Gene-Environment Interplay and Prosocial Behavior

An Analysis of Parent-Child Relationships

by

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ABSTRACT

Several decades of research have concluded that child social functioning is a critical predictor of wellbeing across various developmental domains. Most scientists agree that both genetic and environmental influences play defining roles in social behavior; the processes by which they concurrently affect child development, however, has been the subject of less research. This work examines distinct mechanisms that shape child prosociality by examining genetic and environmental influences on development, via two empirical studies. The first study analyzed the evocative-reactive and the evocative-socially-mediated hypotheses as gene-environment correlation (rGE) mechanisms connecting the arginine vasopressin receptor 1a (AVPR1a) and dopamine receptor D2 (DRD2) genes, child prosocial behavior, and parent differential treatment (PDT). Findings present modest evidence for the evocative-reactive rGE hypothesis; specifically, AVPR1a marginally influenced child prosociality, which subsequently predicted mother preference in adolescence. The second study examined several gene-environment interactions (GxEs) in exploring how social environmental variables- positive and negative parenting- predicted child prosociality, as moderated by socially-implicated genes, DRD2 and dopamine receptor D4 (DRD4). Findings indicated that while positive parenting was predictive of child prosociality regardless of genetic variants, the effects of negative parenting on child prosociality were dependent on child genetic variants. Together, findings from these studies suggest modest genetic and environmental influences on child behavior in middle childhood and adolescence, consistent with previous research and theory. Directions for future research are offered, and intervention and policy implications are discussed.

DEDICATION

For my mother, father, and sister, who saw me through five long years with the unconditional support, patience, strength, and love that made this possible. Thank you.

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CHAPTER 1

INTRODUCTION

The study of genetic and environmental interplay in human behavior has had a long, controversial, and often misguided history. While human development research has swayed through phases of genetically-heavy and environmentally neglectful eras and the reverse, it is now a widely accepted notion that genes and the environment have bi-directional influences on each other, and together make significant contributions to human behavior. Scientists have identified a number of different mechanisms through which genes and the environment work together to influence human behavior, including gene-environment correlations (rGEs), gene-environment interactions (GxE), and epigenetics, among others. While each type of gene- environment interplay undoubtedly contributes to a more comprehensive understanding of human behavior, both typical and atypical, the focus of the current study was on the effects of rGEs and GxEs on social behavior. Together, the analyses presented here measured two distinct processes by which genes and the environment work in concert to affect child social functioning.

The general aim of these studies was to examine genetic variation in the context of social environmental variation, with respect to their collective effects on child social functioning. The first study analyzed how socially-implicated measured genes predicted child social functioning, as mediated by a social environmental variable, parent differential treatment (PDT). The second study identified how social environmental variables, positive and negative parenting, predicted child social functioning, as moderated by socially-implicated genes. The goal of the work presented here was to

reveal distinct and potentially complimentary mechanisms that shape eventual child social functioning by examining genetic and environmental influences. To that end, the basis of this work assumes that child genes influence early behaviors, which subsequently affect the social environment. The social environment then influences future behavior, the extent of which is dependent on child genes (see Figure 1). In this way, via rGE-GxE interplay, genes and the environment jointly influence social behavior. Though these studies do not test the entirety of this basis, they provide a promising starting point for examining how genes "get outside the skin" to influence development over time. Because it is now a widely accepted notion that biology and the social environment, together, shape behavior, developmental researchers must move beyond studies focused solely on biological *or* environmental factors and center their efforts on interdisciplinary work to move the field's understanding of development forward.

Theoretical Framework

Most behavioral geneticists agree that genes influence most behaviors, in a variety of capacities, throughout the life course. Few behavioral geneticists would argue, however, that genes are deterministic to individual outcomes because although genetic influences are present in most behaviors, so too are environmental influences. Genes and the environment interact at various levels and through numerous mechanisms throughout the life course, forming a constant back and forth effect between genetic and environmental influences that ultimately shape behavior and competencies. One mechanism through which genes and the environment work together is the rGE. In rGEs, genes influence early behaviors, which are then met with corresponding responses from

the environment; these environmental responses then have causal effects on future behavior. A second mechanism by which genes and the environment influence behavior is through gene-environment interactions (GxEs), whereby the degree of the environment's effects on subsequent development is partially reliant on genetic variants. Because of this codependency between genes and the environment, it is difficult to truly understand human behavior without taking biological and environmental variation into account. These studies assume genes and the environment function jointly in interactive and dynamic ways throughout development, and that together, rGEs and GxEs can explain two such processes that shape social behavior. Though not directly tested, these studies also lay a foundation to suggest that in addition to gene-environment interplay, gene-environment mechanism interplay, such as rGE-GxE interplay, also plays an important role in explaining development.

The multiplier effect (Ceci, Barnett & Kanaya, 2003; Dickens & Flynn, 2001) provides a framework to explain rGEs. The effect is described as a process through which genetically influenced environmental selection and genetically influenced environmental responses to behavior, set a trajectory for future environmental selections and environmental responses, with each experience feeding off of the previous. The framework holds that individuals are born with certain biologically based abilities, such as the ability and motivation to attend to and process important external stimuli, including social stimuli. These initial genetically influenced abilities are the base skills infants use to interact with and learn from their environment. From very early in life, these innate characteristics initiate a series of rGEs where each initial behavior is matched with a

corresponding environment. Once individuals are in a genetically correlated environment, the environment has causal properties of its own, typically reinforcing the genetically influenced behavior that evoked the initial environmental response (Caspi, Roberts & Shiner, 2005; Moffitt, 1993). Over time, this constant interchange between genes and the environment serves to shape trajectories and eventual outcomes. As an example of this process, an infant who displays low levels of positive affect may elicit less positive affect in return from parents; these lower levels of positivity directed toward the infant, may in turn affect the infant's future social development. In this way, an infant's genetically influenced initial ability to orient to social stimuli or display positive affect, will be predictive of and reinforced by the social environment (parenting), absent intervention, further contributing to functioning later in development. Importantly, in the case of the infant with low positive affectivity, the response elicited by his or her environment does not *have* to correlate with the behavior; that is, if a parenting intervention is introduced, for example, parents may learn how to react positively even when faced with negative outputting behavior, which can initiate an environmentally catalyzed multiplier effect.

Gene-environment interactions are a distinct mechanism through which genes and the environment shape eventual outcomes. In GxEs, genetic variants place conditions on the behavioral outcomes of environmental influences. The differential susceptibility hypothesis is one theoretical framework proposed to explain GxEs (Belsky, 1997). The framework holds that genetic influences can cause individuals to be moderately, hypo- or hyper-sensitive to their environmental surroundings, for better or for worse. That is, if an individual has genetic variants that increase their sensitivity to environmental influence, a

rich and supportive environment may be more beneficial than it would be for individuals in a similarly positive environment without this genetic variant; likewise, an individual with this same variant in a negative environment may experience more detrimental outcomes than individuals in comparable environments without the environmentally sensitive genetic variant. Through genes shaping unique sensitivity levels to environmental influence, the differential susceptibility framework explains differential outcomes to similar rearing environments. Returning to the example of the infant who demonstrates low affect, it is possible that the infant's genetic variants make him or her highly susceptible to the environment. Under this scenario, a parent's low levels of positivity would prove much more deleterious on the infant's development, with outcomes likely mirroring the extent of low positivity. Conversely, an infant demonstrating and receiving similarly low levels of positive affect but with genetically influenced low environmental susceptibility, would be less negatively impacted by a parent's low demonstrations of positivity. Combined, rGEs, GxEs, and their interplay, can have important effects on social relationships and child adjustment. Given the codependency of genes and the environment and their joint influences on outcomes, it is imperative for the field of developmental science to begin to form research questions and hypotheses under the assumption that a true understanding of development cannot be attained without examining, and at the very least considering, both critical factors in the equation.

Statement of Problem

These studies contribute to the field by answering previously unexplored research questions, each of which will be discussed below, while also addressing a number of larger scope issues facing the field and offering promising directions for the future of intervention. First, prosociality, an important part of social functioning, is the central behavior of interest in these studies. The importance of social functioning lies in the prominent role it plays in the general wellbeing of all humans as well as the saliency of its deficit across numerous disorders. While intervention in physical medicine, such as cancer and heart disease treatment, have progressed by leaps and bounds over the last several decades, progress in interventions for psychopathology is slow, with little comparative progress. One reason for this may be the field's reliance on case-control designs based on often biologically unsupported diagnostic categories that erect arbitrary walls between genetically and phenotypically similar conditions. Biological-environmental causal pathways may be more rapidly uncovered by taking a dimensional approach. That is, for example, studying individuals with similar social deficits, regardless of diagnosis, to understand the underlying causes of social disruption. Though the studies presented here only examine one indicator of the social developmental dimension—prosociality— implications for psychopathology are discussed using this framework.

Next, even though most scientists accept that both genes and environments influence development, most research remains environmentally *or* biologically based. Segregated silos of study are the norm and collaboration is scarce, a significant

impediment precluding broader and more rapid progress in the field. Genes and the environment generally do not function independently and rarely are their effects on development simple and additive, as the compartmentalization of research genres would suggest. This is especially true in the study of social behavior. The lack of empirical studies incorporating both genes and the environment has left an unacceptable dearth in the knowledge and data necessary to develop comprehensive, effective, biologically-supported but socially-focused interventions. This unaddressed problem is detrimental to the well-being of individuals who experience social difficulties, including children and adults with a wide range of disorders, from autism spectrum disorder (ASD) and attention deficit/hyperactivity disorder (ADHD) to mood disorders and schizophrenia. The research presented here will join the small but growing field of gene-environment work in demonstrating a more comprehensive way to study the processes involved in social behavior.

In addition to contributing to the field's understanding of factors that influence social development, these studies have important implications for the future of intervention science. By further understanding genetic risk, rGEs, and the multiplier effect, clinicians may be able to detect risk and provide intervention for social difficulties earlier in life and at "trajectory dependent" points in development. These interventions can focus on preventing deleterious rGEs by targeting parents' responses to children's behavior, such that responses will be based on the science of positive parenting practices rather than on children's challenging behaviors, preventing a history of negative parent-child interactions from forming. Furthermore, currently, intervention studies often

struggle to demonstrate large or even moderate effect sizes that indicate intervention effectiveness. A plausible reason for this may be differential susceptibility to environmental influences; that is, some children may be more susceptible to their environment and therefore gain larger benefits from certain interventions, while others may be less genetically susceptible to their environment and gain less benefit from these interventions. Failing to take differential susceptibility into account may result in masking the effectiveness of interventions for each individual group, preventing the examination of specific intervention effects and inhibiting progress with respect to individualized treatment. Finally, the allocation of intervention is often based purely on environmental criteria, which may mask the urgency of intervention for some children who may possess biological and environmental risk. Through learning more about gene-environment interplay, eventually clinicians may be able to assess risk based on biological and environmental factors and target those with the most urgent needs. While the current study did not specifically test intervention effects, findings warrant the use of biological and environmental perspectives in designing, targeting, and evaluating interventions.

Finally, ample research has shown that genes and the environment both influence child development; the *process* by which they concurrently affect child development has been the subject of much less research, however. Research on the genetic influences of social behavior in itself has been slow to develop, likely due to a host of factors, including findings indicating that most behavior is genetically complex involving multiple genes and processes, many of which remain unexamined. Because of these and

other reasons, many behavior geneticists have focused their efforts on identifying statistically significant links between genes and behaviors or disorders, and in doing such, have left process out of the discussion. That is, the focus has been "do genes affect behavior?" rather than "how do genes affect behavior?". The same has been true of environmentally-based research. A plethora of studies have analyzed environmental risk and protective factors; few however, have taken biological influences and their effects on process into account. Although increasing numbers of researchers are beginning to explore the complex processes involved in gene-environment interplay, a large segment of behavioral genetic research continues to analyze purely genetic heritability estimates with environmental studies mirroring this approach in their respective field. The studies presented here join a growing minority in the field by moving in the direction of explaining *how* genes and the environment shape development over time, demonstrated through an analysis of rGEs and GxEs in social behavior.

CHAPTER 2

GENE-ENVIRONMENT CORRELATIONS: PARENT DIFFERENTIAL TREATMENT AND CHILD SOCIAL FUNCTIONING

Several decades of research have concluded that social functioning is a critical predictor of wellbeing across various developmental domains (Ladd, 2005; Ladd, Herald-Brown, & Andrews, 2009; Parker & Asher, 1987). Most scientists agree that both genetic and environmental influences play defining roles in social behavior; the processes by which they concurrently affect child development are the subject of little research, however. Gene-environment correlations (rGEs), defined as a process through which parental or child genes affect environmental exposure and subsequent adjustment, are one such mechanism in which genes and the environment function together to shape social behavior. More clearly identifying the processes through which rGEs exert influence on social behavior can inform the field's understanding of social development, the result of which will benefit individuals with social impairments through informing and strengthening social interventions.

Using the multiplier effect as a theoretical framework, the current investigation examined two distinct processes by which socially-implicated measured genes affect social behavior and evoke environmental exposure. The first, often referred to as the reactive path (Reiss & Leve, 2007), tested how the Arginine Vasopressin Receptor 1a (AVPR1a) gene and the D2 Dopamine Receptor (DRD2) gene, independently, combined as a composite, and multiplied as a product, directly affect child prosocial behavior, which consequently elicits parent differential treatment (PDT). The second path, often

referred to as the socially-mediated path (Reiss & Leve, 2007), has scarcely been tested in the literature and explains how the aforementioned genes, independently and combined, predict PDT, which subsequently affects later child social functioning (see Figure 2). Combined, these paths have the potential to shed new light on the roles that specific genes and aspects of the social environment play on child social behavior.

Despite evidence that suggests that genes and the environment, together, have strong effects on social behavior, very few studies have analyzed the ways in which measured genes and specific environmental exposures affect development, through their effects on each other, longitudinally. In particular, research has not focused enough on the ways specific genotypes relate to environmental factors, such as home environments or parent-child relations. Moreover, most studies that have analyzed gene-environment correlations in social contexts have studied negative behaviors, such as aggression or negative affect; as a result, there is limited information about positive behaviors, such as prosocial behavior. While negatively-focused research can provide information on factors that are detrimental to development, without complementary positive-focused research, it is difficult to design interventions that can correct these negative influences. Previous work has not explicitly identified the implications and benefits that an understanding of rGEs can have on social interventions. By more accurately understanding the processes through which parenting behaviors can mediate the relation between child genes and outcomes, parents and clinicians can intervene at critical points to change social-behavioral trajectories.

Theoretical Framework

The theoretical perspective that best explains the role of rGEs over time in social development is the multiplier effect (Ceci et al., 2003; Dickens & Flynn, 2001), a framework that maintains that human behavior, and in particular developmental trajectories and outcomes, are the products of a self-reinforcing cycles of interplay between biological and environmental factors. The multiplier effect posits that infants are born with a set of genetically influenced abilities, such as the ability and motivation to attend to and process relevant environmental stimuli, including social stimuli. These initial innate abilities are the foundational skills that infants utilize to interact with their environment. From very early in life, these innate characteristics "kick-start" a series of rGEs where each initial competence or skill is matched with a corresponding environment, through self-selection or through responses elicited from others. Once individuals are in a genetically correlated environment, the environment has causal properties of its own, often- but not always- reinforcing the genetically influenced trait or behavior that elicited the original environmental response (Caspi et al., 2005; Moffitt, 1993). The increasingly complex series of rGEs that subsequently ensue, influence childhood outcomes and eventual adult competencies.

In the context of social behavior, certain genetic variants contribute to early behaviors such as social orienting, emotional reactivity, and frequency of social initiations. These early behaviors may affect the responses elicited from important communication partners, especially parents. Over time, and particularly throughout the sensitive neural development period, the frequency and quality of social interactions,

influenced by individual differences in motivation, competencies and environmental responses, may contribute to effectiveness or impairments in socializing and will likely affect future social behavior and adjustment. This example demonstrates how initial conditions can be matched by environmental exposure and how environmental exposure can further reinforce the initial behavior to perpetually affect development. Given this pattern, children with initial social impairments who progress through social and emotional development without intervention, may be left further and further behind their peers in what can be labeled a "snowball effect" (Ceci et al., 2003). To expand on this idea, most children are born with a set of initial social abilities. They progress in their development by experiencing learning opportunities that correspond, in part, to their initial competencies. These environmental learning opportunities further advance their social abilities. Children who face developmental delays in their social functioning may have a smaller or less effective set of initial social abilities, which, absent intervention, may subsequently be matched with fewer natural environmental learning opportunities. The cumulative effects of fewer initial social abilities and less corresponding environmental stimulation may inhibit progress in social development, affecting personal relationships, and overall adjustment. Theoretically, this pattern will cause the gap between those with and without social difficulties to grow larger over time, given developmental progression. The multiplier effect and rGEs may also partially explain previously established evidence of behavioral rank stability over time, specifically in social competence (Vaughan-Sallquist et al., 2009), such that individuals with genetically influenced social impairments early in life will likely be matched with corresponding

environments and remain socially delayed, compared to same-aged peers, later in life, assuming no intervention. In these ways, over time, rGEs can have multiplicative effects on human development, particularly on social trajectories.

Previous evidence has been established to support this continuous back and forth between genetic and environmental influence throughout development. For example, Zadeh and colleagues (2010) studied the bidirectional influences of child externalizing behavior and mother negativity and found evidence of a feedback loop whereby children's externalizing behavior influenced parental negativity, which further predicted child externalizing behavior later in development. Child externalizing behavior has previously been found to be moderately to highly heritable (Heath & Hen, 1995; Rhee & Waldman, 2004). This transactional model demonstrates that genetically influenced child behaviors can result in corresponding environmental exposure, which is correlated with the initial eliciting behavior; this environmental exposure, then exerts added influence over the behavior of interest, later in development, creating a multiplier effect. We use this framework and extend previous studies by taking into account child genetic variation in the context of parent-child relationships. At the simplest level, in the case of PDT, we hypothesized that children with certain variants of DRD2 and AVPR1a would display like behaviors and be exposed to corresponding parenting environments, which will subsequently influence later social behavior.

Gene-Environment Correlations and Social Behavior

Gene-environment correlations (rGEs) are one type of gene-environment interplay that suggests genes are predictive of the type of environment individuals experience, as

mediated by self or parental phenotypes, through personality characteristics or behavioral repertoires. Previous work has conceptualized three types of causal mechanisms through which rGEs operate: passive, evocative and active rGEs (Plomin, DeFries, & Loehlin, 1977); the current study focuses on evocative rGEs. Evocative rGEs are defined as the relation between genes and genetically influenced behaviors or personality characteristics and the responses they evoke from others (Plomin et al., 1977). They speak to the interactive role children play in relationships and highlight that children are not passive beings, but instead are active in forming relationships and evoking responses from others (see Ambert, 1997). This type of rGE is especially important to children's social development, given that impaired social behavior can greatly affect the reactions elicited from important figures in children's lives and have deleterious effects on forming secure attachments and meaningful relationships.

Many environmentally-based investigations have examined the role that children and adolescents play in eliciting behaviors from social partners, though most have not been studied using genetically sensitive designs. For example, studies have shown that infants with difficult temperaments, who demonstrate irritability and negative affect, elicit less responsivity from parents (Bates, Maslin & Frankel, 1985; van der Boom & Hoeksma, 1994). Conversely, infants who display more positive affect and higher attentional focus, elicit more responsivity from parents (Kyrios & Prior, 1990). Other studies have analyzed activity level and found that high activity children tend to evoke more hostility and physical intrusion from parents (Buss, 1981). Research on children with autism spectrum disorder (ASD) and other developmental delays has found that

parent involvement in interactions is dependent on child skills; specifically, the less interactive skills the child possesses, the more involved the parent becomes (Bruner & Sherwood, 1983; Meek, Robinson, & Jahromi, 2012), indicating that child skills evoke differential parenting responses.

