderate the effect of *COMT* on aggression (Gogos et al., 1998; Lachman, Morrow, et al., 1996). Intelligence was controlled because (a) we used a narrative story-telling task to assess attachment representations and (b) prior research indicated that children's attachment narratives are associated with verbal intelligence (McElwain, Booth-LaForce, Lansford, Wu, & Dyer, 2008; von Klitzing, Stadelmann, & Perren, 2007), as is c) *COMT* (Wacker, Mueller, Hennig, & Stemmler, 2012).

We adopted a continuous approach for measuring disorganization because it generated more variation and statistical power than pure categorical approaches (Futh, O'Connor, Matias, Green, & Scott, 2008; O'Connor et al., 2011). Moreover, meta-analytic evidence has shown little if any difference in the predictive validity of categorical and dimensional scoring (Schneider, Atkinson, & Tardif, 2001). Additionally, DeCoster, Iselin, and Gallucci (2009) observed that a continuous approach is preferable under most circumstances and that a categorical measure never performs substantially better than a continuous one. Other approaches to the measurement of preschool attachment that do not rely on the Strange Situation procedure have also applied dimensional scoring (e.g., Q-Sort; Waters & Deane, 1985). Ultimately, because dimensional scoring of the Q-sort has good convergent validity with the Strange Situation procedure and is regarded as a valid measure of attachment (van Ijzendoorn, Vereijken, Bakermans-Kranenburg, & Riksen-Walraven, 2004) was central to our decision to use this method and scoring approach with the MCAST.

Method

Participants and Recruitment

Two birth cohorts (born in 2003 or 2004) of children and their parents living in the city of Trondheim, Norway were invited to participate in the Trondheim Early Secure Study (TESS). Details concerning the procedure and recruitment have been presented elsewhere (Wichstrom et al., 2012); only a brief outline is provided here. The Strengths and Difficulties Questionnaire (SDQ) 4-16 version (Goodman, 1997), together with an invitation letter, was mailed to the parents ($N = 3,456$). Completed SDQs were returned at the ordinary community health checkup for 4-year-olds at well-child clinics, which all Norwegian children (are expected to) attend (3,358 families attended). Parents with inadequate proficiency in Norwegian were excluded ($N = 176$). The health nurse did not ask 166 parents to participate.

At the well-child clinic, the eligible parents ($N = 3,016$) were informed of the study using procedures approved by the Regional Committee for Medical and Health Research Ethics. Written consent was obtained from the parents of 2,475 children (82.1% of children were eligible).

The SDQ total difficulties scores were divided into four strata. Using a random number generator, the defined proportions of parents in each stratum were selected to participate in a further study. The selection probabilities increased with increasing SDQ scores. Of the 1,250 parents invited to participate, we tested 936 (74.9%). The subsequent dropout rate did not vary by SDQ strata ($\chi^2 = 5.70$, $df = 3$, $p = .13$) or gender ($\chi^2 = 0.23$, $df = 1$, $p = .63$). Altogether, 762 children participated in the follow-up assessment two years later (T2). Among these children, 704 were successfully genotyped for the *COMT* Val158Met polymorphism; these children formed the basis of the analysis sample.

Attrition analyses revealed no differences between the children genotyped and those not genotyped for the disorganization scores at Time point 1 (T1) (OR = .78, CI = .36-1.69, $p = .52$). At T1, the genotyped children had slightly fewer aggressive behaviors (OR = .97, CI = .94-1.0, $p = .04$) and higher verbal ability scores (OR = 1.01, CI = 1.00 - 1.02, $p = .01$) than those not genotyped. No differences were observed for social competence (OR = 1.01, CI = .99-1.03, $p = .45$) or gender (OR = .98, CI = .78-1.23, $p = .85$). Multivariately, the only significant predictor of participation at Time point 2 (T2) was aggressive behavior (OR = .95, $p = .02$). In combination, the above-mentioned discriminating variables explained .9 % of the attrition according to the Cox and Snell proxy R^2. Table 1 indicates that nearly 25% of cases were missing data for the disorganization measure. This result was due to the fact that some children were too immature to participate (12 %), some were not motivated or refused to participate (6.9%), other problems occurred (1.0 %), or technical problems contributed to the remainder of the missing data (e.g., no picture, no sound, other recording problem, 4.7 %).

No significant differences emerged between those with and without missing data on the other primary study variables with one exception: more boys than girls had missing data (29.3% vs. 19.5%, $\chi^2 = 9.05$, $df = 1$, $p = .03$).

/Table 1 about here/

Procedure

After completing the SDQ, the parent who attended the well-child clinic visited the university with the child, typically within 2-4 weeks. Re-examination, including the collection of saliva samples for genotyping, occurred 2 years later when the child began first grade (T2). Most children attended the clinic with the identical parent at both T1 and T2: among the children who were with their mother at T1 (n=563), 30 were with their father at T2 (5.3%). Among the 103 children who were with their father at T1, 12 returned with their mother at T2 (11.7%). Gender information was missing for 38 parents.

Measurements

The predictor measurements are described first followed by descriptions pertaining to dependent constructs and finally the control variables.

Predictor Variables

Attachment disorganization. Disorganization was measured using the MCAST (Green et al., 2000). The MCAST has been applied in studies with low- and high-risk samples (Barone et al., 2009; Futh et al., 2008; Green, Stanley, & Peters, 2007; Leuzinger-Bohleber et al., 2011; Minnis et al., 2009; Minnis, Green, O'Connor, & Liew, 2009; Minnis et al., 2010; Wan & Green, 2010), and a number of results emphasize its reliability, internal consistency and validity (e.g., Barone et al., 2009). Not only are MCAST scores stable over time, they correlate in expected manners with other key attachment measures (Green et al., 2000). In particular, disorganization has been observed to correlate positively with a mother's

unresolved status measured using the Adult Attachment Interview (AAI; George, Kaplan, & Main, 1996) and independent teacher ratings of behavioral problems (Goldwyn, Stanley, Smith, & Green, 2000). Moreover, Futh et al. (2008) observed that disorganization in the children's attachment narratives in the MCAST were associated with greater teacher- and parent-reported problems.

The MCAST uses doll-play and story-stems to elicit attachment representations. Procedurally, the child is initially shown a non-attachment-related vignette (i.e., a breakfast vignette) that is used to determine whether the child understands and can follow the procedural instructions. This vignette is followed by four attachment-related distress stories that are completed by the children. The administrator establishes a story, which includes a child doll and a mother or father doll (depending on the gender of the parent that accompanied the child to the clinic). The child's identification with the doll figures is emphasized (e.g., "let's pretend this doll is you; this doll is your mother"). The stories begin with everyday events in which something bad/scary suddenly occurs (e.g., the child doll hurts its knee or has a nightmare). These stress inductions are designed to activate the child's attachment system and aim to facilitate specific attachment-related thoughts and behaviors comparable to the use of separation in the Strange Situation procedure (Ainsworth, Blehar, Waters, & Wall, 1978) or the "five adjective question" in the AAI (AAI: George et al., 1996). When the story climaxes, the administrator asks, "what happens next?" to facilitate the completion of the story by the child. The child is then asked about the feelings of the child/parent dolls.

In this study, the doll play was videotaped, and trained and reliable coders, who were unaware of any information regarding the child, coded each attachment-related story. The videotapes were scored according to a detailed coding manual (Green, Stanley, Goldwyn & Smith, 2007), which specifies how disorganization should be scored on the basis of the

child's behavior and his or her narrative during each vignette. Behavioral and narrative indications of disorganization included freezing or lapses at critical narrative points (e.g., a reunion between the child and mother dolls), narratives with no goal direction or major internal contradictions (e.g., proximity-seeking then freezing), explicit expressions of the child doll's fear of the parent doll, disoriented or bizarre reactions or multiple and incompatible strategies within a vignette (e.g., freezing, stilling, incomplete movements).

We measured disorganization on a dimensional, rather than categorical, basis. The primary categorization (A, B, C, or D) of each vignette was coded as 1 (present) or 0 (absent), and a secondary classification was coded as 0.5 (present) or 0 (absent). A D-score was computed by averaging the primary and secondary scores (range 0-1) across the four vignettes. Hence, a child who attained a primary classification of D on two vignettes and a secondary classification of D on one vignette would be provided a D score of .625 ([1 + 0 + 1 + 0.5]/4). Accordingly, the highest D score attainable was 1.0. A random 10% of the MCAST stories were recoded by additional raters who were blind to all information concerning the child and family, which resulted in an inter-rater reliability of ICC = .76 for the D scale across multiple pairs of raters. For the insecure avoidant (A) scale, the ICC was .71 and .70 for the insecure ambivalent (C) scale. Because of the categorical nature of D scores in each vignette (present or absent), theta was used to calculate internal consistency across the four vignettes, $\theta = .79$.

COMT. Two milliliters of saliva were collected using the Oragene DNA/Saliva Kit (DNA Genotek, Ottawa, Ontario) to genotype the children. DNA was later extracted and stored according to the manufacturer's protocol. The genotypes of the *COMT* Val158Met polymorphism were determined using a LightCycler Real-time PCR machine (Roche Diagnostics Scandinavia AB, Bromma, Sweden) (Wittwer et al., 1997). The PCR was performed in 20 µL of reagent in a LightCycler System using 2 µL of genomic DNA and a

LightCycler-FastStart DNA Master Hybridization Probes Kit (Roche Diagnostics, Bromma, Sweden) with previously published PCR primers and hybridization probes (Holmen et al., 1990). Based on the melting-curve profiles, the genotypes of the participants were classified as Val/Val, Val/Met or Met/Met. The *COMT* genotype frequencies were consistent with the Hardy-Weinberg equilibrium. The children's genotypes were divided into three groups: Val/Val ($N = 151(21.4\%)$), Val/Met ($N = 355 (50.4\%)$), and Met/Met ($N = 198 (28.1\%)$). In the analysis, the Met carriers were entered as one group ($N = 553$) with Val/Val carriers as the comparison group.