In addition to environmentally-based studies, researchers have examined rGEs using adoption and twin designs. Much of this work has focused on the construct of child aggression. Three genetically informed adoption studies on neurotypical individuals, ranging from middle childhood through adolescence, examined the evocative influences of child aggression on parenting (Ge, Conger, Cadoret, Neiderhiser & Yates, 1996; O'Connor, Deater-Deckard, Fulker, Rutter & Plomin, 1998; Riggins-Caspers, Cadoret, Knutson, & Langbehn, 2003). Each study measured child genetic risk for aggression using a measure of biological parents' psychopathology; the design's logic maintains that biological children of parents with psychopathology are at higher genetic risk for demonstrating antisocial or aggressive behavior, and as a result are likely to elicit more negativity from adoptive parents than adopted children without psychopathological genetic risk. All three studies found that children's aggressive behavior mediated the relation between biological parents' history of psychopathology and adoptive parents' discipline and control, indicating evocative effects. Using a twin design, Pike and colleagues (1996) similarly found that children and adolescents (ages 10 to 18) who demonstrated more negativity, irritability and aggression also elicited more negative parenting. Narusyte and colleagues (2007) examined the mediating role of parental criticism in the relation between early adolescent aggression and later adolescent

delinquency in typically developing twin pairs. They found evidence of evocative rGE suggesting that heritable early aggressive behavior evoked parental criticism and that the resulting criticism in combination with early aggressive tendencies influenced later delinquency. Knafo and Plomin, (2006) studied rGEs in the context of prosociality and found that at ages three, four, and seven, deficits in prosocial behavior were related to negative discipline and withdrawal of affection from parents; child genetic influences were found to account for a large part of these associations, indicating an evocative rGE. Prosocial behavior, as well as other positive and desirable social behaviors, should hold a larger presence in future psychopathological research in order to inform positive-oriented approaches to intervention. Tremblay and Dionne (2013) ventured outside of parent-child relations and examined rGEs in the school context. Disruptive behavior was associated with- and predictive of- difficulties with peer relations, and genes accounted for most of the association. Combined, these studies suggest that genetically influenced problematic behaviors, such as aggression or low prosociality, may put children at higher risk for eliciting negative responses from parents and peers, which may lead to further worsening of initial behaviors and adjustment difficulties.

Most rGE studies to date have been conducted using twin or adoption designs and have not incorporated molecular data. One of the growing number of molecular rGE studies to date, conducted by Hayden and colleagues (2010), examined DRD2 in the context of parent-child relationships. Researchers found that the Taq1A polymorphism of the DRD2 gene was related to supportive parenting, as partially mediated by child negative emotionality. In a follow-up study, investigators found that carriers of certain

variants of the dopamine transporter gene (DAT1) experienced more hostile parenting and less guidance, as partially mediated by negative emotionality (Hanna et al., 2012). More recently, an association between the 9-repeat variant of the DAT1 gene and negative parenting, as mediated by negative child affectivity, was identified (Hayden et al., 2013). Two additional molecular genetic studies examined rGEs in parent-child relations and found that certain variants of the DRD4 and DRD2 genes were related to less warm and responsive parenting (Mills-Koonce et al., 2007; Propper, Willoughby, Halpern, Carbone, & Cox, 2007). The serotonin transporter has also been associated with positive parenting, as mediated by self-control in preschool-aged boys (Pener-Tessler, Avinun, Uzefovsky, Edelman, Ebstein, & Knafo, 2013). In perhaps the most comprehensive molecular rGE study to date, Propper and colleagues (2012) found that certain variants of DRD4 predicted girls' academic outcomes and withdrawn behavior, as mediated by sensitive parenting; for boys, variants of the DRD2 gene predicted emotion regulation (which predicted teacher-reported academic behavior), as mediated by sensitive parenting.

Another molecular rGE study, conducted by Dick and colleagues (2006), studied the correlation between variants of the GABRA2 gene, alcohol dependence, and marital status. The authors found that alcohol dependence partially mediated the relation between a high risk GABRA2 variant and marital status. Specifically, individuals with the risk variant were less likely to be married than those without it, as mediated by alcohol dependence. The mediation was only partial, indicating that the GABA2 variant's relation to marital status was still significant, albeit weaker, after alcohol dependence was

put into the equation. It is possible that alcohol usage evoked less emotionally meaningful responses from potential romantic partners, although it is difficult to decipher if the correlation results were evocative or active in nature. Interestingly, recent investigations have found irregularities in GABA receptor binding sites in individuals with ASD, (Fatemi, Reutiman, Folsom, & Thuras, 2009; Ma et al., 2005; Samaco et al., 2005) a disorder characterized in large part, by social deficits. It is possible that genetic variants of the GABA receptor are associated with a larger aspect of social engagement, manifested in Dick et al., (2006) as marital status, but potentially expressed as other forms of social difficulties in different contexts and populations.

Burt and colleagues employed a molecular rGE approach in their examination of the serotonin receptor 2A gene (5HT2A) and its relation to peer relations, as mediated by rule-breaking behavior (Burt, 2008). Adolescent boys who were homozygous for the A allele (1438A/G) engaged in more rule-breaking behavior and were better liked by same-aged, unfamiliar peers during experimental group activities. Like GABA receptor binding sites, the serotonin transporter and various receptor genes have also previously been implicated in ASD (Cook, Bennett, & Leventhal, 1997; Devlin et al., 2005; Veenstra-VeenderWeele et al., 2002) indicating that this system may play an important role in social behavior and relationships.

A recent study by Fowler and colleagues (2011) also found evidence of rGE using a molecular design. The researchers examined childhood friendships as predicted by the DRD2 genotype. Findings revealed significant homophily between children depending on the Taq1A polymorphism of DRD2; that is, children tended to be friends with their peers

who shared the same allelic variant. While this may appear to be purely an active mechanism, it is possible that responses elicited from peers with like allelic variants were more favorable than responses evoked from peers with different variants, implicating evocative mechanisms that reinforce or encourage peer selection.

Perhaps the most important strength of the reviewed molecular rGE studies is their incorporation of both biological and environmental variables in their contribution to understanding social behavior. Studies such as these go beyond showing simple correlations between genes and disorders or behaviors and examine potential behavioral mechanisms through which genes influence environmental exposure. This study contributes to the field by expanding on the few molecular rGE studies to date and longitudinally examining child prosocial behavior, as influenced by socially-implicated child genes, AVPR1a and DRD2, and PDT.

Socially-Implicated Genes: AVPR1a and DRD2

The genes chosen for this analysis were selected under the assumption that neural functioning mediates the relation between genetic influence and behavior. Although structural and functional neural factors were not analyzed in the current investigation, taking biological causal pathways into account is a hypothesis-driven approach that provides biological and theoretical rationale for analyzing a proposed set of genes, particularly given the inconsistent and often incoherent genetic findings identified by the literature thus far. The AVPR1a gene and the DRD2 gene were chosen for the current analysis because of their established connections to the ventral striatum neural region, one of the most heavily socially implicated regions in the brain. Additionally, these genes

have previously been directly implicated in social behavior, in animal and human models. Of note, researchers have found that this genetic combination may influence social behavior in a co-dependent manner (Insel, 2004; Lim et al., 2004).

AVPR1a. Arginine vasopressin is a neuropeptide produced in the hypothalamus, stria terminalis, and the amygdala (DeVries & Buijs, 1983). AVPR1a, arginine vasopressin receptor 1a, is a vasopressin receptor widely distributed throughout regions of what is referred to as the "social brain", including the ventral striatum, amygdala, parts of the prefrontal cortex and the anterior cingulate cortex (Skuse & Gallagher, 2009). The AVPR1a gene has been the subject of substantial research in both animal and human models, and converging evidence widely implicates it in social behavior (Caldwell, Lee, Macbeth & Young, 2008). Animal studies have discovered that monogamous, social animals have a higher concentration of AVPR1a in the ventral striatum, relative to less social, non-monogamous animals (Hammock & Young, 2005; Insel & Young, 2001). Animal studies have also provided evidence suggesting that variation in the length of specific microsatellites (i.e. RS1 and RS3) on AVPR1a may contribute to social behavior, such that monogamous, highly social species show more extended microsatellites than non-social species (Hammock & Young, 2006).

Promising findings in animal models have sparked interest in analyzing the role of AVPR1a in humans (Donaldson & Young, 2009), particularly in those who experience social difficulties, such as individuals with ASD. To date, five studies have found a link between AVPR1a and ASD, each with varying results in terms of significantly identified loci and associations (Kim et al., 2002; Tansey et al., 2011; Wassink et al., 2004; Yang et

al., 2010; Yirmiya et al., 2006). The most recent of these was a study by Tansey and colleagues (2011), who found that individuals with ASD were more likely to have a short variant of RS1, and that this allele was related to less promoter activity. This may indicate reduced transcription of AVPR1a, resulting in lower density AVPR1a in multiple regions of the brain, including the ventral striatum and the amygdala. Previous investigations on healthy adults have shown that the short version allele of RS1 on AVPR1a is related to increased amygdala activation (Meyer- Lindenberg et al., 2009), which is in turn related to increased social anxiety and potential social withdrawal (Stein, Goldin, Sareen, Zorilla, & Brown, 2002). Of note however, the amygdala is complex, connects with numerous other neural regions, and has been associated with various functions. Interestingly, the same study found that the long version of RS3, another AVPR1a microsatellite, was associated with higher amygdala activation, indicating that length functionality may differ depending on microsatellite, even within the same gene.

Providing further evidence of the functional importance of allele length, Knafo and colleagues (2008) found that in healthy adults, short variants of the RS3 microsatellite (i.e. 325 bp or less) were related to less hippocampal activation, which was then linked to less prosocial behavior. A similar study in preschool-aged children found that children with at least one copy of the RS3-327bp allele were the least likely to show altruistic behavior, when compared to children with all other alleles (Avinun, Israel, Shalev, Gritsenko & Bornstein, 2011). Walum and colleagues (2008) found that individuals with the AVPR1a RS3 334bp allele had poorer quality marriages, higher marital problems, and were less likely to be married. The RS3 327bp and 334bp alleles

would be coded as "long" by previous investigations that have dichotomized the variable by length, indicating that more research is needed to identify a more precise and functionally meaningful cut-off point for defining long versus short alleles and for studying microsatellites of AVPR1a in general. Given the association, albeit in uncertain directions, between microsatellite allele lengths and social behavior, AVPR1a is a promising gene to examine, particularly as it relates to social behavior and consequential environmental exposure. Combined, these potential biological pathways leading from genes, to neural functioning, and ultimately to social behavior provide an auspicious justification for analyzing variations of this gene in the context of parent-child relationships and child social functioning.

DRD2. Dopamine is a neurotransmitter that is produced and projected to numerous areas in the brain including the amygdala, hippocampus, and the ventral striatum, among others. Decades of neurological research has found that the dopaminergic system is highly relevant in social behavior through establishing reward value and motivation (Ikemoto, 2007; Schultz, 2007) and influencing emotional responses (Greba, Gifkin, & Kokkinidis, 2001; Gurraci & Kapp, 1999). Dopaminergic activity is mediated by five dopamine receptors, D1 through D5, which are coded by genes DRD1 through DRD5, respectively. DRD2 is the gene that encodes for the D2 subtype of the dopamine receptor family. This gene and its respective receptors may play an important role in social development. Animal studies, both classic and recent, have demonstrated the critical role the dopamine system plays on pairing social behavior with reward value (see Wise, 2004). Specifically, high density D2 receptors in socially

implicated neural regions have been shown to increase reward value for social stimuli and facilitate pair bonding, while low density D2 receptors seem to indirectly block pair bonding, via excess cyclic Amp synthesis (see Skuse & Gallagher, 2009; Aragona and Wang, 2007). Animal studies have also found that mice with impaired dopamine systems are not motivated to push a lever for food, water, or sexual contact (Spyraki, Fibiger & Phillips, 1982, 1983). These studies and others suggest that a dopamine-impaired system results in the loss of motivational value for stimuli that are naturally reinforcing. Social interaction is generally naturally reinforcing for social species such as humans. However, if the dopaminergic system is impaired in particularly social areas of the brain, it is possible that the pairing of reward with social stimuli will be disturbed, which may impact early social motivation, social attention, initiation, and reciprocity; this lack of social behavior may subsequently influence environmental exposure, and future social functioning.

Animal and human models have also found that certain variants of D2 receptors influence facial processing and emotional behavior, including emotional control, and fear and anxiety-related behaviors in social contexts (Blasi et al. 2009; Greba et al., 2001; Gurraci et al., 2000). This is likely partially due to DRD2's influential presence in the amygdala. One study found that administering a D2 receptor agonist was related to increased positive affectivity (Depue, Luciana, Arbisi, Colins & Leon, 1994), potentially indicating that genetic variants that generate a higher density of D2 receptors in social areas of the brain, versus variants that generate a lower density of D2 receptors, may influence early evoking behaviors. Together, through reward value and emotional

responses, and likely through other mechanisms not yet determined, DRD2 may have important implications on the development of early social behaviors and consequential responses from the environment.

Previous studies have identified a functional intronic single nucleotide polymorphism (SNP) relevant to social behavior, the Taq1A polymorphism (rs1800497), located over 10 kilobase-pairs downstream of the coding region of DRD2. Scientists have recently discovered that the Taq1A polymorphism, traditionally associated with DRD2, is located on a neighboring gene, ANKK1 (Neville, Johnstone, & Walton, 2004; Smith, Watson, Gates, Ball & Foxcroft, 2007). The A1+ genotypes (i.e. A1A1 or A1A2), as opposed to the A1- genotype (i.e. A2A2) of Taq1A, are associated with ASD, ADHD, Tourette's syndrome, schizophrenia, alcohol dependency, and a variety of internalizing symptoms (Comings et al., 1991; Glatt, Faraone, & Tsuang, 2003; Lawford, Young, Noble, Kann, & Ritchie, 2006; Saraceno, Munafo, Heron, Craddock & van den Bree, 2009). As reviewed, a number of studies have found evidence of rGE between the Taq1A allele and social settings, within peer- and parent-child contexts (Fowler et al., 2011; Hanna et al., 2012; Hayden et al., 2010; Mills-Koonce et al., 2007; Propper et al., 2007). In addition, a recent study found a higher frequency of T allele homozygotes (A1+) in an all-male ASD group compared to a control group. The same study found that the A1+ genotype was also associated with more severe social and communication deficits, and increased stereotypic behaviors (Hettinger et al., 2012), further implicating this polymorphism in social behavior. The A1+ variant has also been linked to reward deficiency syndrome, a disorder characterized by insensitivity to reward (Comings &

Blum, 2000), attachment disorganization (Lakatos et al., 2000), and social problems (Marino et al., 2004).

These particular allelic variations (A1+) may result in a lower density of D2 receptors in the brain (Noble, Ritchie, Montgomery & Sheridan, 1991; Thompson et al., 1997), which may prompt a decrease in the reward value placed on specific stimuli, including social stimuli. Decreased reward value for social stimuli may reduce opportunities for social engagement through less social initiations, which may negatively impact social development through lack of practice of social skills. Given this evidence, it is likely that DRD2 variants and corresponding reward value may have important effects on social functioning. We expand the literature on DRD2 and human social behavior by examining the relation between variations in the TAQ1a polymorphism, social behavior, and PDT.

As previously stated, in addition to findings that suggest that DRD2 and AVPR1a independently influence social behavior, research has found that these genes may function co-dependently to influence certain aspects of social behavior. Pharmacological animal studies have found that non-monogamous voles injected with AVPR1a showed increased levels of social behavior, but only if D2 receptors were functioning normally; if D2 receptors were blocked, social behavior did not increase (Lim et al., 2004). It has been suggested that vasopressin augments the value of social stimuli by activating regions highly populated with dopamine receptors known to influence reward perception, such as the ventral striatum. Insel and colleagues (2004) suggested that in voles, vasopressin may link social information to dopamine reward pathways in the brain in

order to facilitate partner preference formation. During mating, vasopressin would activate the dopaminergic reward circuits and condition high reward with social behavior. It is possible that similar processes occur in humans considering the findings reviewed and the physical proximity of social neurotransmitters and neuropeptides to dopaminergic circuits in the brain. Due to this evidence, in addition to testing the effects of each of these genes independently, the effects a gene-gene interaction were also examined. Finally, due to previous research identifying independent effects of these genes, a composite formed from the sum combination of AVPR1a and DRD2 was also examined.

Parent Differential Treatment

Parent-child relationships are bidirectional and are the product of a number of constructs, including child social behavior and parenting behavior. The effects of parent-child relationships on child outcomes have been well documented by previous research (Park & Ladd, 1992). These important relationships have been shown to effect children's later self-esteem, peer competence, peer interactions and friendships in childhood and into adulthood (Bowlby, 1973; Cassidy, Kirsh, Scolton & Parke, 1988; Strouf & Fleeson, 1986; Strouf, 1983). The attachment between parent and child, in addition to being established on a history of availability and responsiveness, is made up of the quality rather than the quantity of these reciprocal interactions over time (Elicker & Englund, 1992). Studies have shown, however, that parents do not always treat their children equally or exhibit the same parenting behaviors across children; in fact, researchers have identified that between 33 to 67 percent of parents exert differential treatment on their

children, in constructs such as affection, attention, closeness, control, and overall preference (Shebloski, Conger, & Widaman, 2005; Volling & Elins, 1998). Building on these findings, Boll and colleagues (2003) found that differential treatment can have detrimental effects on the critical parent-child relationship. Given the pervasiveness of parent differential treatment and the heavy influence of parent-child relationships on children's adjustment, it is important to understand the processes involved in differential treatment; particularly, if and how child genetic and behavioral influences affect certain types of PDT and if this treatment subsequently goes on to affect future child adjustment.

The study of PDT was most influentially initiated by Plomin and colleagues' (1987) article that tasked researchers with understanding why twins and siblings who are raised in the same family are strikingly different. Since then, researchers have identified several variables that predict differential treatment, among those are child, context, and parent-specific variables. Researchers have also identified a number of troublesome child outcomes associated with differential treatment. Although findings have been inconsistent over the years, this body of research lends evidence to the idea that PDT is common, influenced by a variety of factors, and may have adverse effects on child development.

With respect to factors that contribute to PDT, certain child-specific characteristics or behaviors have been implicated. For example, child age, with younger children receiving more preferential treatment (Dunn, Stocker & Plomin, 1990; Feinberg et al., 2000; Jenkins, Rashbash, & O'Connor, 2003; Volling & Ellis, 1998) child

temperament, with children with more difficult temperaments receiving less affection and more discipline, (Brody et al., 1992; Jenkins et al., 2004) and child behavior, with more aggressive children receiving more negative parenting and more demonstrably positive children receiving more positive parenting (Anderson, Lytton, & Romney, 1986), have each been found to influence differential treatment. Importantly, although each of these child characteristics have been shown to predict differential treatment, scholars have agreed that child behavior and differential treatment is bidirectional, dynamic, and developmentally-dependent (Burt, Mcgue, Kruger, & Iacono, 2005; Meunier, Wade & Jenkins, 2012; Neiderhiser, Reiss, Hetherington, & Plomin, 1999).

While evidence has found that child characteristics or behaviors may contribute to PDT, studies have also found that differential treatment, in turn, also influences future child outcomes. A number of adverse child outcomes, including poor child health (Browne & Jenkins, 2012), poor self-worth and self-esteem, increased internalizing and externalizing behaviors (Dunn, Stocker, & Plomin, 1990; Feinberg et al., 2000; McHale et al., 1995; Singer & Weinstein, 2000), lower quality sibling relationships (Boll, Ferring & Fillip, 2003; Brody, Stoneman, & Burke, 1987; Volling & Belsky, 1992), and hostile parent-child relationships (McHale & Gamble, 1989) have been associated with differential treatment. Longitudinal analyses have found that differential treatment predicts increases in externalizing behavior (Conger & Conger, 1994; Mcguire, Dunn & Plomin, 1995). Although most studies have found adverse outcomes in children who receive less preferential treatment, some studies have found that differential treatment can adversely affect all children in a family unit, including those who receive more

preferential treatment (Boer, Godehard & Theffers, 1992; Boyle & Jenkins, 2004; Suitor, Sechrist, Plikuhn, Pillemer, & Pardo, 2008). Evidence for these findings remains conflicted, however, with some studies finding that differential treatment only adversely affects those who are disfavored (Mcgyuire, Dunn & Plomin, 1995), other studies finding that it favors those who receive preferential treatment (Reiss, Hetherington, Plomin, & Howe, 1995), and other studies finding that it adversely affects all siblings (Boyle & Jenkins, 2004; Suitor et al., 2008).

As is common with multi-reporter questionnaire data, researchers have found low agreement between parent and child reports of PDT (Daniels, Dunn, Furstenberg, & Plomin, 1985; Kowal, Krull, & Kramer, 2004), with children often reporting higher levels of PDT and parent reports often showing stronger genetic influences (Carbonneau et al, 2002). Given these patterns, it is important to examine PDT, and particularly PDT in the context of rGEs, through both parent and child reports. To my knowledge, no studies have analyzed the effects of child genes on PDT and the subsequent effects on child prosocial behavior, using a molecular design in a longitudinal, multi-reporter, cross-lagged model. As reviewed, studies have found that child characteristics elicit differential treatment in select behaviors, many of which, previous work has shown, are genetically influenced. This connection warrants more genetically-informed research on this topic. Given the important influences child genes may have on early social behavior, the interactive and bidirectional links between child behavior and parent behavior, and the effects of parenting on subsequent child social development and eventual adjustment, it is

imperative to understand the processes that link these influential developmental variables together.