Dependent Variables

     Aggressive behavior. Aggressive behavior was measured by the aggressive behavior narrow band scale of the Children's Behavior Checklist (CBCL), which was completed by the parents (T1 α = .88; T2 α = .84) (Achenbach, 1991). At T1, the 1.5- to 5-year (CBCL/1.5–5) version was used, whereas the 6- to 18-year version was used at T2. A Teacher's Report Form (TRF/ 5-18; Achenbach, 1991) was used to measure the teacher ratings of the children's aggression (T1 α = .93; T2 α = .92).

     Social skills. Social skills were measured using the 39-item Social Skills Rating System (SSRS) (Gresham & Elliot, 1990) completed by the parents, which measures four dimensions: cooperation (T1 α =.74, T2 α =.78) (e.g., helping others, sharing materials, complying with rules/directions); responsibility (T1 α =.66, T2 α =.72) (e.g., the ability to communicate with adults, respect for property or work); assertion (T1 α =.73, T2 α =.80) (e.g., appropriately express feelings when wronged, receive criticism well, participate in organized group activities); and self-control (T1 α =.81, T2 α =.86) (e.g., appropriately respond to teasing, take turns, compromise). Based on the hypotheses, the cooperation and responsibility subscale scores were averaged to create an other-oriented social skills scale, and assertiveness and self-control scores were averaged to create a self-oriented social skills

scale. The correlation between cooperation and responsibility was substantial (T1: $r = .68$, $N = 704$; T2: $r = .70$, $N = 704$, both $p < .001$), whereas the correlation between assertion and self-control was somewhat less substantial at T1 ($r = .49$, $N = 704$, $p < .001$) and large at T2 ($r = .64$, $N = 704$, $p < .001$). The teacher-rated global social competence measure (Gresham & Elliot, 1990) consists of three dimensions: cooperation (e.g., keeps desk clean without being reminded, finishes tasks within time limits), assertion (e.g., invite others to join activities, initiate conversations with peers, help the teacher without being told) and self-control (e.g., control temper in conflict situations, wait his or her turn) (T1 $\alpha =. 93$; T2 $\alpha =.93$).

Covariates

Verbal ability. Verbal ability was measured using the Peabody Picture Vocabulary Test (PPVT-III; Dunn & Dunn, 1997; Williams & Wang, 1997) ($\alpha = .99$). We also included child *gender* as a covariate.

Results

Descriptive Statistics

Table 1 presents the descriptive statistics for all variables included in the primary structural equation modeling (SEM) analysis. Aggression decreased from age 4 to 6 years, whereas social competence, other-oriented social skills and self-oriented social skills all increased, as was expected. Secure attachment had the highest mean level, whereas disorganization and insecure avoidance had similar scores and insecure ambivalent was less frequent, as was also expected. In terms of the disorganized attachment scores, 44.2% of children showed no evidence of disorganization and received a score of zero; 32.3% of children scored between 0.13–.33, and 23.5% of the sample was characterized as highly disorganized (range: 0.38–1.00).

Independent sample t-tests were conducted to compare aggression, other-oriented social skills, and self-oriented social skills scores for the two genotype groups at T1 and T2. There was no significant difference in aggressive behaviors between the genotypes at either T1, (t (641) = -1.83, p =.07), or T2, (t (692) = -.93, p = .35). However, Met-carriers scored slightly higher on the self-oriented social skills than Val homozygotes at T1, score = 27.32 versus 26.58, (t (646) = 1.96, p = .05), and T2, score = 39.66 versus 38.43, (t (690) = 2.19, p =.03). There were no significant differences between the genotypes for other-oriented social skills at T1 or T2, (t (648) = 1.69, p = .09) (T1), (t (689) = -1.04, p = .30) (T2). Independent sample t-tests were also conducted to determine whether the gender of the parent accompanying the child affected the assessment of child aggression and social competence. No such parent gender difference was observed for aggression at T1, (t (639) = 1.17, p = .24), or T2, (t (676) =-1.08, p = .28), or social competence at T1, (t (646) = 1.36, p = .17), or T2, (t (675) = -.27, p = .79).

Table 2 displays the correlations between all study variables. Small but significant negative associations were observed between disorganization and verbal ability, other-oriented social skills (T1), and self-oriented social skills (T1, T2). Aggression was associated with disorganization (T1 only) and low levels of social competence (T1, T2).

/Table 2 about here/

Primary Analyses

We conducted the primary data analyses in two phases using SEM to evaluate whether the *COMT* Val158Met polymorphism moderated the effects of disorganized attachment on aggression and social skills. These analyses were followed by identical analyses focused on components of the social skills composite variable. First, aggressive behavior and other-oriented and self-oriented social skill scores at T2 were regressed on the

following T1 variables: aggressive behavior, other-oriented social skills, self-oriented social skills, gender, disorganization, and language skills. Aggressive behavior and social skills at T2 were allowed to correlate. Multi-group analyses were performed to compare the Met-carriers with the Val/Val carriers to test for gene X disorganization interaction effects. Initially, all path coefficients were freely estimated. This solution was compared to a solution in which the path coefficients between the disorganization outcomes at T1 and T2, aggressive behavior and social competence were fixed to be equal in the two genotype groups. A robust Maximum Likelihood (MLR) estimator was used. Because the χ^2 differences between the restricted and freely estimated models by the MLR were not χ^2 distributed, the two models were compared according to Satorra's procedure (Satorra, 2000).

These primary analyses were performed using Mplus 7.11 (Muthén & Muthén, 2012). With a screen-stratified sample, all parameters were weighted with the inverse of the drawing probability for each subject (i.e., low screen scorers were "weighted up" and high scorers were "weighted down"). This method provided unbiased general population estimates (Horvitz & Thompson, 1952). Missing data among those children who were genotyped were handled according to the Full Information Maximum Likelihood procedure.

Prediction of T1-to-T2 Change in Aggression and Social Competence

Table 3 presents the results of the initial phase of the multi-group SEM analysis designed to determine whether *COMT* moderated parent-rated aggressive behavior and social competence in disorganized children. For Val homozygous individuals, greater disorganization predicted more aggressive behavior and less other-oriented social skills. These children also decreased in self-oriented social skills with increasing levels of disorganization after controlling for the identical measurements (and gender and verbal ability) at 4 years of age. The opposite pattern of results was observed for carriers of the Met allele: greater disorganization predicted a significant decrease in aggression and significant

increase in other-oriented social skills. Comparisons between the models in which the path coefficient was freely estimated and the models in which the path was fixed to be equal across the groups yielded significant differences for aggression ($\Delta\chi^2 = 13.61$ $df = 1$, $p = .0002$), other-oriented social skills ($\Delta\chi^2 = 9.19$, $df = 1$, $p = .002$) and self-oriented social skills ($\Delta\chi^2 = 7.80$, $df = 1$, $p = .005$). Namely, genotype moderated the effect of disorganization on social development in the predicted manner. Because we used a continuous D-score scale in the above analyses, it is possible that the reported results emerged because of trivial changes at the lower end of the D-score continuum. To determine whether the results were maintained for children with high levels of disorganization as was predicted, the D scale was re-scaled, to distinguish children scoring at the top (23%) of the distribution from those scoring low or with no score. The resulting interactions are illustrated in Figures 1 (aggression), 2 (other-oriented social skills) and 3 (self-oriented social skills). The figures reflect subgroup mean comparisons of change from T1 to T2 and contrast the outcome scores for the two genotypes according to D subgroups. Figure 1 shows that although most children showed a decrease in aggression, Met-carrying HighD children showed the greatest decrease, whereas Val-homozygotic HighD children showed the smallest decrease in aggression. This genotypic difference between HighD children was significant, $\chi2$ [1] = 7.13, $p = .008$. However, children whose D-score was zero (labeled "NoD") showed the opposite pattern, such that Val homozygotes decreased the most in aggression and Met-carriers decreased the least, $\chi2$ [1] = 7.11, $p = .008$. Figures 2 and 3 show that all children increased in social skills, but Met-carrying HighD children showed the greatest increase in other-oriented social skills, whereas Val homozygotes with high D scores showed a comparatively smaller increase in other-oriented social skills. This genotypic difference between the HighD scoring children was significant, $\chi2$ [1] = 16.22, $p = .0001$. NoD and LowD children did not differ in other-oriented social skills according to genotype. A similar pattern of development, although less

strong, was observed with respect to self-oriented social skills: HighD children homozygous for the Val allele showed less increase compared to Met-carriers, $\chi 2$ [1] = 3.78, p = .05. Thus, in summary, only HighD children had social developments that changed according to genotype.

To investigate whether the detected interactions between genotype and disorganization were because of an absence of security, the previously reported regression analyses were re-run to control for a composite security score reflecting the sum of MCAST insecure-ambivalence and insecure-avoidance. The COMT X disorganization interaction remained significant in predicting T2 aggressive behavior ($\Delta\chi^2$ [1] = 14.11, p < .0002), other-oriented social skills ($\Delta\chi^2$ [1] = 8.45, p = .004) and self-oriented social skills ($\Delta\chi^2$ [1] = 7.34, p = .007).

/Table 3 about here/

/Figures 1, 2 and 3 about here/

It was predicted that the genetic moderation of the effects of disorganization would be restricted to parental reports based on the view that disorganization is a relationship-specific measure. To examine whether the observed interactions were specific to parents, we re-ran the analyses using the continuous D score with teacher ratings of aggression and social skills. The results indicated that higher D scores did not predict aggression (Val/Val, β = -.01, p =.92, Met-carriers, β = .04, p = .55); however, social skills decreased significantly in Met-carriers (Val/Val, β = -.10, p = .44, Met-carriers, β = -. 12, p = .02).