The Current Study

The current study analyzed evocative rGEs and their effects on child prosocial behavior, in the context of parent - child relationships. The aims of the study are: 1) to test the reactive hypothesis cross-sectionally and longitudinally, by identifying the relation between the reviewed genes and PDT at time one (T1) and separately at time two (T2), as mediated by child prosocial behavior; 2) to test the socially-mediated hypothesis cross-sectionally and longitudinally by identifying the relations between the reviewed genes and prosocial behavior at T1 and separately at T2, as mediated by PDT; 3) to longitudinally analyze the outlined pathways simultaneously using a cross-lagged model. See Figures 3, 4, and 5 for all outlined analyses. These analyses uncover potential processes through which genes affect child social outcomes, taking genetic and environmental variation into account. The reactive path posits that child genes influence child behavior, which subsequently influences PDT; the socially-mediated path suggests that child genes elicit PDT which subsequently affects future child social functioning. By testing both reactive and socially-mediated evocative rGE pathways, the proposed analyses provide evidence for the most plausible path, and illustrate how these paths function together, given the social variables considered.

Methods

Participants

Participants for this study were recruited under the Wisconsin Twin Project (WTP; Lemery-Chalfant, Goldsmith, Schmidt, Arneson, & Van Hulle, 2006), a longitudinal investigation examining healthy development and psychopathology in a representative sample of twins from Wisconsin. Only participants with data on at least one of the genes of interest were included in the current investigation. This resulted in 950 individual children, or 475 twin pairs (*M=95* months, *SD*=10.72), each of whom were followed from birth through adolescence. There were slightly more females (51.8%) than males (48.2%). With respect to race, 92.4% of the participants were White. The remaining 7.6% of participants were African American, Native American, Asian, biracial or of other decent. Regarding household income, 9.6% of families in the sample made under $30,000 a year; 35.9% reported making between $30,000 and $60,000; 36.5% made between $60,000 and $100,000 a year; and 10.3% reported earnings over $100,000 a year. Approximately 7.7% of families chose not to respond. In terms of parent education attainment, 20.9% of mothers and 33.1% of fathers reported high school or below as their highest level of education; 39.7% of mothers and 32.1% of fathers reported having some college, technical or trade training; 27.4% of mothers and 20.3% of fathers reported a college degree as their highest level of education; 10.9% of mothers and 10.5% of fathers reported graduate training or a graduate degree as their highest level of education; and 1.1% of mothers and 4.1% of fathers chose not to respond.

Procedures

Study participants were identified through state birth records after 1989 and were invited to participate by mail, as approved by the Institutional Review Board. After families agreed to participate, they submitted written informed consent and received compensation for their time. Families were first contacted for information when twins were two years of age. At this time, researchers collected information regarding child social, emotional and communicative levels, via questionnaires. When twins were seven years of age, families were contacted to arrange a telephone interview in order to assess a number of constructs, including psychopathology using the Health and Behavior Questionnaire (HBQ; Armstrong & Goldstein, 2003). Families then participated in a five-hour home visit where parent-child interactions were observed and videotaped, parent and child information was gathered via parent and child report or interview, and cells were collected via buccal swabs for DNA analyses. Subsequent questionnaires and interviews were conducted via mail or telephone.

Measures

Genes. For AVPR1a, one variable number tandem repeat (VNTR), the RS3 microsatellite, was typed and analyzed. A total of 16 alleles were identified with varying frequencies. For DRD2, four SNPs were typed (rs1800497, rs6277, rs1799978, and rs1076560); the current study analyzed SNP rs1800497. DNA was obtained via buccal swabs. For analysis, each reaction mixture contained 0.5 mM primer. A ReddyMix master mix was used (Abgene, Surrey, UK) at a magnesium concentration of 1.5–2.5 mM $MgCl_2$. Polymerase chain reaction conditions (PRC) were the following: pre-heating at

95 °C for five minutes, 30 cycles at 95 °C for 30 seconds, 55 °C for 30 seconds, 72 °C for 40 seconds, and a final extension step of 72 °C for ten minutes. The data were analyzed using an ABI 310 DNA Analyzer.

Genetic Coding. AVPR1a has been coded several different ways in the literature. In order to fully explore the effects of the gene, we coded the RS3 microsatellite of AVPR1a in three different ways. First, carriers of what previous studies (Knafo et al., 2008) have labeled the "short" variant (325 or fewer base pairs in length) were given a score of -.5, while those who carried a long allele (i.e. 326 or more base pairs) received a score of .5. Next, carriers of the 327bp, previously identified as a potential "risk variant" were ascribed a .5, while all non-carriers were coded as -.5 (Walum et al., 2008; Avinun et al., 2011). AVPR1a's RS3 microsatellite's length was also coded as a continuous variable by summing the length of each allele for each individual. Initial correlation analyses indicated that the continuous coding of AVPR1a, rather than either dichotomous coding method, was more highly related to the behavior and environmental variables of interest, therefore the continuous variable was used in subsequent statistical analyses. In the analysis of DRD2, rs1800497 (i.e. TAQ1a polymorphism), a SNP previously evidenced to affect social behavior, was coded. TT and TC genotypes (i.e. A1+genotypes) were coded as .5, while CC genotypes (i.e. A1- genotypes) were coded as -.5.

Next, a cumulative genetic composite was formed by summing AVPR1a and DRD2. The most common method for coding AVPR1a, long versus short, and DRD2's coding as explained above were used. The composite was formed by creating groups of

each genetic combination of AVPR1a RS3 microsatellite length and DRD2, yielding four combinations: 1) RS3 short/A1+; 2) RS3 short/A1-; 3) RS3 long/A1+; and 4) RS3 long/A1-. Those with the short variant of AVPR1a RS3 and A1+ of the Taq1a polymorphism were ascribed a 1; those with *either* a short variant of AVPR1a or the A1+ of the Taq1a polymorphism were ascribed a 0; and those with neither risk factor received a score of -1.

The Sibling Relationship Questionnaire. The SRQ (SRQ; Furman & Buhrmester, 1985) is a parent report questionnaire that assesses 15 scales of sibling relationships, including parent partiality. The parent partiality subscale of the SRQ was used as a measure of PDT at T1. The scale assesses questions such as "whose side the parent usually takes", "what sibling is usually treated better", and "who receives more parent attention". Parent report was collected via questionnaire. Mothers assessed their own behavior as well as fathers' behavior on a five point scale, with a score of one indicating the twin is almost always treated better, a score of five indicating the co-twin is almost always treated better, and a score of three indicating no differential treatment or preference. The scores for twin 1 in each family were reverse coded and the scores for twin 2 were left as they were answered so that higher scores consistently indicated more favorable partiality and lower scores means less favorable partiality for the twin in question.

Twins Inventory of Relationships and Experiences (TIRE). The TIRE (TIRE; Carbonneau et al., 2001) is a 48-item questionnaire that captures child-specific information on parent-child and peer-child relationships. This questionnaire was used as a

measure PDT at T2, specifically, maternal and paternal partiality, as reported by mothers, fathers, and children. Mother and father preference questions assessed how much parents have interest in, are proud of, and praise one child over another. Twins and parents rated each question using a five-point scale, with scores of one indicating the twin receives more of the behavior and scores of five indicating the co-twin receives more of the behavior. All scores were reverse coded for ease of interpretation such that higher scores indicated more favorable partiality.

MacArthur Health and Behavior Questionnaire – Parent Version (HBQ). Prosocial behavior scores were derived from the MacArthur Health and Behavior Questionnaire- Parent Version (HBQ, Armstrong et al., 2003). This tool is a parent report measure designed to capture mental health, physical health, social functioning, and school functioning in children and adolescents. The measure was initially developed and validated to capture children's development from ages four through eight (Essex et al., 2002; Lemery-Chalfant et al., 2007), but was recently modified to measure the same constructs in adolescents (Shirtcliff & Essex, 2009), providing a useful mode of continuous measurement from childhood through adolescence. Previous reliability and validity studies have indicated that in the domain of social functioning, the tool has high test-retest stability (r=.68-.83), moderate inter-rater agreement (r=.26-.50), and large effect sizes in discriminating between clinically-referred children (demonstrating both internalizing and externalizing behaviors), and community control groups (Cohen's *d*=.8) (Essex et al., 2002).

The current study used the prosocial behavior subscale of the tool in middle childhood and adolescence. The prosocial scale was originally presented in Weir and Duveen (1981) as an independent measure, where it demonstrated strong alpha levels (.85) in mother and father reports. Parents and twins reported on a three-point scale including options for "never/not true for me/my child", "sometimes true for me/my child", and "often/very true for me/my child". Preliminary analyses indicated that mother-reported prosocial behavior was most robustly related to the other variables of interest therefore mother-reported prosocial behavior was used for all analyses.

Results

All statistical analyses were conducted in Mplus (Muthen & Muthen, 2007). Missing data was accounted for by using Full Information Maximum Likelihood (FIML), where all available data from all subjects are used. To take into account the nested nature of the data, the CLUSTER command was used, which corrects for the biases in estimation of standard errors. All variables had skewness estimates under two and kurtosis estimates under seven. In addition, as suggested by Tabachnick and Fidell (2001), we visually inspected data, given the large sample size, and found that all variables were relatively normally distributed.

Prior to primary analyses, descriptive statistics were calculated (see Table 1) and bivariate correlations were conducted to examine zero-order relations between variables (see Table 2). Results from these zero-order correlations were used to select the most robust variables for mediation analyses. Next, a series of mediation analyses (see Figure 3 and 4) were conducted to test several different processes that connect child genes, PDT,

and child prosocial behavior. Variables identified as promising through the series of mediation analyses, were then entered in a more stringent, longitudinal, cross-lagged model (see Figure 5). Due to the exploratory nature of these analyses, the process of conducting separate, single-mediator regression analyses *prior* to more complex and stringent models was employed, in order to reveal the most robust variables and processes that most likely demonstrate statistical and meaningful significance in a cross-lagged model.

Evocative-Reactive rGE

Genes and Child Prosocial Behavior. The first set of analyses tested the relation between various genes and child prosocial behavior; that is, "path a" in a typical single mediator regression analysis. Age, sex, and SES were entered in each analysis as covariates. Results indicated that AVPR1a was marginally related to child prosocial behavior at T1 (*Standardized β =.07, se=.04, p=.05*), but was not significantly related to child prosocial behavior at T2 (*Standardized β =-.05, se=.04, p=.24*) (see Figure 6a). Next, the relation between DRD2 and child prosocial behavior was tested; results indicated that DRD2 was not significantly related to child prosocial behavior at T1 or T2 (*Standardized β =-.03, se=.04, p=.50; Standardized β =-.01, se=.04, p=.82*). The relation between the cumulative genetic composite (CGC) and child prosocial behavior with parents at T1 and T2 also revealed non-significant results (*Standardized β =.01, se=.04, p=.83; Standardized β =.01, se=.05, p=.79*). Finally, the gene by gene interaction, comprised of the product between AVPR1a and DRD2, was tested in relation to child prosocial behavior at T1 and T2; results were not statistically significant

(*Standardized β =.01, se=.04, p=.83; Standardized β =-.001, se=.05, p=.99*). See figure 6a for significant gene-behavior correlations.

The marginal relation between AVPR1a and child prosocial behavior at T1 justified further analysis of AVPR1a in subsequent mediation models. Due to non-significant findings and the absence of any promising trends between the DRD2, CGC, and GxG and child prosocial behavior, those genetic combinations were not tested in subsequent evocative-reactive models.

AVPR1a, Child Prosocial Behavior, and Parent Differential Treatment. The next set of analyses tested AVPR1a's role in an evocative-reactive rGE. As previously identified, AVPR1a marginally predicted child prosocial behavior at T1. The relation between child prosocial behavior at T1 and mother-reported preference at T1, with AVPR1a in the equation, was not significant (*Standardized β =-.03, se=.03, p=.25*). Because the second path was not significant, mediation was not tested. The same analysis with father-reported preference at T1 substituted in the equation yielded marginal findings (*Standardized β =-.05, se=.03, p=.06*). Indirect effects between AVPR1a and father-reported preference at T1 were not significant (*Standardized β =-.003, se=.002, p=.17*).

The second set of analyses examined the effects of AVPR1a on parent and child reported parental preference at T2, as mediated by child prosocial behavior at T1. The relation between child prosocial behavior at T1 and maternal preference as reported by twins at T2 was not statistically significant (*Standardized β =.06, se=.04, p=.12*). When mother-reported preference was substituted in the equation, a marginal relation between

child prosocial behavior and mother-reported preference at T2 was identified (*Standardized β =.06, se=.03, p=.07*). A test of indirect effects between AVPR1a and mother-reported preference was not significant (*Standardized β=.004, se=.003, p=.20*). In examining father preference, child prosocial behavior did not significantly predict twin-reported father preference (*Standardized β=-.04, se=.05, p=.34*), therefore mediation was not tested. Similarly, the relation between child prosocial behavior and father-reported preference was not significant (*Standardized β=-.001, se=.04, p=.98*).

Evocative Socially-Mediated rGE

Genes and Parent Differential Treatment. The following set of analyses tested the socially-mediated evocative model. First, the relation between each gene and genetic combination of interest was tested in relation to mother and father preference at T1. Results demonstrated that AVPR1a did not significantly predict mother or father-reported preference, respectively (*Standardized β=-.02, se=.03, p=.40; Standardized β=.02, se=.03, p=.44*). Similarly, DRD2 did not predict mother- or father- reported preference at T1 (*Standardized β=-.03, se=.02, p=.27; Standardized β=-.005, se=.02, p=.84*). The CGC also yielded non-significant results in its relation to mother and father-reported preference at T1 (*Standardized β=-.03, se=.03, p=.28; Standardized β=.004, se=.03, p=.88*). Finally, analyses of the GxG indicated a non-significant relation with mother- and father- reported preference at T1 (*Standardized β=.03, se=.03, p=.27; Standardized β=-.01, se=.02, p=.84*).

Following, the analysis of each gene and genetic combination in relation to parental preference at T2 was tested. Analyses revealed that the links between AVPR1a

and mother-reported, as well as father-reported preference were not significant (*Standardized β=-.02, se=.03, p=.46; Standardized β=.01, se=.04, p=.71*). Twin-reported mother and father preference were also not significantly predicted by AVPR1a (*Standardized β=-.05, se=.04, p=.13; Standardized β=.06, se=.04, p=.11*). The relation between DRD2 and mother- and father-reported preference was similarly non-significant (*Standardized β=-.01, se=.03, p=.62; Standardized β=.05, se=.03, p=.08*). Twin-reported mother preference was not significantly predicted by DRD2 (*Standardized β=.03, se=.04, p=.41*), though twin-reported father preference was, at trend levels (*Standardized β=.07, se=.04, p=.07*). Next, the relation between the CGC and parental preference at T2 was examined. The CGC did not significantly predict mother or father-reported preference at T2 (*Standardized β=-.01, se=.03, p=.73; Standardized β=.04, se=.03, p=.25*).Twin-reported mother preference was also not predicted by the CGC (*Standardized β=.004, se=.04, p=.90*). Twin-reported father preference, however, was predicted by the CGC at marginal levels (*Standardized β=.07, se=.04, p=.06*). Finally, the GxG was tested in relation to parental preference at T2. Analyses of the GxG indicated it did not significantly predict mother-reported preference (*Standardized β=.03, se=.03, p=.43*) but yielded marginal results in predicting father-reported preference (*Standardized β=-.07, se=.03, p=.05*).The GxG was not significantly related to twin-reported mother or father preference (*Standardized β=.04, se=.04, p=.37; Standardized β=-.03, se=.04, p=.54*). Because none of the genes or genetic combinations significantly or marginally predicted parental preference at T1, no subsequent analyses investigating the socially-mediated path at T1 were pursued. Only mediation models including father

preference at T2 were probed further, due to the promising results identified. See Figure 6, items b, c, and d for all significant gene-environment correlations.

Genes, Father Preference, and Child Social Behavior. This set of analyses revealed that though DRD2 was marginally related to twin-reported father preference at T2, father preference was not significantly related to child prosocial behavior at T2, with DRD2 in the equation **(***Standardized β=-.04, se=.05, p=.38*). The next potentially promising path was between the CGC and twin-reported father preference. Analyses indicated that the relation between twin-reported father preference at T2 and child prosocial behavior at T2, with the CGC in the equation was not significant (*Standardized β=-.04, se=.05, p=.36*). Finally, the relation between father-reported preference at T2 and child prosocial behavior at T2, with the GxG in the equation was explored; similar to the other socially-mediated paths tested, the relation between father-reported preference at T2 and child prosocial behavior a T2, with the GxG in the equation was not significant (*Standardized β=.02, se=.04, p=.68*).

Cross-Lagged Model: Genes, Prosocial Behavior, and Parent Differential Treatment

The variables that demonstrated promising trends in the aforementioned analyses were further examined in a more stringent cross-lagged model (Figure 5), where concurrent, autoregressive, and cross-lagged paths linking genes, child prosocial behavior and parent preference were examined simultaneously. The first analysis examined the effect of AVPR1a on mother-reported preference at T2 and child prosocial behavior at T2 as mediated by mother-reported preference at T1 and child prosocial behavior at T1 (see Figure 7). Fit indices demonstrated mediocre model fit, with a RMSEA of .07; a CFI of

.93; and a SRMR of .02. The autoregressive path of child prosocial behavior over time was significant (*Standardized β =.56, se=.03, p<.001*). Mother preference at T1, however, was not significantly predictive of mother preference at T2 (*Standardized β = .07, se=.09, p=.47*). The concurrent correlation between child prosocial behavior and mother-reported preference was not significant within T1 (*Standardized β =-.03, se=.03, p=.40*), but was significant within T2 (*Standardized β =.16, se=.03, p<.001*). In this model, the relation between AVPR1a and child prosocial behavior at T1 was marginal (*Standardized β =.07, se=.04, p=.06*). Evocative cross-lagged analyses showed that the relation between child prosocial behavior at T1 and mother-reported preference at T2 was also marginal (*Standardized β =.07, se=.04, p=.06*). The socially-mediated hypothesis showed less promise. AVPR1a was not significantly predictive of mother-reported preference at T1 (*Standardized β =-.02, se=.03, p=.46*) and mother-reported preference at T1 did not significantly predict child prosocial behavior at T2 (*Standardized β =.001, se=.03, p=.98*).

The next cross-lagged model examined the relation between AVPR1a and father-reported preference and child prosocial behavior at T2, as mediated by father preference and child prosocial behavior at T1 (see Figure 8). Fit indices demonstrated model fit ranging from mediocre to good, with a RMSEA of .04; a CFI of .99; and a SRMR of .01. The autoregressive path of child prosocial behavior at T1 and T2 revealed a significant finding (*Standardized β =.54, se=.03, p<.001*). The relation between father preference at T1 and father preference at T2, however, was not significant (*Standardized β =.10, se=.07, p=.17*). Concurrent associations between child prosocial behavior and father

preference were correlated at marginal levels within T1 (*Standardized β =-.05, se=.03, p=.05*) but not within T2 (*Standardized β =-.01, se=.04, p=.80*). The reactive cross-lagged path, which tested the relation between AVPR1a, child prosocial behavior at T1 and father preference at T2, revealed that the path from AVPR1a to child prosocial behavior was marginal (*Standardized β =.07, se=.04, p=.05*). Child prosocial behavior at T1, though, did not significantly predict father-reported preference at T2 (*Standardized β =.01, se=.04, p=.83*). The socially-mediated path revealed that the relation between AVPR1a and father preference at T1 was not significant (*Standardized β =.02, se=.03, p=.50*), though the cross-lagged path between father preference at T1 and child prosocial behavior at T2 was statistically significant (*Standardized β =.07, se=.03, p=.03*).

Discussion

We analyzed the association between various socially-implicated genes, child prosocial behavior, and parent differential treatment (PDT), using the multiplier effect as a theoretical framework. Overall, findings suggest modest genetic and environmental influences on child behavior in middle childhood and adolescence, consistent with previous research and theory. Two particular rGE hypotheses, the evocative-reactive and the evocative-socially-mediated hypotheses, were the focus of the present study. A test of the evocative reactive path, which posits that genes influence child behavior, which subsequently affects the child's social environment, revealed some empirical support, albeit modest. AVPR1a was marginally positively associated with child prosocial behavior in middle childhood, which went on to predict mother, but not father preference in adolescence. Mother preference at adolescence was also positively correlated with

child prosocial behavior at adolescence, though father preference was not. These findings, though modest, shed preliminary light on one behavioral process that may connect AVPR1a and the social environment. The socially-mediated path, distinct from the reactive path in suggesting that genes influence the social environment, which subsequently influences child behavior, was not empirically supported, namely because of the lack of association between genes and the environment. Specifically, child AVPR1a did not predict parental preference in middle childhood. Similar to the reactive path, the socially-mediated path revealed different patterns for mothers and fathers: while mother preference in middle childhood did not predict adolescent prosocial behavior, father preference did.