Secondary Analyses

Although these analyses were not the central focus of this study—because of an absence of the temporal ordering of predictors and outcomes—we examined whether genotypes moderated the effect of disorganized attachment at age 4 on child aggression,

other-oriented social skills and self-oriented social skills when adjusting for the covariation between these social outcomes and gender and language skills. Thereafter, we examined the identical GXA interaction at age 6. The results showed that disorganization was significantly associated with aggression at age 4 among Met-carriers, although this result was not significant compared to Val homozygotes (Val/Val, β = -.08, p = .37, Met-carriers, β = .13, p = .02, χ^2 = 3.18, df = 1, p = .07). Disorganization was not significantly associated with other-oriented social skills (Val/Val, β = .04, p = .71, Met-carriers, β = - .07, p = .19, χ^2 = .81, df = 1, p = .37) at age 4. Regarding self-oriented social skills, there was no association among the Val homozygotes (β = -.12, p = .14), but HighD Met-carriers showed a lesser degree of such skills, β = - .10, p = .04, although this difference in the effect of D between genotypes was not significant, χ^2 = .81, df = 1, p = .37. At age 6, there was no longer any association between disorganization and aggression for any of the *COMT* genotypes (Val/Val, β = .09, p = .33, Met-carriers, β = -.05, p = .25, χ^2 = 1.92, df = 1, p = .17). However, among Met-carriers disorganization was now, as opposed to the situation at age 4, associated with more other-oriented social skills (β = .10, p = .04). This result was not observed among the Val homozygotes (β = -.11, p = .29), which bordered on significance, χ^2 = 3.25, df = 1, p = .07. Disorganization was associated with significantly less self-oriented social skills at age 6 among Val homozygotes (β = -.23, p = .02) but not Met-carriers (β = -.01, p = .77), χ^2 = 3.89, df = 1, p = .05. In sum, there was a significant association between disorganization and aggression and low self-oriented social skills among Met-carriers that was observed at age 4 but not at age 6, whereas the previous non-significant association with other-oriented social skills became significant at age 6. However, disorganization was not associated with social outcomes among Val-homozygotes at age 4, but at age 6, they showed decreasing self-oriented social skills with increasing disorganization.

Treating all Met-carriers as members of a single group rested on the premise that the effects of disorganization on social competence and aggressive behavior would not vary across hetero- and homozygote Met-carriers. To test this premise, we re-ran the analyses investigating the possible differences between the two Met-carrying groups. No differences were observed.

Discussion

For more than 25 years, developmentalists have chronicled the development of children with disorganized attachment histories (Main & Cassidy, 1988; Moss et al., 2005; O'Connor et al., 2011; Wartner et al., 1994). This research has yielded a clinical and empirical consensus that as children age and reaches late preschool or early school age, their disorganization manifests in at least in two different manners. Whereas some disorganized children behave in a punitive and aggressive manner toward their parents, other disorganized children behave in a particularly pronounced cooperative, caregiving manner (Main & Cassidy, 1988; Wartner et al., 1994). Previous research has raised the possibility that these differences are a function of the children's rearing environments (Bureau et al., 2009; George & Solomon, 1998; Moss et al., 2004; Solomon & George, 2006) and may thus reflect different manners of coping with a disorganization-inducing family environment, including parenting.

In this study, we tested an alternative explanation of the divergent developmental legacies of disorganization; namely, that genotype might contribute to the differences in aggressive behavior and social competence displayed by controlling-punitive and caregiving children. The results of this prospective study of a large community sample of Norwegian 4-year-olds was consistent with expectations that Val-homozygous and Met-carrying children who scored high for disorganization as preschoolers would develop in contrasting manners in the transition to school. Highly disorganized children homozygous for the Val allele become

more aggressive over time and show reduced self-oriented social skills compared to less disorganized children, whereas aggressive behavior decreases and other-oriented social skills increase in Met-carrying children who score high on disorganization in preschool compared to those who score low on disorganization. Additionally, these children did not completely match a controlling-caregiving (comparatively little aggression and high other-oriented social skills) or controlling-punitive style (comparatively higher aggression and lower self-oriented social skills) at either age 4 or age 6. Nevertheless, with increasing levels of D, 6-year-old Val homozygotes showed lower self-oriented skills, whereas Met-carriers showed higher other-oriented skills.

These differences at age 6 and because the two genotypes develop in opposite directions—in terms of change over time—with regard to social functioning, suggests that we may be tapping into a *developmental process* that has not yet produced sufficient change to generate differences in functioning at age 6. This suggestion leads to speculation that differences in the direction of growth may become sufficient with more time to generate detectable differences in functioning at older ages. Such a result would be consistent with Bureau et al. (2009) who proposed that behavioral differences in disorganization subtypes (punitive, caregiving, and disorganized profiles) become pronounced by 8 to 9 years of age.

However attractive this proposal is, it remains difficult to explain all the results from this study. Nevertheless, it remains notable and seemingly important that genotype interacted with disorganization when focusing on change over time from ages 4 to 6. Within this time frame, children generally develop more social skills (Berger, 2011; Matthews, Deary, & Whiteman, 2009) and decrease in aggression (Cote et al., 2006; Tremblay et al., 2004). Additionally, cognitive skills increase during this period. Therefore, in this particular developmental phase, genotype may play a more active role than earlier in life, at least with

respect to this particular behavioral phenomenon. It is well appreciated that gene functioning, including expression, varies across life (Meaney, 2010; Szyf, 2009a, 2009b).