Combined, findings provide evidence for genetic and environmental influence on child behavior and justify further cross-disciplinary research into the study of child social behavior. Though preliminary support was found for the evocative-reactive hypothesis and not the socially-mediated hypothesis, given the infancy of the field, future research should continue to examine both hypotheses, and others, in attempting to expand our understanding of rGE. The multiplier effect was not directly tested in this study; however, findings suggest a chain of events stemming from genes, through behavior, to the social environment. Future work can more directly test the framework, using the research presented here as a starting point, by examining the trajectories of children with varying genetic combinations during multiple points in development and in varied contexts over time. The genetic and environmental influences and associations found, discussed in further detail below, add to the growing body of rGE evidence and provide

ideas for further exploration in the context of specific genes, behaviors, and environmental variables.

Genetic Influences and Associations

Promising gene-behavior and gene-environment correlations were identified. Specifically, AVPR1a showed a marginal association with prosociality in middle childhood. DRD2 and the CGC on the other hand, while not directly predictive of child prosociality, were marginally related to father preference in adolescence. Together, these trends indicate that child genes are associated, albeit at modest levels in this case, with child prosociality and father preference.

Gene-Behavior Association. AVPR1a was the only gene of those tested with a promising trend for its relation to child prosocial behavior. Findings indicated a marginal association with prosocial behavior in middle childhood, such that longer AVPR1a RS3 microsatellite variants were related to more prosociality. Previous research has identified an association between AVPR1a length and social behavior in animals and humans, though the direction of reported associations has not been fully consistent and the evidence base is not robust. For example, animal studies indicate that monogamous voles that are more trusting, show preference for familiar partners, and invest more time in pup rearing have extended AVPR1a RS3 microsatellites, compared to non-monogamous voles (Hammock & Young, 2002; 2004; 2005). Studies of humans have found both consistent and dissenting trends. In line with the findings presented here, Knafo and colleagues' (2008) found a positive relation between the length of the RS3 microsatellite of AVPR1a and donating behavior in adults, mediated by the amount of mRNA in the

hippocampus. Conversely, other studies have found that the 327bp allele of the RS3 microsatellite, which would be considered "long" in dichotomous length coding, is associated with less altruistic behavior in preschoolers (Avinun, Israel, Shalev, Gritsenko & Bornstein, 2011) and poorer quality marriages, higher marital problems, and lower likelihood to be married in adults (Walum et al., 2008). Meyer-Lindberg and colleagues (2009) examined the association with respect to the amygdala activation. The long variant of the RS3 microsatellite was related to stronger amygdala activation, which has previously been associated with higher social anxiety and withdrawn behavior (Modahl et al., 2009). The same study found that the long variant of the RS1 microsatellite, another commonly studied microsatellite of AVPR1a, was associated with less amygdala activation, suggesting that microsatellite length may have different, potentially opposite implications among different microsatellites. Of note, amygdala activation is complex in nature, affecting not only fear response and conditioning, but showing lateralized activation in constructs such as emotion recognition and memory, processing of- and attention to- emotional stimuli, and emotional learning (see Phelps, 2006), further complicating its mediation between AVPR1a microsatellite length and prosocial behavior. Finally, Tansey et al. (2011) found that the long versions of both the RS1 and RS3 microsatellites lead to higher promoter activity, which may indicate more AVPR1a in socially-relevant neural regions, and more consequent social behavior.

The findings identified here are consistent with Knafo and colleagues' (2008) observations and are fitting with Tansey's (2011) findings, indicating longer variants of RS3 are in accordance with higher levels of social behavior. Longer microsatellites may

result in more transcription and relative density of certain neuropeptides, such as AVPR1a, in various regions of the brain, including the amygdala and ventral striatum, which may facilitate prosociality at certain points in development. More basic research is needed to clearly delineate the biological pathways implicated in the associations between AVPR1a and social behavior. Though some studies have shed preliminary light on promising neural mediators, such as mRNA density in the hippocampus (Knafo et al., 2007) and amygdala activation (Meyer-Lindberg et al., 2009; Tansey et al., 2011), more neurogenetic work is needed to clarify how AVPR1a affects these neural regions and what other biological factors, such as GxG interactions, neurotransmitter density, protein regulation, white matter, and brain connectivity, are influential to these processes. Only by more clearly understanding genetic function, endophenotypes, and biological causal pathways, will the connection between genes and behavior or the environment be understood.

Interestingly, the marginal relation between AVPR1a and prosociality, present in middle childhood, was missing in adolescence. This inconsistency warrants a discussion on the relevance of developmental timing in behavior genetics. As reviewed, the functionality of length, though promising, has not yet been determined for many genetic variants. It is possible, perhaps likely, that the effects of genes on the brain, behavior, and the environment change over time, resulting in much more complex relations than early behavior geneticists may have anticipated. As the study of epigenetics has shown especially well, gene function is not static; we should not expect its effects on the brain or behavior to be static. Taking a developmental perspective is also consistent with what is

known about the brain's developmentally-and experience-dependent malleability, including regional and functional changes, but also changes in neurotransmitter density over time. For example, preliminary research has suggested that dopamine receptor concentration, which may affect reward dependence and other motivation-based constructs, changes with age and by neural region (Wahlstrom, Collins, White & Luciana, 2011); unfortunately the study of dopamine receptors in the human brain is early in development and cannot offer a definitive map of when density peaks.

In addition to developmentally prompted peaks and lessening of neurotransmitter density, it is possible that individual differences in density may yield benefits at some points in development and risks at different points in development. For example, during early childhood, a highly formative and sensitive neural period, it is possible that a very high level of reward value placed on social behavior is important for various reasons, including more focused attention to social stimuli, increased opportunities for social learning and social practice, and strengthening of synapses that foster healthy social behaviors. During this time, it is possible that a longer RS3 microsatellite is positively correlated with prosociality. Perhaps later in life, in adolescence for example, the highest level of social reward is less useful because it is no longer a time of learning basic social skills and pairing positivity with social behavior. It is possible that an exaggerated eagerness to be liked or receive social reward may eventually cause anxiety or social withdrawal, supporting Tansey and colleagues' (2011) findings of a positive association between AVPR1a RS3 microsatellite length and amygdala activation, which links to social anxiety. Indeed, previous work has found that in adolescent girls, very high levels

of empathy and prosocial behavior, potentially influenced by AVPR1a, may increase risk for mood disorders (Zahn-Waxler, Shirtcliff & Marceau, 2008). In this case, the longer RS3 microsatellite may be negatively related to social functioning and wellbeing.

While the twin genetic literature reports differences in heritability over time (e.g. Bergen, Gardner & Kendler, 2007; Knafo et al., 2006), the literature on measured genes has paid little attention to developmental stages and often times even participant ages. This lack of specificity makes it difficult to track how and if development moderates the relation between genes and behavior. Future behavior genetic research, at a minimum, should design studies with development in mind and report specific information with respect to chronological and developmental age to make comparisons between ages and stages possible. Once studies begin to report findings in accordance to the developmental periods studied, scholars can begin to map genetic influence on behaviors across developmental trajectories.

Finally, development and genes may not only influence individual differences in behavior; together, they may also influence the intensity, onset, duration, progression, and in the case of maladaptive behaviors—intervention effectiveness and likelihood of recovery from certain behaviors. For example, in the case of prosociality, some genes, at key points in development, may not only affect levels of demonstrated prosocial behaviors, but they may also affect developmental onset, how fast it progresses (e.g. multiple settings, beneficiaries, strategies), how frequent prosociality is expressed, and how responsive individuals are to treatment to increase prosociality. Mapping genetic influences on each of these diverse features of behavior across a developmental trajectory

is a complex but highly promising future direction for the fields of developmental science and behavior genetics.

Gene-Environment Associations. In addition to the marginal gene-behavior association identified, trends in gene-environment correlations were also noted. The DRD2 gene was positively related to father preference in adolescence at trend levels. This indicates that children with the A1+ allele of DRD2, or the allele preliminarily identified by the literature as more "risky", were more likely to be preferred by fathers. Although the CGC did not provide any additional information over and above single gene analyses, it did provide additional support for this association, also demonstrating a marginal relation with father preference. This indicates that children with the A1+ allele and short variants of AVPR1a were more preferred by fathers. Furthermore, an inverse correlation was detected between father preference and adolescent prosocial behavior. Though non-significant, prosocial behavior in middle childhood showed an inverse association with father preference at both time points studied. In addition, results consistently showed a negative association between father and mother preference, and mother preference in almost every case was positively associated with child prosociality. Together, this group of findings cautiously suggests an inverse relation between prosociality and father preference, potentially explained by the presence of unanalyzed child behavioral mediators or family and contextual dynamics associated with twin families, as elaborated below.

First, because many child behaviors and tendencies likely affect preference, it is possible that unanalyzed behaviors mediate the association between DRD2 and father

preference. These behaviors may contribute to qualitatively different interactions between children and fathers compared to children and mothers (see Lamb, 2010; Parke, 1995). Previous research indicates that fathers encourage children to take risks, stand up for themselves, and be competitive (see Paquette, 2004). It may be that fathers value those behaviors, which may show inverse relations to prosocial behavior, in determining preference. Given the breadth of literature identifying "rough and tumble" or physically stimulating play as a salient and critical aspect of fathering (Cabrera, Fitzgerald, Bradley & Roggman, 2007; Grossmann, Grossmann, Fremmer-Bombik, Kindler, Scheuerer-Englisch & Zimmermann, 2002; Macdonald & Parke, 1986; Paquette, 2004; Roggman, Boyce, & Cook, 2001), child attributes such as physical abilities, playfulness, outgoingness, or higher activity levels may play a mediating role in the relation between genes and father preference. Looking to the literature on temperament, the domain of novelty seeking (see Cloninger et al., 1987), previously associated with the A1+ allele of DRD2 (Noble, Ozkaragoz, Ritchie, Zhang, Belin, & Sparkes, 1998), may also represent behaviors that are perhaps more acceptable to fathers than mothers or even favorable to the father-child relationship.

Second, it is possible that the observed marginal association between DRD2 and father preference is due to family dynamics, possibly unique to twin families; particularly, processes involved in identifying a preferred child. Mother and father preference were consistently inversely related, as reported by twins and parents; thus, for a given set of twins, one parent tends to favor one twin and the other parent tends to favor the co-twin. Scholars have previously suggested this idea of "father-twin, mother-twin

dichotomy" (Trias, 2006), with some accompanying empirical support (Moilanen & Pennanen, 1997; Jouanjean- I'Antoene, 1997). For example, Moilanen and Pennanen (1997) found that mothers and fathers prefer opposite twins. Father preference was found to be more associated with the physically dominant and more autonomous twin, while mother preference tended to be associated with the twin who developed language earlier. It is possible that a twin-family dynamic (or families with singleton children close together in age) is to divide parenting responsibilities by twin or child rather than by tasks, thus resulting in an environment of one primary caregiver for each twin. A more efficient division of labor by child therefore, may influence more quality time together and subsequent parent preference. If mothers value prosociality more than fathers, the inverse correlation between DRD2 and father preference may be a byproduct of prosociality being a more salient predictor of mother preference, and fathers, by default, assuming a primary caretaking role for the less prosocial child.

Overall, it is clear that both genes and the social environment play important roles in child outcomes, albeit to varying degrees, likely dependent on development. Given that numerous child behaviors likely influence parental preference, future work may benefit from shifting toward studying behavioral dimensions or repertoires, perhaps stemming from temperamental or developmental domains. For example, rather than examine child prosocial behavior as an isolated mediator or outcome behavior, researchers may study a combination of temperamental constructs such as positive emotionality, activity level, and behavioral inhibition, each made up of numerous behavioral indicators. This diverse set of repertoires and behaviors may more accurately capture the child mediators

connecting child genes to both mother and father preference. Expanding and diversifying the set of behaviors examined will require a similar expansion in the genes examined; as such, future work should expand beyond studying single genes and identify a diverse set of genes and genetic families that are functionally connected, as informed by developmental neuroscience.

In terms of study design, observational and longitudinal studies would contribute to the advancement of this topic. Longitudinal studies with numerous time points over the course of child and parent development would determine whether preference shifts or intensifies over time or if groups of behaviors influence mother and father preference differently over the course of development. Longitudinal studies can also provide insights into the effects of preference on various aspects of child development, child and eventual adult-parent relationships, and "spillover" effects into other relationships, including sibling relationships, friendships, or intimate relationships. Incorporating genetics into these developmentally-focused longitudinal studies may allow us to map genetic influence onto the progressing parent-child relationship and examine if certain genes have more salient influences on mother or father preference at different points in time.

While longitudinal and questionnaire data can give us a higher level and broader view of the dynamics involved in preference and parent-child relationships, observational data can give us a closer look at the micro behaviors that may predict larger constructs, on the premise that a long history of micro behaviors may have substantial effects on development and relationships. Observational research can capture a diverse array of behaviors, perhaps grouped into domains of development or positive and negative

constructs, uniquely occurring within interactions between mothers and their children and fathers and their children. This would allow us to determine, for example, whether the frequency of positive affectivity exchanged between a twin and their parent is predictive of preference for mothers and whether a different set and type of micro behaviors influence father-child interactions and preference. Together, these directions suggest promising questions the field can pursue to learn more about how family dynamics, parent-child relationships, and genes, work together, possibly multiplicatively, over time to predict eventual adult competencies, adjustment, and outcomes.

Environmental Influences and Associations

Among the modest genetic influences between AVPR1a and prosocial behavior, and between DRD2 and father preference, several environmental influences, associations, and trends were revealed. Interesting differences were identified between mothers and fathers with regards to the predictors of parental preference and its effects on child prosociality. Findings also revealed strong stability in child prosocial behavior between middle childhood and adolescence. Combined, the environmentally-based set of findings, interpreted in the context of genetic influences, have important implications for intervention and policy directions.

Mothering, Fathering, and Child Prosociality. To reiterate, child prosocial behavior in middle childhood predicted maternal preference in adolescence, albeit at modest levels; the same was not true for father preference. Conversely, father preference in middle childhood predicted child prosocial behavior in adolescence; though the same was not true for mother preference. These findings build on previous research that

indicates that both parents make important influences on child development, with some studies finding that in certain contexts, fathers have greater influence than mothers (Bogels, 2011; Hoeve, Dubas, Eichelsheim, Vanderlan, Smeenk, & Gerris, 2009; Lamb Hwang, Frodi & Frodi, 1982; Vershueren & Marcoen, 1999). Father-child interactions are important to social functioning, with negative father-child interactions predicting less prosocial behavior with peers (Carson & Parke, 1996) and positive father-child interactions predicting higher quality friendships (Youngblade & Belsky, 1992). Furthermore, father involvement predicts higher child empathy and cognitive competence (Lamb, 2010; Pleck et al., 1997; Pruett et al., 1983). The influential effects of the father-child relationship may stem from early father-child interactions, with fathers playing a critical role in providing a secure base during environmental exploration (Grossman et al., 2002). To that end, fathers encourage children to explore novel situations (Paquette, 2004), potentially including novel social situations. Over time, this may allow children to become more comfortable initiating or responding to social interactions, affording them more practice in complex social situations.

The significant effect of father preference in middle childhood on prosocial behavior in adolescence adds to the literature that suggests an important and unique role of fathers in child social behavior and warrants more intentional attempts by the field to include fathers, or absence of fathers, in studies of child development. Currently, many researchers who aim to study parenting, in reality study mothering, excluding the important influences fathers uniquely have on family dynamics and child development. In order to truly understand parent-child or family-child dynamics, pertinent caregivers must

be included. This design would most obviously include fathers, but in the changing makeup of families, researchers should also consider second residential mothers or fathers in lesbian, gay, and transgender families, residential grandparents, and other relatives or step parents.

Importantly, parent and child reports of parental preference were consistently positively correlated, lending reliability to the measures and the reporters. This agreement implicates that each member of the family was reliably aware that one parent preferred one twin, while the other parent preferred the co-twin. Two previous studies have found lower agreement between child and parental report on differential treatment in pre- through middle-adolescence (Daniels, Dunn, Furstenberg, & Plomin, 1985; Kowal, Krull, & Kramer, 2004). Of note, both of these studies examined singleton siblings and differential treatment, as opposed to our study of twins that examined preference, a single construct within differential treatment. As previously discussed, it may be that parental preference is more salient in twin families than in singleton families. It is also possible that parental preference, in general, is more obvious or clear than other aspects of parent differential treatment, possibly evidenced by more time spent together, resulting in more agreement between reporters. More research is needed to examine under what contexts reporters in the same family agree, what biases reporters carry, and the unique effects of twins on family awareness of particular behaviors, including parental preference.

Behavioral Stability. Aside from genetic and environmental associations, findings revealed that child prosocial behavior, influenced by both genetics and father preference, showed strong stability between middle childhood and adolescence. Behavior

stability over the course of six years, particularly during a highly transitional and dynamic period in development, is compelling and in line with previous research. Obradovicc and colleagues (2006) found stability in mean level social competence between the ages of three and 16. Similarly, Vaughan-Sallquist and colleagues (2009) found prosocial rank stability between kindergarten and third grade. These findings imply that the social behavior, including prosocial behavior, children exhibit early in life is in line with the levels that will be exhibited later in childhood and through adolescence. As is further discussed below, this stability is likely influenced by rGEs and corresponding neural development and has important implications for early intervention.

The theory of progressive rGEs over the life course indicates that early genetically influenced behaviors will be matched with like environments. Those environments will then affect future child behavior, over and above initial genetic influences. Taking this perspective, it is logical that prosocial behavior exhibited in middle childhood is stable in adolescence, due to a continuous matching of genetically influenced behaviors with like environments, creating a self-reinforcing cycle. Further, the growing literature on developmental neuroscience indicates that infancy and early childhood are two of the most sensitive or environmentally susceptible periods in development, characterized by pruning and the strengthening of critical synapse connections (Anderson, 2003; Fox, Levitt, & Nelson, 2012; Roth & Sweatt, 2011; Shonkoff, 2011). Combined with research demonstrating that neural networks serve as the "rough draft" for children's later development and recognizing empirical work on the adverse effects of negative early experiences (Felitti, Anda, Nordenberg et al., 1998; Flaherty, Thompson, Litrownik,

2006; Haltigan, Roisman & Fraley, 2013; Koenen, Moffitt, Poulton, Martin, & Caspi, 2007), evidence for the importance of early experiences is solid and growing. The findings identified here compliment these robust bodies of literature and further highlight the importance of early experiences, thus justifying investments in early education and intervention. If the earliest years of life are indeed among the most formative and social trajectories observed in early and middle childhood generally remain stable through adolescence, it is logical to follow that interventions implemented early have the greatest odds of yielding longstanding and thereby cost effective results. This is not to say trajectories cannot be modified later in development, given rigorous intervention or a specific set of experiences; but naturally, prosocial behavior seems to stabilize in childhood.

Taken together, this literature starkly shows the need for high quality early experiences for young children, for example, through positive parenting practices, mitigation of toxic stress, effective teachers and schools, and early intervention as needed. Further, by more thoroughly understanding genetic risk for low prosociality, these early intervention programs may be targeted to children and families with the highest overall risk indices, made up of biological and environmental indicators. This may compensate for low initial skills or low resulting environmental stimulation and alter children's trajectories before behaviors become more rigid and difficult to alter later in life. Interestingly, some behavior geneticists have posited that "social control", via a safe, secure, and structured environment, may inhibit the expression of risky genes (Shanahan & Hofer, 2005). Indeed, the heritability of extraversion/surgency and effortful control

seem to increase in chaotic home environments as does negative affectivity under crowded and unsafe home environments (Lemery-Chalfant, Kao, Swann, & Goldsmith, 2013), potentially affecting early social experiences. This work suggests that structured, secure, and warm early home environments may protect against the expression of risky genetic influence, thus warranting investments in interventions that also focus on promoting healthy home environments. Aside from clinical and practical implications, this body of evidence has valid policy implications, particularly given the timely public discourse on mental health in society. Policy makers may place a more targeted focus on positive social behaviors via allocation of resources and effort spent assuring that young at-risk children have access to appropriate interventions and supports as needed, and that all children are in healthy, enriching, and supportive environments, whether in their home, classroom, or community.