Although we cannot be certain that increases in social competence of disorganized Met-carrying children reflects a controlling-caregiving style of functioning, as we hypothesized, because this result did not emerge when teacher reports were considered and was not observed among the Val homozygotes, suggests that our judgment was not entirely misguided. Further support for this view derives from the fact that the children with disorganized histories showed increases in the other-oriented components of social competence. Such results, although not definitive, appear consistent with the notion that Met-carriers with disorganized histories of attachment become increasingly attentive toward and desirous of pleasing their parents, but not necessarily their teachers. Obviously, it would have been optimal if a less uncertain measure of controlling-caregiving behavior was available. Future research should include such a measure when aiming to extend this gene X attachment research.

In sum, the results of this inquiry suggest that disorganized children *develop* differently in their relationships with their mothers because of their version of the COMT gene or some other reasonably correlated factor. The *COMT* Val158Met accounts for much of the dopamine degradation in the PFC (Karoum et al., 1994) and thus plays an important role in regulating dopamine concentration in this region of the brain that is critical for human behavior. The PFC is involved in complex mental processes (Benton, 1991; Fuster, 2011), including the assessment and control of appropriate social behavior (Allen, 2009; Yang & Raine, 2009). The *COMT* polymorphism has thus been related to self-regulation and attention (Diamond, Briand, Fossella, & Gehlbach, 2004; Egan et al., 2001). Different levels of COMT activity conferred by the Val158Met genotypes may therefore play an important role in stress

response and self-regulating mechanisms, which in turn, may be related to the development of aggressive behavior and social competence, particularly in the case of children with histories of disorganized attachment.

The tonic-phasic theory (Bilder, Volavka, Lachman, & Grace, 2004; Grace, 1991) may offer some explanation of the contributing mechanisms. The tonic-phasic theory states that the dynamics of dopamine regulation occur via two processes: (1) a high- amplitude transitory, phasic dopamine release, which is caused by a dopamine neuron burst firing that is triggered by behaviorally relevant stimuli, and (2) a sustained low-level 'background' tonic dopamine release. Tonic dopamine release is thought to regulate the intensity of the phasic dopamine response through its effect on extracellular dopamine levels (Grace, 1991). Because of different enzyme activity associated with *COMT* Val158Met, *COMT* Val158Met may influence the balance of tonic and phasic dopamine transmission (Bilder et al., 2004). For homozygous Val carriers, the breakdown of dopamine occurs two to four times faster than for Met-carriers (Weinshilboum et al., 1999), which results in decreased overall dopamine concentrations in homozygous Val carriers compared to Met carriers. Therefore, the effect of the Met allele should be an increased tonic dopamine transmission in different regions of the brain. The Val allele is assumed to have complementary effects: increasing the phasic dopamine transmission while decreasing the subcortical tonic dopamine neurotransmission and overall dopamine concentration in the PFC (Bilder et al., 2004). The Val allele is associated with lower tonic dopamine, which is hypothesized to reduce executive function (Bilder et al., 2004; Goldberg et al., 2003), which may facilitate the propensity for reactive aggression when facing provocations, including those from demanding parents. Carriers of the Met allele will have higher D1 and D2 transmission and thus more stable networks for short-term memory (Bilder et al., 2004). The better short-term memory among Met-carriers may equip highly disorganized children with another coping mechanism when

facing stressful situations, such as an unstable or needy parent, thus leading them—over time— to act in a deliberate and planned manner rather than aggressive, which results in other-oriented behaviors over time.

Perroud et al. (2010) contend that with equal environmental exposure, stress-induced phasic dopamine release will be greater in Val allele carriers. This suggestion may explain why Val carriers facing adversities, possibly including disorganized attachment (and the rearing history it reflects), became more aggressive over time than Met-carriers. Namely, this developmental pattern may have been the result of an increase in phasic dopamine transmission in response to environmental stress (Bilder et al., 2004), a suggestion that must be tested in future research before it can be confidently concluded.

The obviously speculative interpretation of the results reported herein is consistent with results of other GXE studies focused on COMT Val158Met, contextual adversity and aggression, for example, data showing that problematic behavior increases among Val homozygotes raised under conditions of socioeconomic disadvantage (Nobile et al., 2010); that low birth weight coupled with Val homozygosity increases the risk of antisocial behaviors (Thapar et al., 2005) and that the identical results are true for children with ADHD (Caspi et al., 2008; Langley et al., 2010).

In accordance with the tonic-phasic hypothesis (Bilder et al., 2004), Met-carriers may have dopamine levels that make self-regulation and cooperative social behavior more likely. Higher dopamine levels have been associated with an internal locus of control (Previc, 2009). Therefore, it is possible that the higher dopamine levels of Met-carriers result in a less spontaneous and more deliberate approach to the threatening environment that disorganized children may experience. This approach may result in more proactive efforts to regulate the environment, including particularly other-oriented behavior, which was observed in our study. Although the primary results were consistent with our expectations and also appeared

consistent with the tonic-phasic hypothesis (Bilder et al., 2004), more research is necessary before strong conclusions and interpretations can be drawn from our results. First, our focus was exclusively on the COMT Val158Met polymorphism. Thus, future research should consider other genes implicated in the development of aggression, social skills and related developmental constructs. Whether the results reported herein, which diverge from those of Luijk et al. (2010), are a function of when and how we measure disorganization must be determined. For this reason, we believe that these results must be replicated with other measures of attachment disorganization (e.g., the Strange Situation procedure). Moreover, we consider it a limitation that mothers were overrepresented in both the attachment sequence and in reporting children's behaviors. Hence, we encourage future studies to rely on other informants.