Limitations and Future Directions

The results presented here should be interpreted in the context of several study limitations. First, most of the gene-behavior and gene-environment associations, with the exception of those discussed, were not significant. This is not surprising given the relatively novel status of the field, especially in the context of social behavior. It is possible that the genes or genetic combinations selected for analysis were not strong enough in themselves to predict behavioral or environmental variables. For example, though a cumulative genetic composite was tested, it consisted of only two genes. Perhaps combining the genes examined here with additional socially-implicated genes, such as other dopamine genes, serotonin genes, or the oxytocin receptor gene, would increase the predictive power and variance accounted for in social behavior. In addition,

while the field knows more about AVPR1a and DRD2 relative to other genes, there is still much unknown about how these genes function in developing humans and under different environmental contexts. No studies of humans, to our knowledge, have examined AVPR1a and DRD2 in combination, whether summed or multiplied, thus there is a lot to be learned about their relationship. Future research should continue to study dopamine-related genes, as well as AVPR1a and OXT, given their numerous commonalities, in isolation and combined with other gene families in order to gain a better understanding of functionality under varying environmental and developmental contexts.

On the environmental side, this study measured child prosocial behavior and parental preference, a very specific behavior and type of environmental exposure. Future studies may bear more fruitful results in examining broader behavioral dimensions or repertoires, made up of numerous behavioral indicators with common neural underpinnings. The limited context studied —the parent-child dyad—could also be expanded upon and improved by future research. Studies, like that of Proper and colleagues' (2012) have begun to move in this direction by expanding beyond a single environmental context into studying multiple relevant child contexts, including school, peer, and family relations. As various developmental stages likely affect the influence of genes on behavior and the environment, different environments influence behavior in distinct ways as well, making it important to study rGEs in numerous contexts. Further, as explained by the multiplier perspective, examining rGEs in various contexts will help

the field identify environmental kick-starters that may be highly valuable in informing intervention.

As reviewed, the socially-mediated hypothesis was not empirically supported, likely due to a host of reasons. One obvious reason is that genes and the social environment in middle childhood are too distal in a causal chain of variables to show a significant association. Countless proximal variables, including other genes, neural endophenotypes, and early child and parent behaviors, stand between them (Jaffe & Price, 2007). A more realistic depiction of the socially-mediated pathway may have been possible given additional data points. For example, a parent behavior measured in infancy or early childhood could have been studied as a mediator between genes and child behavior in middle childhood; subsequently, the effects of child behavior in middle childhood could have been tested as a predictor of parenting in adolescence. This would have provided a more comprehensive and transactional test of socially-mediated gene-behavior-environment interplay. Given a predictive genetic risk composite, an additional wave of data included after early adolescence may have also assisted in building the case for the socially-mediated pathway, such that environmental effects on later development could have been assessed. We should not assume that all genetic influence is transmitted to behavior and the environment through a single mechanism; to that end, it is likely that the socially-mediated pathway may be supported in some circumstances while the reactive pathway may be supported within other contexts and behaviors. In sum, future research should not discount the socially-mediated hypothesis yet, as the field remains in

its infancy and much remains to be learned about how genes influence development, via behavior and the social environment.

Incorporating parental or child attributes as moderators between child genes and the social environment may have also clarified potential rGEs. It is possible that the extent of the effects of child genes on parental behaviors is moderated by parental stress, chaotic home environments, or parent education, for example. Aspects of parents' personality have recently been found to moderate the relation between child genes and parenting (Oppenheimer et al., 2013). It is conceivable that parental stress, for example, influences how careful parents are in showing differential parenting; that is, under high levels of stress, parents may be more reactive to their children's heritable behaviors, whereas under lower stress, parents may be more intentional in their behavior toward each of their children. Future rGE work should take parental and child attributes as well as family circumstances into account as moderators, particularly in the study of parenting, in order to clarify how rGEs exert influence under various contexts.

In terms of methodology, the fact that different measures of parental preference were used at each time point is a limitation. Further, father report of preference was not collected in middle childhood; rather, mother-reported father preference was measured, potentially contributing to lack of stability in father preference over time. All data, with the exception of genetic data, was collected via parent and child report. Future studies should aim to collect and examine more observational data, in combination with participant-reported data, in order to identify differences in genetic influence between observed and reported behaviors, as well as micro indicators of broader behavioral

repertoires. With objective observation, participant perception, which is likely influenced by genes, may have a less pronounced effect on findings.

As reviewed, there are three identified types of rGEs: evocative, passive, and active. We restricted our focus to the evocative type, but it is possible that passive and active rGE mechanisms influenced the findings. For example, in the case of fathers, it may be that factors not analyzed in this study, such as shared interests, affect their preference, which may be influenced by shared genes, or a passive rGE. In these cases, children would share their fathers' genes and also be reared in an environment with high exposure to whatever the shared interest is, simultaneously increasing quality time with the parent. In terms of active rGEs, it could be that children choose their preferred parent early in life and that this selection is then reciprocated or elicits parents' preference. Though it is unrealistic and likely impossible to test for all rGEs in any given study, interpreting their potential contributions to study findings is an important consideration.

The most important future direction of gene-environment, and particularly rGE work, is its translation into clinical practice and intervention. Early intervention science can make substantial gains by understanding genetic influence and the biological-environment processes that unfold to ultimately predict outcomes. Knowledge gained from genetic risk can be used to inform parents early in their child's life what behaviors to expect and how to respond appropriately to those behaviors, especially negative or asocial behaviors, in effect allowing parents to "get ahead of the curve". Parental responses to child behavior will thus be guided by evidence-based positive parenting practices, rather than by challenging child behavior, preventing a multitude of negative

parent-child interactions in early childhood that influence maladaptive trajectories. For example, for asocial children, like many of those with ASD and related disorders, parents can be taught specialized techniques to scaffold their child's attention and provide learning opportunities so that they too can benefit from the rich early experiences that help develop the brain and set developmental trajectories. Overall, by early detection and prevention of deleterious, potentially multiplicative rGEs, gene-environment work can help inform and improve intervention, particularly social interventions, to the benefit of young children and families in need.

Conclusion

We simultaneously examined genetic and environmental influences, via gene-environmental correlations, on child prosocial behavior over the course of middle childhood and adolescence. Findings revealed modest evidence for the evocative-reactive rGE path, indicating that child genes influence early child behaviors, which subsequently elicit parental behaviors. Interesting patterns with respect to mother- and father-child relationships emerged and highlight the importance of including fathers in child development research. Despite these important contributions, multiple questions remain with respect to genetic influence, behavioral and environmental mediators, and processes that affect prosocial behavior, both environmental and biological. Future research addressing these questions could inform early intervention and social policy.

Though the field of behavior genetics continues to answer more questions about human behavior, it remains in the early stages of truly understanding the influences of genes on complex human behavior; our progress is even more elementary in understanding behavior genetics in the context of development. What is known for

certain, both theoretically and empirically, is that genetics and the environment jointly influence human behavior and development. The field of behavioral genetics must advance from examining time-locked gene-behavior or gene-disorder association and linkage studies, to analyzing the processes by which genes influence behavior in multiple contexts and at multiple time points throughout development. Similarly, environmental studies must expand beyond solely measuring the environment's effect on behavior, given all that is known about the influences of genetics and neural functioning on behavior. Only by pivoting to a truly integrated research agenda, where processes of biology and the environment are studied simultaneously over time, will we attain a true understanding of development, and be equipped to design the most effective interventions for children, adults, and a society in need.

CHAPTER 3

DOPAMINE RECEPTOR GENES AND PARENTING: INFLUENCES ON CHILD PROSOCIALITY

For decades the concept of parental influence on child development has received a wealth of empirical support from social scientists. Although the extent to which parents influence various aspects of child development has been a topic of disagreement, most developmental researchers agree that, to a certain extent, parenting matters. More recently, with increasing accessibility to molecular data, this concept and its accompanying environmentally-based empirical evidence, has been under renewed scrutiny prompting researchers to rethink the processes through which parents influence child development. Researchers are increasingly veering away from the linear relation, once thought to directly connect parenting to child outcomes, and are moving toward studying more dynamic, non-linear hypotheses of developmental outcomes. Of particular interest is the concept of gene-environment interactions (GxE), which explore the moderating role of genes in the association between environmental exposure and development. Belsky et al., (1997) offered an explanation of GxEs through their proposed framework of differential susceptibility, which posits that the extent to which environmental exposure affects developmental outcomes depends partially on child characteristics (i.e. genes). The inception of the differential susceptibility framework in combination with newly accessible molecular data has driven developmental scientists to explore the ways in which the effects of parenting interact with child genes to influence child outcomes. The current study adds to the growing body of GxE research, in the

context of parent-child interactions, by examining the moderating effects of socially implicated genes on the association between parenting and child social functioning.

The importance of social functioning on childhood and eventual adult adjustment has received a great deal of empirical support over several decades (Hawkins, Kosterman, Catalano, Hill & Abbott, 2005; Ladd, 2005; Ladd, Herald- Brown, & Andrews, 2009; Parker & Asher, 1987). Healthy social development and socially-based interventions have been linked to work and school productivity, mental, sexual, and emotional health, and reduced rates of delinquency in adolescence and adulthood (Hawkins et al., 2005; Hawkins et al., 2008; Tremblay, Pagani-Kurtz, Vitaro, & Masse, 1995). Positive peer relationships, attained and maintained through healthy social functioning, can also promote improved outcomes by facilitating skill acquisition, educational goal-attainment, access to meaningful supports, and improved academic success (Agostin & Bain, 1997; Kraemer, McIntyre, & Blacker, 2003; Ryndak & Fisher, 2001). Social functioning, therefore, has been shown to be one of the most influential domains of development. Understanding the biological and environmental bases of social functioning becomes increasingly important in the study of psychopathology, considering not only the important lifelong implications social functioning has on wellbeing, but also recognizing that numerous disorders share a deficit in social functioning. By further understanding the interactive relationship between parenting, child genes, and child social outcomes, the proposed study can build on the growing base of gene-environment work and serve to inform the study of healthy social development as well as intervention research aimed at

developing more comprehensive and precise personalized treatment for those at risk and those in need.

Although researchers are now beginning to analyze GxEs in social contexts, few have examined these processes longitudinally. In addition, most socially-focused GxE studies have centered on either young children or adolescents, leaving a substantial gap in the developmental understanding of how genes moderate the relations between the environment and outcomes over the course of childhood and into adolescence. Ellis and colleagues' (2011) influential work recently stressed the importance of analyzing GxEs through a developmental framework, using longitudinal designs, because susceptibility likely fluctuates over the life course. The proposed study aims to longitudinally examine the processes involved in GxE from middle childhood through adolescence, providing new insights regarding developmental process.

The Differential Susceptibility Framework

The differential susceptibility framework, as it was initially proposed, was grounded in evolutionary theory (Belsky et al., 1997; Boyce et al. 1993). In this context, researchers proposed that the uncertainty of the future, particularly the effectiveness or harmfulness of certain child-rearing practices, prompted humans to "hedge bets" and rear children that varied in their environmental susceptibility. Accordingly, if rearing practices proved to have adverse consequences on children, only those who were highly environmentally susceptible would be negatively impacted; likewise, if certain rearing techniques proved to be highly effective, those who were environmentally susceptible

would benefit most, and because of inclusive fitness, could also indirectly transmit these benefits on to siblings, parents, or other close kin.

Given this basis, the framework holds that the magnitude of environmental influence on child development is affected by the child's susceptibility to the environment, implying that those children who are highly environmentally susceptible are most intensely influenced by their environment, for better or for worse. That is to say, children who are highly environmentally susceptible will benefit most from supportive environments but will also be most negatively affected by adverse environments. Belsky and colleagues (1997, 2005) proposed that varying levels of environmental susceptibility are largely genetically influenced, notwithstanding the potential role of the environment. The focus on "for better *and* for worse" makes this framework unique to previously proposed frameworks, such as dual risk and diathesis stress. Given Belsky's hypothesis, genes are not seen as "risky" or "protective" as previous frameworks have labeled them; rather, genes are seen as influencing developmental "plasticity", whereby highly environmentally susceptible children are characterized as more plastic than less environmentally susceptible children. Establishing evidence for this framework requires a specific set of conditions to be met. In addition to identifying that a specific "plastic" allele, met with a negative environment, results in the most negative outcomes, data must show that the allele in question, when faced with an enriching and supportive environment, results in the most positive outcomes, over and above those experienced by individuals (without the "plastic" allele) who are surrounded by similarly positive environments.

The differential susceptibility framework has important implications on the domain of social development. Decades of environmentally-based research has concluded that healthy social relationships, particularly parent-child relationships, are critical to positive development. These studies have shown that positive parent-child relationships predict a number of favorable outcomes for children including academic adjustment, popularity amongst peers, and positive long-term social outcomes (Black & Logan, 1995; Morrison, Rimm-Kauffman & Pianta, 2003; Pianta & Harbers, 1996). These crucial relationships have also been positively associated with a variety of specific social skills such as peer competence, peer interaction and friendship (Bowlby, 1973; Park & Ladd, 1992; Ladd & Pettit, 2002; Strouf & Fleeson, 1986). The differential susceptibility framework posits that the importance of parent-child relationships on child social development is intensified for some children, implying that, while growing up in a safe and supportive environment is important for all children, the stakes are heightened for the sub-population of children who are most environmentally susceptible. The current study aims to study the effects of positive and negative parenting on child social functioning, as moderated by DRD2 and DRD4, through a differential susceptibility lens. Under this perspective, it is hypothesized that children with certain genetic variants indicative of plasticity will have the poorest social functioning and the best social functioning in the context of negative or positive parenting, respectively.

Differential Susceptibility to Parenting: DRD2 and DRD4

Scholars have suggested that one mechanism through which genetic variability may lead to environmental susceptibility is through dopaminergic circuits that regulate

responses to reward (Bakermans-Kranenbur & van Ijzendoorn, 2007; Belsky & Pluess, 2009). Decades of animal studies and neurological research have found that the dopaminergic system is linked to social behavior and is highly relevant in establishing reward value (Ikemoto, 2007; Schultz, 2007; Wise, 2004). Dopamine receptors mediate dopaminergic activity in the brain. The five identified dopamine receptors, D1 through D5, are analyzed as two functionally different groups, referred to as D1-like receptors and D2-like receptors. Biologically-based theory and evidence would suggest that D2-like receptors, particularly D2 and D4, and the genes that code for them, DRD2 and DRD4, play an instrumental role in social development. In addition, a group of studies on humans have identified DRD4, and to a lesser extent DRD2, as "plasticity" genes that influence differential susceptibility to context. Among those studies, some have specifically analyzed the moderating role these genes play in the context of parent-child relations (Bakersmans-Kraenburg, van Ijzendoorn, & Pijlman, 2011; Knafo, Israel, & Ebstein, 2011; Mills-Koonce et al., 2007; Proper et al., 2007; Proper et al., 2008; Sheese et al., 2007; van Ijzendoorn & Bakermans-Kranenburg, 2006). Due to their evidenced effects on social behavior and preliminary evidence that they influence plasticity, DRD2 and DRD4 were selected as the genetic foci of the presented study.

DRD2. The DRD2 gene is located at chromosome 11q23.1. Variants of the DRD2 gene influence D2 receptor production, density, and functionality. Of particular interest to environmental susceptibility and social behavior is the TAQ1a polymorphism, consisting of two major alleles (A1+ and A1-). Studies have identified this polymorphism as influencing environmental susceptibility within parent-child dyads. Mills-Koonce et al.,

(2007) found that the relation between parental sensitivity and affective difficulties was moderated by DRD2. Results indicated that children with an A1+ variant had the most and least affective problems, based on their mothers' levels of sensitivity. Berman and Noble (1997) found that family stress predicted reduced cognitive processing skills, but only in adolescents with an A1+ allele of the DRD2 gene. Strien et al., (2010) found that adolescents with an A1+ allele of DRD2 were the least and most likely to eat emotionally, depending on their parents' levels of psychological control. Processes of dual risk have also been identified with DRD2. Zwaluw and colleagues (2010) found that adolescents with highly permissive parents and an A1+ allele of DRD2 consumed significantly more alcohol than any other group. Finally, association studies have found that the A1+ allele is related to a number of socially-relevant behaviors and disorders including, ADHD (Farone et al., 2001; Rowe et al., 1999), attachment disorganization (Lakatos et al., 2000), and social problems (Marino et al., 2004). This study investigates the role of TAQ1a polymorphism of DRD2 as a moderator in the relation between parenting and child prosocial behavior and examine if patterns of dual-risk or differential susceptibility are observed.

Given the complexities involved in gene-environment interplay and development, it is likely that genes serve multiple functions, including directly influencing behavior and moderating the environment's effects on outcomes. More research is needed to examine DRD2's role in social development, particularly in young children and within the parent-child context. As is evident, there has been limited work analyzing the moderating effect of DRD2 on the relationship between environmental exposure and

outcomes, particularly in young children and in social behavior. This may be because the literature base has been centered on DRD4, which has likely increased interest around this gene, to the detriment of research on DRD2. As reviewed, biologically, DRD2 and DRD4 are hypothesized to play similar roles in dopaminergic reward pathways, warranting increased research attention on both DRD2 and DRD4.

DRD4. The DRD4 gene, located at chromosome 11p15.5, is highly polymorphic with multiple functional variants. Variants differ on the number of 48 base pair tandem repeats in the coding region of the gene. The 7-repeat variant of DRD4 has generated the most robust evidence with respect to environmental susceptibility effects. Studies have found that compared to those produced by the 2- or 4- repeat alleles, dopamine receptors coded by the 7- repeat allele are less efficient at transcription, translation, and second messenger generation (Robbins & Everitt, 1999; Schoots & Van Tool, 2003). Decreased efficiency in the dopamine system is related to decreased attentional and reward sensitivity, which, depending on the context, can result in negative or positive outcomes (Bakermans-Kranenburg & van Ijzendoorn, 2011; Robbins & Evertitt, 1999). Scholars have suggested that the 7-repeat allele of the DRD4 gene differs from the 2- and 4- repeat alleles with respect to cAMP activity (Asghari et al., 1995; Skuse & Gallagher, 2009), previously linked to social reward value, further indicating that this variant may functionally affect reward value and sensitivity to reward.

In comparison to other genes, DRD4 has been among the most studied in the GxE literature, with respect to parenting and child outcomes. van Ijzendoorn and Bakermans-Kranenburg (2006) were one of the first teams to find evidence of DRD4 influencing

differential susceptibility to environmental exposure. The authors found that parental unresolved trauma was related to children's disorganized attachment, but only for children who carried the 7-repeat allele. Those with the 7-repeat allele had both the lowest and highest levels of disorganized behavior, dependent on parental unresolved trauma. More recently, Bakermans-Kranenburg and van Ijzendoorn (2011) found that attachment status predicted donating behavior in children, but only for those with the DRD4 7-repeat allele. Specifically, children with the 7-repeat allele in securely attached parent-child relationships donated more than any other group; conversely, those with the 7-repeat allele in disorganized attachment relationships donated less than any other group. Combined, these studies illustrate that attachment can be influenced by the interaction between parent mental health and child genetic variants and that attachment interacts with child genetic variants to influence child outcomes, each of which establishes preliminary support for the differential susceptibility framework. While the reviewed attachment studies found that the 7-repeat allele predicts increased sensitivity to environmental exposure, the field has not arrived at full consistency. Gervai and colleagues (2007) found that the relation between parental atypical behavior and disorganized attachment was moderated by child DRD4 7-repeat allele, but found that the relation was stronger for those children *without* the 7-repeat variant of DRD4. Given the complexities involved in development, including countless gene-by-gene interactions, gene by environment interactions, gene-environment correlations, epigenetics, and regional genetic diversity, among many other phenomena, more research is needed to

more accurately identify the role of DRD4 in parent-child relationships and child outcomes.

Other studies have analyzed more specific parenting behaviors, with respect to DRD4 and child outcomes. For example, Bakermans-Kranenburg and van Ijzendoorn (2006) and Dilalla (2009) both examined parental sensitivity and its effect on child externalizing behavior. Results demonstrated that preschool aged children with the 7-repeat allele of DRD4 demonstrated the lowest *and* highest frequencies of externalizing behaviors, dependent on parental sensitivity, further supporting the differential susceptibility framework. van Ijzendoorn and Bakermans-Kranenburg (2007) later found similar results for parental responsive behavior; that is, children with the 7-repeat allele displayed the lowest and highest levels of externalizing behaviors, based on levels of parental responsiveness. Most recently, Knafo and colleagues (2011) found that the relation between positive or negative parenting and child prosocial behavior was correlated in the expected directions, but only for children with the 7-repeat DRD4 variant; correlations were not statistically significant for children who were not carriers of the 7-repeat allele. Of note, the interaction between positive parenting and the allele of interest was statistically significant but the interaction between negative parenting and the 7-repeat allele only approached significance, indicating that more research is needed to confirm these results. In addition to negative and positive parenting, the researchers found that the association between unexplained discipline and child prosociality was positive for children with the 7-repeat variant, but expectantly negative for non-carriers, indicating there is much to be learned about the interaction between this gene and

parenting, with respect to social behavior. Finally, Sheese and colleagues (2007) analyzed the quality of parenting in relation to activity level and impulsivity, as moderated by DRD4. The authors found that children with the 7-repeat allele were more susceptible to the quality of parenting they received, with respect to impulsivity, such that children with the 7-repeat allele were less impulsive than all other children under circumstances of high quality parenting, and were more impulsive than all other children under circumstances of low quality parenting (Sheese, Voelker, Rothbart, & Posner, 2007). While each of these studies demonstrated a full range of positive and negative environmental exposure, the dependent variables, with few exceptions, were often restricted to either a negative behavior or absence of negative and positive behaviors. A lack of externalizing behaviors does not equate to demonstrating, for example, high levels of prosocial behavior and vice versa. Because of this, these studies are only preliminary in their support of the differential susceptibility paradigm. Further research that captures a full range of environmental exposure and outcomes is needed to provide more solid evidence for this framework. The current study aims to overcome this limitation by testing a range of positive and negative predictors and a continuous outcome.

The studies reviewed provide preliminary evidence and warrant continued research in the field, however, their results are not conclusive. Controlled experimental studies offer the most convincing evidence of differential susceptibility. The only intervention study to examine outcomes with respect to parenting and DRD4 was employed by Bakermans- Kranenberg and van Ijzendoorn (2008). The authors conducted a randomized control parenting intervention study where participants were randomly

assigned to a control or parent training intervention group. After random assignments and intensive parenting intervention, child scores were analyzed with respect to intervention group and child DRD4 plasticity. Results indicated that the intervention, aimed at increasing positive parenting and sensitive discipline, was more effective for children with the 7-repeat allele of DRD4, compared to those with other variants, indicating that improvements in parenting most strongly affected children who were more genetically plastic and environmentally susceptible. Although results must be replicated, this study provides evidence of the moderating role of DRD4 in the relation between parenting and child outcomes, and more importantly, offers a prospective glimpse into the potential clinical utility of GxE research. Although the current investigation did not examine controlled environments or intervention effects, its results may be used to inform future clinical work, particularly in the realm of parenting interventions.

Cumulative Genetic Plasticity Index. As reviewed, most GxE studies to date have examined single candidate genes in their analyses. While these analyses have provided valuable insight into GxE processes, preliminary evidence has indicated that compositing groups of theoretically related genes may bear more powerful and meaningful results. Lead scholars in the field have recently begun using genetic composites, referred to as cumulative genetic plasticity indices (CGPI; Belsky & Beaver, 2011), due to the premise that a higher count of plastic alleles results in cumulatively higher sensitivity to the environment. These cumulative genetic plasticity indices aim to capture the number of plastic alleles an individual carries, which should correspond to individuals' levels of sensitivity to environmental exposure.

Multiple studies have found empirical evidence for this premise. For example, Belsky and colleagues (2009) tested the relation between childhood exposure to divorce and quality of adult relationships, as moderated by a cumulative genetic plasticity index comprised of DRD2, DRD4, and COMT. As hypothesized, the authors found increasing effects of divorce on adult relationships as the number of plasticity alleles increased. More recently, Belsky and Beaver (2011) took a similar approach in testing the relation between supportive parenting and self-regulation. Following the pattern identified in their earlier study, the researchers found that the more plasticity alleles males carried, the stronger the relationship between supportive parenting and self-regulation. Studying intergenerational parenting, Belsky and colleagues (2012) for a third time found a similar pattern. Individuals who carried a higher quantity of plastic genetic variants experienced the strongest link between the parenting they experienced as adolescents and the parenting they practiced with their own children, when compared to individuals who carried fewer or no plastic alleles. Finally, Simons et al., (2012) recently found that the relation between children's social environments and aggressive behavior was moderated by a CGPI and that the strength of the association intensified as the number of plastic alleles increased. Scholars have suggested that researchers follow the example of the aforementioned studies and begin to form genetic composites in order to encompass more genetic complexity, capture more variance, identify stronger effects, and garner more understanding of genetic and developmental processes (Belsky & Pluess, 2009). In addition to testing DRD2 and DRD4 independently, we tested the moderating role of a CGPI, comprised of DRD2 and DRD4.

The Current Study

The study of GxEs is quickly expanding, particularly in the analysis of dopamine-related genes, as increasing numbers of studies continue to identify the relevant role DRD2 and DRD4 play in parent-child relations and child outcomes. Despite this rapid growth, few studies have analyzed how DRD2 and DRD4 may interact with parenting variables to influence child prosocial behavior. As reviewed, social functioning, of which prosocial behavior is an integral part, plays a critical role in most aspects of development, and has strong influences on important outcomes such as school success and psychological well-being. In addition, social functioning is a core or associated symptom of multiple disorders, most notably, ASDs. Given the importance of social functioning on human development, and given the recent surges in prevalence of childhood disorders such as ASDs, examining the role of DRD2 and DRD4 on social functioning is an important next step in GxE work. Further, the strong influence of early relationships on the development of social competence and eventual social functioning suggest that parenting is a promising predictor in this analysis. The target environmental and outcome variables selected are particularly appropriate for testing the differential susceptibility framework due to their encompassing of a positive and negative ends of the behavioral spectrum for parenting as well as prosocial behavior.

The following research questions were explored: 1) Does positive and negative parenting interact with variants of DRD2 to predict child prosocial behavior, cross-sectionally and longitudinally? 2) Does positive and negative parenting interact with variants of DRD4 to predict child prosocial behavior, cross-sectionally and

longitudinally? 3) Does positive and negative parenting in middle childhood interact with a CGPI, comprised of DRD2 and DRD4, to predict child prosocial behavior, cross-sectionally and longitudinally? See Figure 9 for all outlined analyses.

Methods

Participants

Participants for this study were drawn from the Wisconsin Twin Project (WTP; Lemery-Chalfant, Goldsmith, Schmidt, Arneson, & Van Hulle, 2006), a longitudinal project on child and adolescent development and psychopathology in a representative sample of Wisconsin-born twins. Participants with data on at least one of the genes of interest were included in the current investigation. This resulted in 950 individual twins (*M=95* months, *SD*=10.72). Of these, 48.2% were male and 51.8 were female. Twins were tracked from birth through adolescence. Of participants investigated in the current analysis, 92.4% reported being White while the remaining 7.6% reported being African American, Native American, Asian, biracial or of other decent. With respect to household income, 9.6% of families in the sample made under $30,000 a year; 35.9% made between $30,000 and $60,000 a year; 36.5% made between $60,000 and $100,000 a year; and 10.3% reported earnings over $100,000 a year. The remaining 7.7% of families chose not to respond. Education levels varied, starting at 20.9% of mothers and 33.1% of fathers reporting high school or below as their highest level of education; 39.7% of mothers and 32.1% of fathers reporting having some college, technical or trade training; 27.4% of mothers and 20.3% of fathers reporting a college degree as their highest level of education; 10.9% of mothers and 10.5% of fathers reporting graduate training or a

graduate degree as their highest level of education; and the remaining 1.1% of mothers and 4.1% of fathers choosing not to respond.

Procedures

Participants in the current sample were identified through state birth records after 1989 and were recruited by mail. If families agreed to participate, they submitted written informed consent. Data regarding child social, emotional and communicative skills were first collected when twins were two years of age, via parent reported questionnaire. When twins were seven years of age, families participated in a telephone interview and participated in a five-hour home visit. During the home visit, parent-child interactions were observed, and additional data on development, psychopathology, and family relations was gathered via parent and child report or interview. Buccal swabs were used to collect cells for DNA analyses. Additional data was collected at adolescence using questionnaires and interviews, via mail or telephone.

Measures

Genes. For DRD2, four SNPs were typed, including rs6277, rs1800497, rs1799978, and rs1076560; rs1800497 or the TAQ1a polymorphism was used for the current analyses. For DRD4, one VNTR was typed, Exon III, 48bp repeat, consisting of repeat alleles ranging from two to eight. A ReddyMix master mix was used (Abgene, Surrey, UK) at a magnesium concentration of 1.5–2.5 mM $MgCl_2$. PRC conditions began with pre-heating at 95 °C for five minutes, followed by 30 cycles at 95 °C for 30 seconds, 55 °C for 30 seconds, 72 °C for 40 seconds, and concluded with 72 °C for ten minutes. An ABI 310 DNA Analyzer was employed for analyses.

Genetic Coding. DRD2 and DRD4 were effect coded with respect to alleles. For DRD2 SNP rs1800497, TT and TC genotypes (i.e. A1+genotypes) were ascribed a code of .5, while CC genotypes (i.e. A1- genotypes) were ascribed a code of -.5. DRD4 has been coded using different methods by the literature; this study coded DRD4 using two methodologies. First, those with the 7-repeat allele were ascribed a score of .5 and those who are not carriers were coded as -.5. The second methodology, also dichotomous, ascribed codes based on length: those with a 7-repeat allele or more repeats were ascribed a score of .5, and those with a 6-repeat allele or fewer repeats received a score of -.5. Preliminary findings suggested that the long/short dichotomous coding of DRD4, rather than the 7-repeat dichotomous coding, was more promising in relation to the variables of interest, therefore all analyses of DRD4 were conducted using the long/short coding.

Cumulative Genetic Plasticity Index (CGPI). The CGPI was formed by summing participants' plasticity scores for each individual SNP, as detailed in the previous section (Belsky & Beaver, 2011). Scores ranged from -1 to 1, with a score of 1 indicating an A1+ of DRD2 and a long repeat allele version of DRD4; a score of 0 indicating *either* the A1+ genotype or a long version of DRD4; and a score of -1 indicating an individual is a non-carrier of both A1+ of DRD2 and the long version DRD4. Higher scores of each genetic code consistently corresponded to higher anticipated plasticity, as identified in previous literature.

Positive and Negative Parenting. Positive and negative parenting at T1 was measured using the Child Rearing Practices Report (CRPR; Block, 1980). The CRPR is a 91-item measure of various parenting attitudes and behaviors, including a positive

parenting subscale and a negative parenting subscale. Mothers and fathers both completed the survey. Early studies on the CRPR revealed reliability between maternal self-report and observed parenting behaviors (Block, 1980; Kochanska, Kuczynski, & Radke-Yarrow, 1989). Positive and negative parenting at T2 was measured using the Twins Inventory of Relationships and Experiences (TIRE; Carbonneau et al., 2001). The TIRE is a 48-item questionnaire that captures child-specific information on parent-child and peer-child relationships. Mothers, fathers, and twins each completed the TIRE. Negative parenting was captured by reporter ratings of whether parents tended to become angrier-, punish children-, and have stricter rules than other parents. Positive parenting was captured by reporter ratings of whether parents spend more quality time, praise children, and show interest in children's activities, than other parents. Mother and father-reported parenting for both measures was averaged to create a parent-reported positive and negative parenting score at T1 and separately at T2; child reports of positive and negative parenting were examined as independent variables.

Prosocial Behavior. Data on prosocial behavior were collected as part of the MacArthur Health and Behavior Questionnaire, Parent Version (HBQ, Armstrong et al., 2003). The HBQ is a parent and teacher report measure designed to capture mental health, physical health, social functioning, and school functioning in children and adolescents. The current study used the prosocial subscale of the parent report tool to measure prosocial behavior in middle childhood and adolescence. This subscale, originally developed as a standalone measure titled the Prosocial Behavior Questionnaire (Weir & Duveen, 1981), has demonstrated high alpha levels (.85) in mother and father

reports. Mothers reported on each item using a three-point scale including options for "never/not true for my child", "sometimes true for my child", and "often/very true for my child".

Results

All analyses were conducted using MPlus (Muthen & Muthen, 2007). Full Information Maximum Likelihood (FIML) was employed to account for missing data. Scholars have indicated that the FIML technique may be superior to other missing data techniques due to its ability to take all available data into account (Enders & Bandalos, 2001; Schafer & Graham, 2002). Skewness and kurtosis analyses indicated that all skewness statistics were below 2 and all kurtosis statistics were below seven; in addition, visual inspection of the data demonstrated that all variables were relatively normally distributed. Mean, standard deviation, and range for each variable of interest can be found in Table 3.

Both twins' outcomes were modeled simultaneously in an actor partner interdependence model (APIM), though partner effects were not examined in the current investigation. In order to account for the nested nature of the data, both twins' data were entered into each equation, to control for the effects of each twin on his or her co-twin, consequently correcting standard errors. To assure that opposite-sex DZ dyads were interchangeable, constrained and non-constrained models were compared (Kenny & Kashy, 2011), where twin predictor and outcome variances and covariances were either constrained to be equal or unconstrained. A chi square test comparing the opposite sex

DZ twins using a constrained and unconstrained model was not significant $X^2(25) = 11.72$, $p=.97$, thus it was assumed that all dyads were interchangeable.

Prior to conducting primary analyses, sex, age, SES and race were tested as possible covariates. Age, SES, and race were not significantly related to any of the variables of interest, though sex was related to prosocial behavior at T1 and T2. Therefore analyses were conducted using sex as the only covariate. All continuous predictor variables were grand mean centered. Interaction terms were created by multiplying each centered continuous predictor variable (positive and negative parenting) and each moderator variable (DRD2, DRD4, and the CGPI). After preliminary analyses, a series of moderation analyses were conducted to test the proposed models (see Figure 9).

Parenting Main Effect Analyses

Analyses of main effects of positive and negative parenting were examined prior to GxEs. Results indicated that positive parenting at T1 was significantly related to prosocial behavior at T1 and T2. Twin-reported positive parenting at T2 was also associated with prosocial behavior at T2.The relation between parent-reported positive parenting at T2 and child prosocial behavior at T2 was marginal. In the analyses of negative parenting, results revealed that parent-reported negative parenting at T1 was not related to child prosocial behavior at T1. Further, negative parent-reported parenting at T1 and T2 were not significantly predictive of child prosocial behavior at T2.Twin-reported negative parenting at T2, however, was significantly inversely related to prosocial behavior at T2.

Genetic Main Effect Analyses

Next, genetic main effects were examined, in relation to child prosocial behavior. Analyses revealed non-significant direct effects of DRD2 on prosocial behavior at T1 and T2. Similarly, analyses of DRD4 indicated that DRD4 was not significantly predictive of child prosocial behavior at T1 or T2. A genetic main effect was identified in the relation between the CGPI and child prosocial behavior at T2. The same finding was not significant for child prosocial behavior at T1.

Moderation Analyses: DRD2, Parenting, and Prosocial Behavior

As suggested by previous research (Belsky, Bakermans-Kranenburg, & van Ijzendoorn, 2007), prior to GxE analyses, each set of variables was tested for gene-environment correlations (rGEs). With respect to DRD2 and parenting, the only significant correlation that emerged was between DRD2 and parent-reported negative parenting at T2 (r=.09, p=.01). Correlations between all other parenting variables and DRD2 were not significant, thereby establishing independence of those variables.

Statistics for all moderation analyses at T1 and T2 appear in Tables 4 and 5, respectively. The first set of moderation analyses examined the moderating role of the TAQ1a polymorphism of DRD2 in the relation between parenting and child prosocial behavior. Results revealed that DRD2 did not significantly interact with positive parenting at T1 in relation to child prosocial behavior at T1. The interactions between DRD2 and parent reported positive parenting at T1 and T2 were also not significantly predictive of child prosocial behavior at T2. Similarly, the interaction between twin-reported positive parenting and DRD2 was not significant.

The next set of tests examined the relations between negative parenting and prosocial behavior, as moderated by DRD2. Analyses revealed that the interaction between twin-reported negative parenting at T2 and DRD2 was not significantly related to child prosocial behavior at T2. Results of parent-reported parenting indicated the interaction between DRD2 and negative parenting at T1 did not significantly predict prosocial behavior at T1 and T2. Parent-reported negative parenting at T2 however, did interact with DRD2 at marginal levels in its relation to child prosocial behavior at T2 (see Figure 10). Probing of this interaction revealed that for carriers of A1+ alleles, the relation between negative parenting and prosocial behavior was not significant (*Standardized β=.03, se=.08, p=.67);* for A1- carriers, the relation was negative and significant (*Standardized β=-.17, se=.08, p=.04)*.

Moderation Analyses: DRD4, Parenting and Prosocial Behavior

Following, DRD2 was substituted with DRD4 to examine whether it interacted with parenting to predict child prosocial behavior. Preliminary correlation analyses indicated that DRD4 was not significantly correlated with any of the parenting variables of interest, therefore variable independence was assumed. Moderation results indicated that DRD4 did not interact with positive parenting at T1 in its relation to child prosocial behavior at T1. Similarly, DRD4 did not significantly interact with parent-reported positive parenting at T1 or T2 to predict child prosocial behavior at T2. Finally, twin-reported positive parenting did not significantly interact with DRD4 in its association with child prosocial behavior at T2.

The next set of analyses examined the relation between negative parenting and child prosocial behavior, as moderated by DRD4. There was a significant interaction between parent-reported negative parenting at T1 and DRD4, in relation to child prosocial behavior at T1 (see Figure 11). Investigation of this interaction showed that for children with the long variant of DRD4, the relation between negative parenting and prosocial behavior at T1 was non-significant (*Standardized β=.10, se=.08, p=.26)*; however, for those with the short variant of DRD4, negative parenting at T1 was significantly inversely related to child prosocial behavior at T2 (*Standardized β=-.12, se=.06, p=.04)*. Analyses of parent-reported negative parenting at T1 and T2 showed a non- significant interaction with DRD4 in predicting child prosocial behavior at T2. Similarly, DRD4 did not significantly moderate the relation between twin-reported negative parenting at T2 and child prosocial behavior at T2.

Moderation Analyses: CGPI, Parenting, Prosocial Behavior

The final set of analyses substituted DRD4 with the CGPI, made up of DRD2 TAQ1a and DRD4, to test its role as a moderator in the relation between parenting and prosocial behavior. Initial correlation analyses indicated that the CGPI was not statistically significantly correlated with parent- or child- reported negative and positive parenting. Interaction analyses revealed that the CGPI did not significantly moderate the relation between positive parenting at T1 and prosocial behavior at T1. Similarly, the CGPI did not significantly interact with positive parenting at T1 or T2 in predicting child prosocial behavior at T2. Finally, the relation between twin-reported positive parenting at T2 and child prosocial behavior at T2 was not moderated by the CGPI.

Analyses of negative parenting and prosocial behavior, as moderated by the CGPI were conducted next. Findings revealed that the CGPI moderated the relation between negative parenting at T1 and child prosocial behavior at T1 (see Figure 12). Investigation of this interaction showed that for carriers of *both* A1- of DRD2 and the short variant of DRD4, the relation between negative parenting at T1 and child prosocial behavior at T1 was negative and significant *(Standardized β=-.25, se=.07, p<.001)*; however, for carriers of *either* the A1+ of DRD2 or the long variant of DRD4, negative parenting at T1 was not significantly related to prosocial behavior *(Standardized β=.06, se=.07, p=.42)*. For those who carried *both* the A1+ allele and the long variant of DRD4, negative parenting at T1 was not significantly associated with child prosocial behavior at T1 (*Standardized β=.21, se=.14, p=.14)*. Analyses of parent-reported negative parenting at T1 and T2 revealed non- significant interactions with the CGPI to predict child prosocial behavior at T2. Twin-reported negative parenting at T2 similarly did not interact with the CGPI at significant levels.

Discussion

We examined the moderating roles of DRD2, DRD4, and their composite (CGPI), in the association between positive and negative parenting and children's prosocial behavior. The effects of negative parenting on prosocial behavior differed, at marginal levels, by child DRD2 and DRD4 polymorphisms, and the CGPI. Positive parenting in middle childhood and adolescence, on the other hand, was predictive of prosocial behavior for all children, regardless of genetic variants. Findings also revealed a gene-behavior correlation between the CGPI and child prosocial behavior, suggesting that

genes can affect behavior through various mechanisms. Overall, results suggest that genes and social environments are critical contributors to child social outcomes in both middle childhood and adolescence.

Negative Parenting

Negative parenting has received ample attention in the child development literature, though scarcely in relation to positive child behaviors, as moderated by child genes. Three GxEs were identified here, each of which indicated a genetic moderation (i.e. DRD2, DRD4, and CGPI) in the association between negative parenting and child prosocial behavior. Variants of the DRD2 gene marginally moderated the association between parent-reported negative parenting in middle childhood and prosocial behavior in adolescence, indicating differential intensity of effects of negative parenting, depending on children's DRD2 variant. Probing of this interaction indicated that for children with the A1+ variant of DRD2, the association between negative parenting and prosocial behavior was not significant. For children with the A1- variant, roughly three-fourths of the sample, the relation was significant in the expected direction; that is, more negative parenting was related to less prosocial behavior.