Nevertheless, although Luijk et al. (2010) diverged from the present study by including different genes and other outcomes, the authors demonstrated the similar interplay between genes and attachment (although not with disorganization) to explain developmental outcomes, thus suggesting that gene X attachment interactions are eligible for further examination. The present study indicates the complex dynamics of how disorganization influences social development from a genetic perspective, and presumably offers a window into the development of controlling-punitive versus controlling-caregiving behaviors in early childhood.

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Table 1. *Sample characteristics (N = 703)*

Variable	*M*	*SD*	Minimum	Maximum	*N*
Demographics					
Child age at T1 (months)	54.79	2.97	48.17	67.81	656
Child age at T2	80.52	1.8	71.88	87.36	647
Male children (%)	50.5%				355
Age of parent at clinic (in years)	35.03	4.72	21.00	57.00	666
Relation to the child					
Woman, brought child to clinic (%)	84.5%				563
Biological parents (%)	98.2%				654
Adoptive parents (%)	1.2%				8
Step-parents (%)	0.2%				1
Foster parents	0.5%				3
Marital status					
Married (%)	54.8%				362
Living together >6 months (%)	34.3%				227
Living together <6 months (%)	1.2%				8
Divorced (%)	6.8%				45
Separated (%)	1.7%				11
Never lived together (%)	0.9%				6
Widow	0.3%				2
Ethnicity					
Ethnicity male parent (%)	94.8%				633

Norwegian

Ethnicity female parent (%)

Norwegian	96.4%		644

Descriptive statistics for variables

in the analyses

Aggression T1	5.75	5.03	643
Aggression T2	2.77	3.50	694
Other-oriented social skills T1	11.11	2.24	651
Other-oriented social skills T2	26.55	3.34	692
Self-oriented social skills T1	13.35	2.28	650
Self-oriented social skills T2	29.37	3.61	693
Disorganized attachment T1	.19	.23	531
Secure attachment T1	.52	.34	531
Insecure avoidant attachment T1	.21	.23	531
Insecure ambivalent attachment T1	.08	.14	531
Verbal ability T1	92.92	21.53	656
Aggression, teacher rated T1	4.22	6.44	626
Aggression, teacher rated T2	2.21	4.44	650
Social competence total score, teacher rated T1	57.45	12.35	624
Social competence total score, teacher rated T2	87.29	13.35	629

Genotype		704
Genotype Val/Val (%)	21.4%	151
Genotype Val/Met (%)	50.4%	355
Genotype Met/Met (%)	28.1%	198

Table 2. *Correlations between variables.*

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1 COMT_r [a]	1	.12**	-.07	-.06	.08	.06	-.02	-.04	.002	.05	-.06	-.05	-.08	-.10
2 Gender [b]		1	-.33**	-.01	-.06	-.10**	-.16**	-.17**	.16**	.20**	.12**	.13**	.07*	.06*
3 Disorganization			1	-.07**	.11*	.02	.06	.08**	-.14**	-.19**	-.09*	-.01	-.12**	-.08*
4 Verbal ability				1	-.12**	-.03	-.06	-.10**	.16**	.10**	.06	.01	.16**	.07**
5 Aggression T1					1	.57**	.24**	.27**	-.18**	-.18**	-.33**	-.31**	-.43**	-.37**
6 Aggression T2						1	.32**	.38**	-.25**	-.21**	-.17**	-.35**	-.27**	-.41**
7 Aggression, teacher rated T1							1	.46**	-.53**	-.26**	-.10**	-.16**	-.18**	-.20**
8 Aggression, teacher rated T2								1	-.27**	-.51**	-.09*	-.17**	-.18**	-.23**
9 Social competence teacher rated T1									1	.31**	.16**	.17**	.23**	.21**
10 Social competence teacher rated T2										1	.12**	.19**	.18**	.22**
11 Other-oriented social skills T1											1	.56**	.68**	.45**
12 Other-oriented social skills T2												1	.51**	.79**

13 Self-oriented social skills T1   1   .63**

14 Self-oriented social skills T2   1

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 * indicates the correlation is significant at the 0.05 level, and ** indicates the correlation is significant at the 0.01 level.

 [a] COMT: Met/Met and Val/Met= 0, Val/Val=1.

 [b] Gender: Boys= 1, Girls=2.