Neither group demonstrated a "for better or for worse" set of findings, thus the results are not indicative of differential susceptibility (Belsky et al. 1997). Instead, under low levels of negative parenting, both genetic groups demonstrated similar levels of prosocial behavior, whereas under high negative parenting, the A1- group demonstrated lower levels of prosocial behavior. Thus, results were more consistent with the diathesis-stress model (Zuckerman, 1999), though unexpectedly the A1- allele, rather than the A1+

allele, was identified as the risk variant, such that the combination of the A1- allele and negative parenting resulted in the lowest levels of prosocial behavior. Although implications should be approached cautiously due to the marginal nature of findings, it appears that the A1+ allele may buffer effects between negative parenting and prosocial behavior.

Building on what is known about the biological bases of DRD2 and D2 receptors, it is possible that children with this variant are less rewarded by social interactions, which may translate to children being less affected by social interactions in general, whether positive or negative. As reviewed, decades of animal models indicate that the dopamine system is highly involved in reward value, motivation, attention, and consequent pair bonding (Aragona et al., 2005; Mirenowicz & Schultz, 1996; Wise, 2004). D2 receptors in particular seem to facilitate social behavior and pair bonding in voles, while other dopamine receptors (i.e. D1) block it (Aragona et al., 2005; Skuse & Gallagher, 2009). Focusing on the A1+ allele, fewer D2 receptors have been identified in the brains of carriers of this variant (Noble, Ritchie, Montgomery & Sheridan, 1991; Noble & Cox, 1997; Thompson et al., 1997). In humans, A1+ is associated with a broad array of relevant behavioral phenotypes including avoidance and indifference in response to social cues (Blum et al., 2000), reward deficiency syndrome (Comings & Bloom, 2000) and social problems (Marino et al., 2004). A large body of evidence also implicates the A1+ allele in impulsive-type disorders; most notably alcoholism and substance abuse (see Bowirrat & Berman, 2005), potentially explained as the result of low natural reward

sensitivity and a subsequent attempt to compensate via high novelty seeking and risky behavior.

Taken together, this body of evidence implicates A1+ in low reward sensitivity and dependence, which may, in some cases, be translated to low environmental sensitivity in general. Looking to the literature on temperament, individuals who score low on reward dependence are indeed less influenced by positive and negative environmental factors, such as social praise or criticism; on the other hand, those who score high on reward dependence are more easily affected by disapproval or criticism (Cloninger, 1987; Cloninger et al., 1994). This finding may explain why an association exists between negative parenting and prosocial behavior for children who have higher reward dependence and potentially a higher density of D2 receptors in socially relevant neural regions, as evidenced by the A1- allele. The tendency to be either sensitive or insensitive to social reward affects social attention and attunement to social cues, which also likely influences components of social competence, such as prosocial behavior. This interpretation of the A1+ allele and reward dependence has different implications depending on the environment and behavior of interest. If, for example, a child is in an adverse environment with high levels of negative parenting and the behavioral outcome of interest is positive (i.e. prosocial behavior), this insensitivity to the environment and low regard for positive or negative social input may be beneficial or show a buffering effect, as is presented here. The same child placed in an intervention program to increase base levels of prosocial behavior may experience less fruitful results given their low sensitivity to reward and environmental stimuli.

Though this interpretation is not consistent with previous studies that have found the A1+ allele to be more plastic, none of the previous studies examined the DRD2 gene as a moderator between a negative environmental variable and positive behavior, such as prosociality. It is possible that the extent to which the A1+ allele is risky or environmentally sensitive partially depends on the behavior under investigation and whether that behavior is positive or negative, normative or pathological. The interaction between this gene and negative environments may affect outcomes differently, potentially with a stronger influence on negative outcomes, as previously studied, and less effect on positive outcomes, as is presented here. Though an established body of evidence indicates that DRD2 plays a role in social functioning, clearly more research is necessary to determine its exact role, particularly under varied environmental contexts and in relation to positive, negative, normative, and pathological behaviors.

In addition to DRD2, DRD4 was also found to moderate the association between parent-reported negative parenting and child prosocial behavior. However, different from DRD2, DRD4 moderated the relation between negative parenting and prosocial behavior in middle childhood rather than adolescence. Analyses revealed that for children with the short variant of DRD4, approximately two thirds of the sample, the relation between negative parenting and prosocial behavior was negative, as expected. For the third of the sample that carried the long variant of DRD4, the relation between negative parenting and prosocial behavior was not significant. Similar to the DRD2 interaction, this test shows an expected and significant pattern for most children, and a non-significant pattern for children who carry the less common, previously labeled “risky” or “plastic” allele.

Findings are in line with those of Gervai and colleagues (2007), such that the relation between parental atypical behavior and disorganized attachment was stronger for the majority of the sample who did not have the 7-repeat variant, or the short variant of DRD4.

One explanation of this finding may be gained from the DRD4 and ADHD literature. A large body of evidence implicates the long variant of DRD4 in ADHD (see Gizer, Ficks, & Waldman, 2009). Interestingly though, a recent study by Gizer and Waldman (2012) found that DRD4 was only associated with the attention domain of ADHD, not the hyperactivity domain. Other investigators have also identified a relation between the DRD4 long variant and inattention in healthy samples (Laucht, Becker & Schmidt, 2006; Schmidt, Fox, Perez-Edgar, Hu, & Hamer, 2001). It is possible that children who carry the long variant of DRD4 are less effective at attending to social stimuli, which may result in difficulty reading and interpreting, and therefore internalizing subtle social cues, including subtle negativity. It may be that more overt and severe negative parenting, which is much rarer, is required to substantially affect the social development of children who carry this allele. This line of reasoning also speaks to the importance of differentiating normative and non-normative ranges of the environment and behaviors of interest. It is possible that when faced with extreme negative parenting, this group of children is indeed more susceptible to negative effects, particularly if they already face deficits in social skills (e.g. reading social cues) due to an rGE.

Another plausible interpretation is based on previous work that suggests that the long variant of DRD4 is associated with weaker transmission of intracellular dopamine

signals (Robbins & Everitt, 1999). As discussed, weak transmission of signals may affect the effectiveness or efficiency of pairing reward value (via dopamine) with social behavior (via "social" neuropeptides and transmitters). Similar to the processes potentially catalyzed by DRD2, it may be that children with the long variant of DRD4 place reduced reward value on social interaction, thus interrupting the deleterious effects of negative interactions.

The results presented here do not support the differential susceptibility framework and are not consistent with several other studies that have identified the 7-repeat variant as more plastic (Bakermans-Kranenburg & van Ijzendoorn, 2007, 2008, 2011; Dillala, 2009; Knafo et al., 2011; Sheese et al., 2007). Only one of these studies, however, examined DRD4 as a moderator between parenting and prosocial behavior (Knafo et al., 2011). Knafo et al., (2011) did not find evidence of DRD4 moderation between negative parenting and child prosocial behavior; though they did find evidence of moderation between positive parenting and prosociality, such that the association between parenting and prosocial behavior for children who carried at least one 7-repeat allele, but not for those who carried no 7-repeat alleles, was significant. An important distinction between Knafo (2011) and the current investigation is the age of participants. Whereas Knafo et al. (2011) studied children's prosocial behavior at age three, this study analyzed prosociality at age eight, a substantial leap ahead in development, implicating more advanced cognitive, social, and emotional functioning, including higher levels of prosocial behavior (Eisenberg & Fabes, 2006). Given what is known about the malleability of the young human brain, it is possible that neurotransmitters vary in

density throughout development and alter the interaction between genes and the environment. Indeed, previous work has found differences in dopamine density dependent on human age, though this evidence base is small and inconsistent (Wahlstrom, Collins, White & Luciana, 2011). In addition, as recent data has begun to suggest, it is possible that genes prompt different effects on behaviors at different points in development (Dick et al., 2013; Irons, Iacono, Oetting, & McGue, 2012). For example, a single gene can influence a behavior in a specific direction at one point in development, and have lessened effects or even directionally opposite effects on the same behavior at a later point in development. In the case of DRD4, parenting, and prosocial behavior, it may be that in early childhood, negative parenting similarly influences all children, and positive parenting is more impactful for subgroups of children depending on genes; whereas in middle childhood the opposite effect is seen. Given that this is only the second study to examine DRD4, parenting, and any positive behavior or trait, further research is needed to clarify the processes involved in these interactions.

Another possible, but unlikely, contributing factor to the discrepancy between the findings here and those of Knafo and colleagues' (2011) may be differences in coding the alleles. Whereas Knafo et al. (2011) coded DRD4 dichotomously as 7- present or 7- absent, we coded the gene dichotomously as long versus short, where carriers of at least one 6-repeat variant or longer constituted the long group and carriers of two 5-repeat variants and shorter, constituted the short group. By including carriers of the 6-repeat variant and higher in the long group, the "long" or what would be the "7-repeat" group expanded by 12 participants, or approximately 5 percent. Although neither method is

ideal due to the use of an arbitrary dichotomy, there is justification for using the short/long coding methodology, as research on other genes (Knafo et al. 2008; Meyer-Lindenberg et al., 2009; Tansey et al., 2011) has offered preliminary evidence of the functional significance of allele length. Thus, dichotomizing by length is an appropriate direction to pursue. Future genetics research must utilize larger samples to explore differences in allelic variation as they relate to functionality in order to inform gene-environment research and bring a greater accuracy and methodological consistency to the field.

The last significant interaction revealed that the CGPI, comprised of DRD2 and DRD4, moderated the association between negative parenting and prosocial behavior in middle childhood. Specifically, for children who carried A1+ of DRD2 and the long variant of DRD4, the relation between negative parenting and prosocial behavior was not significant. Similarly, for carriers of either the A1+ alleles of DRD2 *or* the long variant of DRD4, the association was not significant. For the largest group, consisting of children who carried the A1- allele and the short variant of DRD4, the relation was significant and negative, as expected. Consistent with the single gene GxEs, children with no hypothesized risk or plastic alleles show the expected associations between parenting and prosocial behavior, whereas children with one or more plastic or risk alleles, show a non-significant association. Though these findings do not corroborate with differential susceptibility and do not validate A1+ DRD2 and the long variant of DRD4 as plastic, they do illustrate a pattern of atypical behavioral responses to environmental exposure for carriers of these alleles, leaving much room for additional research on these subgroups of

individuals. Overall, the CGPI did not provide any additional insights over and above analyses of single genes. That is, no observable differences in plasticity or effects otherwise were noted by combining variants of DRD2 and DRD4. This may be due to the fact that only two single genes from the same genetic family made up the CGPI. It may also be that their effects on development are distinct and not additive.

Of note, we found two trends that appeared to support previously published findings from Knafo's (2011) study, with respect to the direction of the association between the environment and child behavior. A positive, albeit non-significant (p = .26), slope in the association between negative parenting and prosocial behavior was noted, but only for children with the long variant of DRD4. Similarly, in examining the CGPI, the slope for children who carried the long version of DRD4 and the A1+ of DRD2 was positive, though non-significant (p = .14), indicating that for this group of children, more negative parenting seemed to trend in more prosocial behavior. Knafo and colleagues (2011) found that for 7- repeat carriers, but not non-carriers, the relation between unexplained discipline and prosocial behavior was also positive. Though the environmental constructs are different, the pattern of negative environmental exposure associated with a prosocial behavior for children with the long variant of DRD4, independently or combined with the A1+ allele of DRD2, is unexpected. Even promising directions should be approached with caution due to the non-significance of the results identified here, but important patterns and implications may emerge from further exploring this trend.

Aside from GxEs, interesting environmentally-based findings were revealed with respect to negative parenting. Twin-reported, but not parent-reported negative parenting was associated with prosocial behavior in adolescence. This discrepancy between reporters may be partly due to parents' hesitations or discomfort self-reporting negative parenting practices, thereby potentially diminishing the association (Schwarz, Barton-Henry & Pruzinsky, 1985). In fact, previous work has found that mothers in particular, tend to self-report more favorable parenting scores than their children or partners (Bogels & van Melick, 2004). Furthermore, children tend to report less positive indicators of family functioning than do parents (Bogels et al., 2001; Sawyer, Sarris, Baghurst, Cross & Kalucy, 1988). It is also possible that twin reports of negative parenting may be a byproduct of unaccounted for mental health difficulties or overall adjustment, associated with poor prosocial behavior. Furthermore, it was outside the scope of this study to capture neglect and abuse as separate and extreme components of negative parenting. The detrimental impacts of neglect and abuse on all aspects of human development are well documented (Twardosz & Lutzker, 2010), and should therefore continue to be focal points for clinical intervention and policy action. Regarding future research, the field would benefit from additional studies examining discrepancies between child- and parent- reported negative parenting, its effects on different types of prosocial behavior, and additional moderating variables, including genes, endophenotypes, and child- or environmental attributes, that could make certain subgroups of children more vulnerable than others.

Positive Parenting

Positive parenting showed a different pattern of findings than negative parenting. Both as reported by parents in middle childhood and twins in adolescence, positive parenting was positively associated with prosocial behavior for all children, regardless of genetic variants. Interestingly, positive parenting in middle childhood was as strongly related to child prosocial behavior in adolescence as was positive parenting in adolescence, providing a compelling case for the importance of positive parenting in early childhood, and the lasting influence of parenting context across development. Though complex, the effects of positive parenting on prosocial behavior are well documented (Clark & Ladd, 2000; Eisenberg, 2006; Knafo et al., 2006; Krevans & Gibbs, 1996). Parents serve as children's first and most important social partner. The parent-child relationship, perhaps more than any other, plays a critical role in helping children establish a secure social-emotional foundation, made up of developing social and emotional competence, trusting relationships, motivation to engage with familiar social partners, and interest in exploring new social opportunities. Some evidence suggests that children in securely attached parent-child dyads demonstrate more prosocial behavior (Iannotti, Cummings, Pierrehumber, Milano & Zahn-Waxler, 1992). This secure attachment likely increases the quantity of positive social interactions, and with it, children's social attention and motivation to engage with parents, eventually affording them the security, autonomy, and skills necessary to explore novel social situations and further advance their social competence. In addition, other positive parenting behaviors, such as modeling prosociality, involving children in helping behaviors, and discussing

how helping benefits others, also influence child prosocial behavior (see Eisenberg & Valiente, 2002).

Biologically, the "use it or lose it" and "practice makes perfect" concepts, which maintain that the more frequently behaviors are practiced, the stronger corresponding synapse connections are formed and the less likely those connections will be pruned away, have important implications for social development (Nelson, Thomas & DeHann, 2008; Segalowitz & Schmidt, 2003). Positive parenting and a history of positive parent-child interactions during the highly sensitive neural period early in life may help strengthen synapse connections important to social functioning later in life. Thus, affording children warm and secure relationships with ample opportunities to practice social exchanges, while encouraging autonomy and exploration of novel social situations may, together, form a strong social-emotional base of which prosociality is a meaningful part. Finally, given that prosocial behavior is heritable (Knafo & Plomin, 2006), it is important to consider the potential role of passive rGEs in the relation between positive parenting and child prosociality. Parents and children's common genes may contribute to like prosocial tendencies; these shared genetic influences in combination with a rearing environment that is reflective of these genes can result in a dual impact on child prosocial behavior.

The findings on parenting and prosociality identified here and elsewhere, taken together with research on the importance of early experiences, warrants attention from policy makers. Specifically, allocating resources to improve parenting preparation prenatally and positive parenting practices in infancy and early childhood is a promising

policy direction to pursue in order to support young children's rapid social-emotional development, primarily via parent training programs. Because evocative rGEs have taught us that children are active partners in forming relationships rather than passive beings (Pener-Tessley et al., 2013; Hanna et al., 2013; Hayden et al. 2013), these programs may be partially targeted toward improving parental responses to children's behavioral outputs, for example, lack of self-control, aggression, or negative affectivity. Other critical components of improving parenting practices may include public awareness campaigns, a larger focus on prenatal and parental mental and physical health, and efforts to mitigate the effects of toxic stress on families. An early focus on positive parenting has the potential to prevent more costly mental health interventions later in life, when children advance into adolescence and adulthood. In addition, given the millions of children in early childhood settings on a daily basis, employing modified strategies to similarly improve the quality of adult-child interactions in these settings is imperative to healthy social development.

Gene-Behavior Correlation

Though the primary aims of this study were to examine GxEs, one gene-behavior correlation emerged. The CGPI predicted child prosocial behavior in adolescence, though DRD2 and DRD4 did not show effects independently. The association was negative, meaning that children with the A1+ allele of DRD2 and the long variant of DRD4 were the least prosocial; conversely, carriers of the A1- and short variants of DRD2 and DRD4 respectively, were reported to be the most prosocial. This is consistent with some previous empirical findings and proposed biological hypotheses. Specifically, as

reviewed, some researchers have argued that longer variants of DRD4 result in less efficient transcription, translation, and second messenger generation (Robbins & Everitt, 1999; Schoots & Van Tool, 2003), which is related to decreased attentional abilities. Taken together with the body of evidence that implicates the A1+ allele of DRD2 in decreased reward value (Comings & Bloom, 2000; Wise, 2004), it may be that this genotype (i.e. long DRD4 and A1+) makes for a combination of impaired attentional and processing skills as well as reduced reward sensitivity. These influences may simultaneously decrease social attention and social motivation, which may make the *ability* to learn new prosocial skills more difficult and the *desire* to learn new prosocial skills less likely. This combination may result in a child who is not successful in social interactions, by virtue of fewer attempts and practice, and inherent difficulty attending to and therefore reading and interpreting social cues. More research is needed to test this hypothesis and disentangle the effects of these genes, if- and how- they function co-dependently, and under which circumstances they influence greater or less sensitivity- or attention- to environmental stimuli.

The rGE finding presented here highlights the complexity in genetic influence and suggests that DRD2 and DRD4, in particular, may influence social development via multiple processes over middle childhood and adolescence. Specifically, while certain DRD2 and DRD4 alleles may present risk to subgroups of children, or make them more susceptible to their environment, results indicate that together, they also directly influence prosociality in adolescence for all children. Although it is unrealistic to expect every gene-environment study to test every form of gene-environment interplay, future

work in this area should at a minimum check for rGEs prior to testing GxEs and interpret findings accordingly. Among other things, this may help us determine dual impacts of genes, that is, how genes may directly influence behaviors or environments, but also intensify the association between behaviors and the environment, broadening and advancing our understanding of gene-environment interplay. The rGE identified in the current study also supports a less-studied but promising dimension of DRD4 research (Lakatos, Toth, Nemoda, Ney, Sasvari-Szekely, & Gervai, 2000), which has predominantly studied this gene in the context of plasticity or moderation, rather than in direct associations with behaviors or environments.

Limitations and Future Directions

This study has important limitations to consider and offers several future directions to pursue. The exclusive focus on dopamine receptor genes, though biologically supported, may have restricted our ability to detect larger genetic influences. DRD2 and DRD4 were chosen, in part, because both demonstrated some evidence of influencing social behavior and plasticity. In identifying genes to study, future investigations may consider forming plasticity composites using larger groups of genes known to interact, influence one another, or work together at molecular levels and within various functionally connected neural regions. For example, in examining social reward and motivation, future studies may form a composite made up of DRD1, DRD2, AVPR1a and OXTR, given that all four genes are hypothesized to play substantial roles in socially-implicated cellular interactions within relevant brain regions. After mating, dopamine is released into various regions in the brain, prompting also the release of

dopamine receptors. While D1 receptors bind to stimulatory G-proteins, an action which decreases reward value (via Cyclic Amp production), D2 receptors bind to inhibitory G-proteins, which increases reward value (via depression of Cyclic Amp production). Because both D1 and D2 receptors are found in regions also highly populated with vasopressin and oxytocin receptors, it is possible that these freshly released dopamine receptors are further activated by AVP and OXT receptors, as has been suggested may be the case in animal models (Insel, 2004). This activation may catalyze the pairing of social behavior with high reward value, the extent of which partially depends on the density and balance between D1 and D2 receptors. By piecing together functional pathways from genetics, molecular biology, and neuroscience, future studies may composite more comprehensive systems of genes, rather than single genes or a small number of genes within the same family.

Given the often inconsistent findings identified in the field of behavior genetics and GxE research in particular, it remains a challenge to composite genes whose directional effects on plasticity remains unknown or conflicted. As further demonstrated here, a consensus on genetic plasticity for any gene remains uncertain. In addition, because of the lack of precise information known about genetic functionality, investigations are forced to use somewhat arbitrary coding schemes, which may be one contributing factor to inconsistent results in the field. Basic genetic research, informed by cellular biology and neuroscience, must continue to expand the field's understanding of functionality in order to inform gene-environment interplay and child development studies.

With respect to the environmental factors examined here, analyses of positive and negative parenting were tested separately. While this approach may more precisely capture the effects of positive and negative parenting behaviors, in reality, children's environments and the amount of negative and positive parenting they receive does not present separately. Future studies may consider incorporating negative and positive parenting dimensions into the same model to more accurately identify how these dimensions, individually and combined, influence child development. In this way, the effects of different combinations of positive and negative parenting (e.g. high positive, high negative) can be studied in relation to child genes and social developmental trajectories.