Table 3. *Prediction of aggressive behavior and social competence in 4- to 6-year-olds in accordance with disorganization and genotype*

Values at T1	Met carriers				Val homozygotes (Val/Val)			
	Aggressive behavior							
	B	S.E	Beta	p-value	B	S.E	Beta	p-value
Other-oriented social skills	.06	.03	.09	.05	.06	.07	.08	.36
Self-oriented social skills	-.07	.03	-.11	.03	-.02	.06	-.03	.77
Aggressive behavior	.39	.04	.57	<.001	.41	.06	.60	<.001
Disorganization	-1.67	.51	-.12	.001	2.47	1.28	.15	.04
Gender (References=boy)	-.58	.23	-.10	.01	-.22	.42	-.03	.60
Language skills	.01	.01	.06	.13	.01	.01	.05	.53
R^2	.35				.37			
	Other-oriented social skills							
Other-oriented social skills	.51	.03	.35	<.001	.80	.18	.51	<.001
Self-oriented social skills	.37	.09	.25	<.001	.12	.15	.08	.42
Aggressive behavior	-.17	.06	-.11	.003	-.14	.11	-.10	.20
Disorganization	4.71	1.32	.15	.001	-4.69	2.40	-.13	.08
Gender (References=boy)	1.74	.57	.13	.002	-.24	1.00	-.02	.80
Language skills	-.03	.01	-.08	.03	-.01	.02	-.04	.60
R^2	.38				.39			
	Self-oriented social skills							
Other-oriented social skills	.03	.09	.02	.77	.18	.19	.11	.33
Self-oriented social skills	.88	.09	.57	<.001	.72	.16	.47	<.001

Aggressive behavior	-.23	.06	-.14	<.001	-.21	.11	-.18	.08
Disorganization	1.60	1.18	.05	.18	-7.30	2.39	-.21	.004
Gender (References=boy)	.78	.56	.06	.16	-2.39	1.01	-.17	.01
Language skills	-.01	.01	-.02	.71	-.04	.02	-.11	.08
R^2	.41				.44			
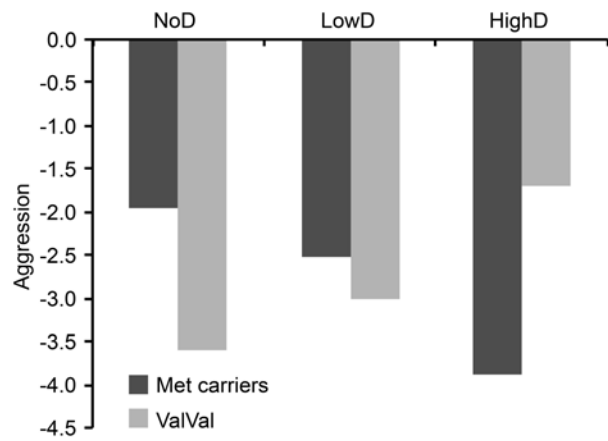
Figure 1. The subgroup mean comparison predicting change in aggression from age 4 to 6 according to the disorganization score at age 4 in Met carriers and Val homozygotes, respectively. NoD= no disorganization; LowD = low disorganization score; HighD= high disorganization score.
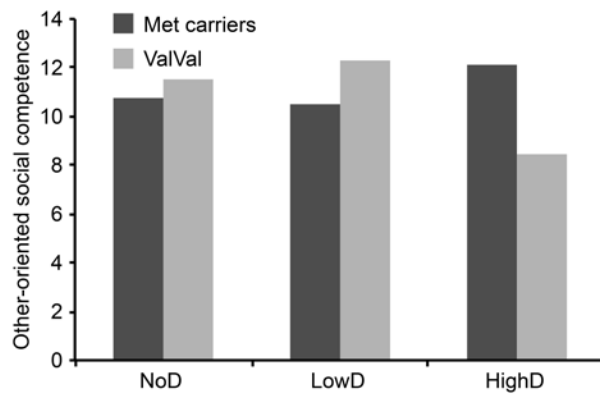
Figure 2. The subgroup mean comparison predicting change in other-oriented social competence from age 4 to 6 according to disorganization scores at age 4 in Met carriers and Val homozygotes, respectively. NoD= no disorganization; LowD = low disorganization score; HighD= high disorganization score.
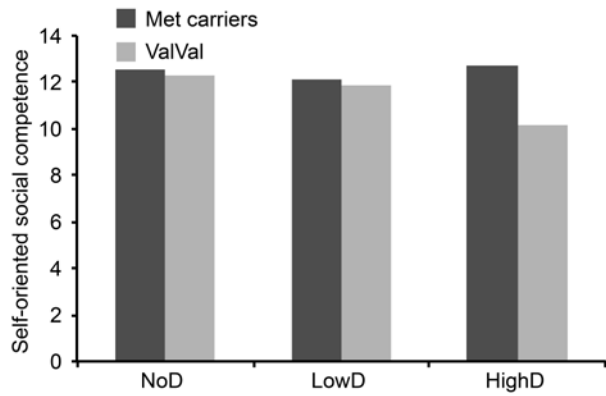
Figure 3. The subgroup mean comparison predicting change in self-oriented social competence from age 4 to 6 according to disorganization scores at age 4 in Met carriers and Val homozygotes, respectively. NoD= no disorganization; LowD = low disorganization score; HighD= high disorganization score.