With regard to prosociality, although it is a key aspect of healthy social-emotional development, future studies should incorporate additional positive social-emotional behaviors to more fully capture the social dimension of development. For example, other positive social-emotional behaviors like cooperation, behavior and emotion regulation, social initiations and responses to social bids, and positive peer and sibling relations, along with negative social-emotional behaviors like asocial, withdrawn, aggressive, or hyperactive behavior could be composited to form a more comprehensive behavioral repertoire that would represent the construct of social functioning. This would result in a shift away from studying single behaviors within larger dimensions to instead examining behavioral repertoires made up of numerous biologically-related behavioral indicators. This shift may help the field gain a more comprehensive understanding of the effects of parenting and genes on specific developmental dimensions. This could be done by using

a person-based approach and assigning composited dimensional scores to individuals, both phenotypic and genetic, to paint a fuller and richer picture of the biological and environmental systems that influence developmental dimensions.

There are several key considerations for future research in addition to those previously mentioned. Among those is a call for special attention on how gene-environment processes function differently for positive versus negative and normative versus non-normative outcome behaviors and environments. Because the field has been so firmly focused on negative behaviors and psychopathology, expanding the focus to cover both negative and positive behaviors, and examining how these fit together, will result in a greater understanding of the influences of genes and environments on development and will undoubtedly inform intervention. Though there is some consistent data on the factors that increase risk, there is less known about the factors that protect against risk or facilitate resiliency and healthy development, particularly with respect to the role of genetics (Lemery-Chalfant, 2010).

Another key consideration for future gene-environment work is to ground studies in developmental science. Bringing developmental perspectives into behavior genetics has the potential to bridge the divide between genetic risk and intervention, in order to prevent genetic risk from metastasizing. For example, Belsky and colleagues (2013) recently found that an empirically supported genetic risk composite did not predict smoking initiation; rather, it predicted how rapidly adolescents and young adults progressed from smoking initiation to being heavy smokers and nicotine dependent. If this study had only examined smoking in adolescence, it would not have revealed the

alarming progression in smoking behaviors, influenced by the genetic composite. By examining adolescents and young adults over time, and so too the development of their smoking habits, Belsky et al., (2013) identified a critical public health message: if policy measures can be taken to prevent first exposure to smoking, the genetic risks of becoming nicotine dependent and facing the steep health consequences of that dependence, can be ameliorated or at least reduced. In understanding the general developmental timeline of smoking, that is, that initiation generally happens in adolescence, and dependence shortly thereafter, interventions and resources can be targeted at this fragile developmental stage, eventually with a heightened focus on those who are genetically at risk. If the field is to truly identify the interplay between genes, behavior and environments, it is critical that researchers take into account that humans are not static beings; rather, they are dynamic and demonstrate changes in behavior over time. These behavioral changes are likely influenced by changing genetic and environmental influences over time. While we included two developmental time points, our work would have benefited from additional data from infancy, early childhood, and late adolescence.

With respect to the theoretical perspectives that inspired this work, though the GxE findings presented here do not support differential susceptibility, atypicalities in children with less common genetic variants were consistently noted. All gene-environment work remains in the early stages of development, therefore all theoretical perspectives should continue to be pursued until a solid base of evidence is established. This is especially true given the likelihood that certain behaviors and environments are

likely explained by differential susceptibility, while others may be explained by dual-risk, and yet others by potentially unidentified mechanisms.

Conclusions

The findings identified here have important implications for the biological and environmental basis of social development. Further, because social dysfunction is an underlying deficit observed across numerous disorders, ranging from ASD and schizophrenia to depression and anxiety, the findings presented here, though not conclusive, have important implications for psychopathology. Taking a dimensional developmental perspective in behavior genetics, as suggested here, will allow scientists to make much larger strides across various mental illnesses and may ultimately result in detachment from strict labels imposed by the DSM, many of which are not biologically supported. If the underlying biological and environmental contributors to social deficits, or like dimensions, can be the unit of study in future studies, rather than disease or disorder labels, psychopathology etiology and intervention can make a progressive leap to clarifying biological causal pathways and identifying and treating underlying conditions rather than groups of symptoms, which has thus far not been robustly effective. With this information, early intervention can shift downward to infancy, during a time when we know the brain is most malleable and interventions are most likely to have lasting effects. A new wave of next-generation neurologically-informed gene-environment studies on social development, therefore, have much to contribute to millions of individuals with ASD and other socially-affected disorders around the world

and their counterparts who suffer from like deficits, though may be categorized differently.

It is premature to draw broad policy and clinical implications from the GxE findings presented here, given that the study of GxE in positive behaviors is in its infancy and many, or most, research questions remain unstudied, and therefore unanswered. Nonetheless, the potential clinical and policy implications that may result from more high quality, process-oriented and biologically and environmentally informed research may change the face of clinical intervention and have large-scale policy implications. Identifying how the environment differentially affects development, via different genetic combinations and biological processes, will lead to earlier detection and prevention of mental illness and if needed – individualized interventions that can more effectively address these complex mental health needs. As Thomas Insel, Director of the National Institute of Mental Health recently stated, after an "era of discovery" clinical neuroscience can now look forward to an "era of translation" (Insel, 2013a). The work of testing the differential effectiveness of behavioral techniques or pharmaceutical interventions, based on genotype, has already begun in topics as diverse as genetic susceptibility to behavioral intervention for cardiac surgery-triggered PTSD (Hauer et la., 2013) and genetic susceptibility to pharmaceutical intervention to decrease the cortisol response to acute social stress (Cerit, Jans, Van der Does, 2013). As researchers continue to disentangle which existing approaches are most effective for subgroups of the population, lessons learned can be applied to novel intervention work, targeted at helping subgroups of the population who are less responsive to existing interventions.

With respect to policy, if certain genes are consistently and reliably identified as "plastic" or "risk" genes, then programs that provide resources and services targeted to families may distribute resources in a way that is biologically *and* environmentally sensitive. In theory, genetic plasticity in the context of adverse environments, such as impoverished neighborhoods, stressed families, or chaotic households, result in more detrimental outcomes. Similarly, risky genes met with these adverse environments, may increase the likelihood of detrimental outcomes. If science eventually provides reliable and convincing evidence for these mechanisms, incorporating genetic markers into more sophisticated risk indices, made up of environmental and biological factors, may provide a more informed basis for determining what level and intensity of services and supports families need to have the best odds at physical, emotional, and financial wellness. These risk indices may be seen as more comprehensive screening instruments for intervention allocation, which may be particularly useful in eras of scarce resources. The continued efforts by the research community to answer the many outstanding questions in gene-environment work combined with a strong bridge between scientists, clinicians, and policy makers, may greatly improve the effectiveness of services and supports provided to children and families in need, through more targeted efforts and individually tailored effective interventions.

CHAPTER 4

CONCLUSION

The work presented here provides evidence of genetic and environmental influence on the development of prosocial behavior, via two distinct mechanisms: rGEs and GxEs. As reviewed, rGEs indicate that genes influence the social environment via behavior, while GxEs suggest that the extent of the environment's influence on behavior varies, partially based on genotype. Together, these mechanisms explain how biological influences get "outside the skin" to affect social developmental trajectories. A complex gene-environment pathway, as illustrated in Figure 1, encompassing of both rGEs and GxEs, served as the basis of these studies. There was a trend in findings, suggesting that genes were directly associated with social behaviors, which predicted the social environment. Some aspects of the social environment subsequently affected social behavior, the extent of which was partially dependent on genes. Together, these findings suggest interplay between gene-environment processes. Because the work presented here did not test the entire pathway in one model or with one set of variables, it is not appropriate to interpret this work as a seamless test of that model. This work does, however, serve as a promising starting point for future research that can extend beyond these analyses to examine the dynamic effects of genes, the environment, and rGE-GxE interplay on developmental trajectories over the life course. Together, these studies add to the growing body of literature that suggests that neither biology nor the environment, in isolation, nor a single gene-environment mechanism, determine social behavior; rather,

biology and the environment work together, through various mechanisms, to predict social outcomes.

Trends presented in these studies suggest that for positive forms of environmental exposure (i.e. preference and positive parenting) rGE processes seem to be more salient to prosociality, as associations were identified regardless of genotype. That is, positive-type environments were marginally associated with genes (i.e. DRD2) and predictive of prosociality, regardless of genotype. Conversely, for negative-typed exposure (i.e. negative parenting), GxE mechanisms seem to play a role, with stronger effects on children with certain genotypes and non-significant effects on children with different genotypes. This speaks to the importance of incorporating both negative and positive environments and behaviors in gene-environment analyses. Examining spectrum-wide variables may clarify under which contexts or circumstances certain genes function via rGEs, GxEs, or other mechanisms, across various stages in development.

The work presented here also contributes to the field's understanding of AVPR1a, DRD2, and DRD4 as important genes for social relationships. The promising results identified in the first study, suggest that the evocative-reactive model is one potential social behavioral mechanism through which AVPR1A affects parents' behavior. Our findings not only affirm the association between AVPR1a and social behavior, but also offer preliminary support for the contention that the microsatellite's length and developmental timing may be important factors that may predict individual differences in various features of social behavior. These factors, and likely others, may begin to explain inconsistent findings in the field (Knafo et al., 2008; Meyer-Lindberg et al., 2009; Tansey

et al., 2011). Because this notion is only speculative, as we did not explicitly test these factors, future work must continue to explore the directionality by which this and related microsatellites' lengths affects social behavior, at different points in development. To attain a better sense of process, other behavioral mediators that connect AVPR1a to the social environment as well as neural mediators that connect AVPR1a to social behavior, should also be the subject of future research.

DRD2, DRD4, and their composite were studied in the context of parenting and child prosociality, via GxE. Both genes and their composite interacted with negative parenting, but not with positive parenting, to predict prosociality. Findings consistently revealed an expected negative association between negative parenting and prosociality for most children, specifically those who were not carriers of any previously identified risk alleles (i.e. A1+ or long DRD4). For children who carried at least one of the risk alleles, the relation between negative parenting and prosociality was not significant. For these children, the pattern indicates an atypical response to an environmental influence, partially attributed to genes. As suggested, this may be due to lowered reward sensitivity or less attention to subtle negative social cues. Overall, much more research is needed to investigate the processes involved in these GxEs, especially because previous evidence has found both consenting and conflicting results (e.g. Gervai et al. 2007; Bakermans-Kranenburg and van Ijzendoorn, 2006; Dilalla, 2009). Empirical progress may benefit from more comprehensive and expansive genetic composites, made up of various functionally related genetic families, including perhaps dopamine, serotonin, hormone, and neuropeptide genes that can explain different complexities of social behavior.

Findings for DRD2 were particularly interesting given that this gene was examined across both studies, in the context of both rGE and GxE. Findings suggested a marginal association with father preference in adolescence (but not middle childhood) and a trend interaction with negative parenting in middle childhood (but not adolescence). These patterns may indicate that DRD2 exerts influence and interplays with the environment in different ways over the course of development, though this hypothesis is in need of further research. Somewhat similarly, AVPR1a influenced child prosociality in middle childhood, but not adolescence. Together, these findings indicate that genes may influence behavior differently depending on environmental exposure over the course of development, and that their interplay with the environment may also change, depending on age. As discussed at length, more developmentally aware and focused research is needed in behavior genetics so as to move beyond the mapping of genes on behavior at single points in time, as if behavior were static, to mapping genetic influence on developing behavior over time.

Although there is some research on DRD2 in the context of social behavior, it remains one of the less studied genes in this context. The literature on DRD2 is scattered, with influences identified across several disorders, including alcoholism, schizophrenia, Tourette's syndrome, ASD, ADHD, and internalizing symptoms (Comings et al., 1991; Glatt, Faraone, & Tsuang, 2003; Lawford, Young, Noble, Kann, & Ritchie, 2006; Saraceno, Munafo, Heron, Craddock & van den Bree, 2009). As is evidenced here, in a handful of other human studies (Fowler et al., 2011; Hanna et al., 2012; Hayden et al., 2010; Mills-Koonce et al., 2007; Propper et al., 2007), and in animal studies (see

Aragona et al., 2005; Skuse & Gallagher, 2009), DRD2 is implicated in social behavior. Perhaps a deficit in the dimension of social functioning is a common denominator between each of the listed disorders, with respect to DRD2. If the field shifts away from the discrete categorical definitions of the DSM, many of which are not biologically supported, and continues toward a more dimensional approach, where for example, the genetic underpinnings of social functioning (affected across all of these disorders) is the unit of analysis, more precise identification of biological pathways may be revealed, which will facilitate research into how those pathways lead into- and interact with- the social environment in different ways over the life course. The National Institute of Mental Health has recently announced a shift in this direction with the release of their Research Domain Criteria Project, focusing its funding on underlying dimensions of functioning (i.e. negative valence systems, positive valence systems, cognitive systems, systems for social processes, and arousal/modulatory systems), rather than on DSM-based categories (Insel, 2013b). This approach may ultimately bring a more cohesive set of conclusions on DRD2 and other genes and environmental processes.

The environmental aspects of both studies centered on aspects of the parent-child relationship: positive and negative parenting and parental preference. Positive parenting demonstrated the most robust findings with respect to its association with child prosocial behavior. Positive parenting is likely an indicator of a secure and healthy parent-child relationship and parents' positive behavior likely serves as a model for children's prosociality (see Eisenberg & Valiente, 2002; Iannotti, Cummings, Pierrehumber, Milano & Zahn-Waxler, 1992). In terms of parental preference, only father preference predicted

later child prosocial behavior, possibly due to the unique roles fathers play in social development, as previous work has found (Carson & Parke, 1996; Lamb. 2010; Youngblade & Belsky, 1992). For mothers, while their preference was not associated with later child prosociality, child prosociality did seem to influence their preference. Aforementioned unique twin- family dynamics or unanalyzed child behavioral mediators may explain the different environmental patterns noted between mothers and fathers.

Finally, findings revealed stability in child prosocial behavior between middle childhood and adolescence, consistent with previous work (Vaughan-Sallquist et al., 2009; Obradovicc et al., 2006) and complimentary of related research on the importance of early experiences (Anderson, 2003; Fox, Levitt, & Nelson, 2012; Roth & Sweatt, 2011; Shonkoff, 2011). If prosocial behavior stabilizes in middle childhood, or earlier, it is logical to follow that interventions implemented early will likely have lasting effects. Taken together, this evidence warrants increased policy action assuring that all children are in warm, secure, and enriching environments, whether at home, in early childhood settings, or in the community.

The most important contributions of these studies and similar work are the implications on the future of intervention, particularly in the domain of social functioning. The dimension of social development is not only important because well-being in humans is partially reliant on their abilities to form and maintain social relationships, but also because deficits in social functioning are present across numerous disorders, most notably ASD, but also mood and anxiety disorders, schizophrenia, ADHD, and others. By identifying the complex biological underpinnings of social

behavior—and how those underpinnings affect subtle social environmental changes— we can more appropriately intervene at critical time points to prevent, effectively ameliorate, or at least improve this dimension of psychopathology. Regarding rGEs specifically, with further research and understanding, clinicians may identify genetic risk and begin intervention much earlier than is currently customary, training families on what behaviors to expect and appropriate responses to those behaviors. This would allow parents to "get ahead of the curve", rather than try to intervene after two or three years of potentially maladaptive, trajectory-setting, parent-child interactions have passed. Parent responses to child behavior would be based on the science of positive parenting practices, rather than on potentially challenging child behavior, in effect breaking up naturally progressing deleterious rGEs. This may be interpreted as kick-starting an environmentally-based multiplier effect where the child's future behavior will correspond to the parent's positive responses, and so forth.

In the case of GxEs, clinicians and researchers may begin to catalogue which interventions show strong evidence for certain genotype-family combinations and which genotype-family combinations require different approaches to attain the same results. At a policy level, once more definitive information is understood about GxEs— for example, clarity regarding when GxEs operate under diathesis stress (i.e., risk) versus differential susceptibility (i.e., plasticity) — policy makers may assess total risk using environmental and biological factors, making for more robust screening tools to target those with the highest needs. Combined, rGEs and GxEs have much promise for the future of clinical

practice, through earlier detection, more personalized intervention, and more comprehensively informed targeting of the highest needs individuals.

Though the base for gene-environment research is growing rapidly, it is not yet the norm in the field of developmental science: too many environmental studies do not take biological influences on behavior into account, while too many biological studies pay little regard to the critical influences the environment has on behavior *and* biology. The majority of scientists accept that most behavior is explained by these joint influences, per theory and the recent compelling findings in GxE, rGE, and epigenetic research, but this knowledge has not yet catalyzed the important and necessary shift in the field toward much more interdisciplinary work, or at least more mutually informed work. This call for interdisciplinary work is not to say that research more narrowly focused on either biology or the environment is no longer necessary. For example, clearly more basic genetic and neurogenetic research is necessary to identify the function of genes and determine how they affect the brain, much in the same way that studies of attachment interventions can still offer important contributions to intervention science. In order to move to the next level, however, attachment researchers must understand the biological factors that contribute to their intervention's effectiveness in some families but not in others; similar to how geneticists and neurogeneticists must take into account how environmental influences, such as poor parent-child relationships, affect neural and genetic functioning differently over the course of human development. If environmentally-focused researchers understand biological processes and biological researchers understand social dynamics, the field's discoveries of causal pathways in developmental science may

accelerate and ultimately improve clinical interventions and child and family outcomes. Rather than a call to end narrowly focused research, a call for more interdisciplinary work demands these two fields form a more intentional link between their worlds when designing and interpreting studies. Cross-pollination between fields, whether in graduate classrooms or through more diverse research conferences and empirical journals, will bring two traditionally separate fields closer together.

The findings presented here demonstrate highly complex interplay between genes and various aspects of the social environment to influence one aspect of social functioning: prosocial behavior. Various future directions for the field were offered, including more dimensional and interdisciplinary research that mirrors the interplay between biology and the environment; increased attention to functional genetic and neurogenetic work, in order to identify precise biological causal pathways; continued and expanded attention to the role of biology in enhancing personalized treatment or developing interventions based on environmentally kick-started multiplier effects; and more urgent policy action, most notably increased funding and attention paid to early childhood development and family programs. Establishing a coordinated research agenda between behavior geneticists, developmental neuroscientists, and developmental scientists, paired with a seamless translational bridge to clinical intervention and policy may catalyze faster progress in developmental science and psychopathology, which will more accurately inform interventions that can help individuals of diverse diagnostic categories attain a higher quality of life.

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TABLES

Chapter Two

Table 1

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Twin Age (T1)	948	67.00	146	95.13	10.72
AVPR1a Continuous	850	637.90	691.00	662.85	7.35
DRD2	736	-.50	.50	-.13	.48
Prosocial Behavior (P-T1)	922	.00	2.00	1.34	.36
Prosocial Behavior (M-T2)	739	.00	2.00	1.39	.38
Mother Preference (M-T1)	926	1.00	5.00	3.00	.38
Father Preference (F-T1)	910	1.00	5.00	3.00	.48
Mother Preference (M-T2)	735	1.00	5.00	2.99	.30
Mother Preference (Tw-T2)	721	1.00	5.00	3.00	.47
Father Preference (F-T2)	423	1.00	5.00	2.99	.43
Father Preference (Tw-T2)	703	1.00	5.00	3.04	.54

Note: M= Mother; F= Father; Tw= Twin; T1= Time one; T2= Time two.

Table 2

Zero Order Correlations

Variable	AVPR1 (C)	DRD2	GxG	CGC	PS (M-T1)	PS (M-T2)	FP (F-T1)	MP (M-T1)	FP (F-T2)	MP (M-T2)	FP (Tw-T2)	MP (Tw-T2)
AVPR1 (C)	1	-.088*	.14**	-.38**	.052	-.070	.021	-.022	.024	-.026	.068†	-.047
DRD2		1	-.66*	.80*	-.042	.019	-.008	-.025	.050	-.013	.061	.044
GxG			1	-.63	.007	.001	.013	.013	-.04	.029	-.013	.031
CGC				1	.024	.033	-.010	-.010	.030	-.011	.047	.014
PS (M-T1)					1	.558**	-.053	-.034	-.018	.062†	-.052	.075†
PS (M-T2)						1	.037	-.011	-.022	.174**	-.090*	.167**
FP (F-T1)							1	-.174**	.112*	-.091*	.072*	.010
MP (M-T1)								1	-.164**	.069	-.045	.101*
FP (F-T2)									1	-.122**	.407**	-.222**
MP (M-T2)										1	-.129**	.342**
FP (Tw-T2)											1	-.222**
MP (Tw-T2)												1

Note: GxG= Gene by gene interaction; CGC: Cumulative genetic composite; PS= Child prosocial behavior; FP= Father preference; MP= Mother preference; M=Mother; F=Father; Tw= Twin; T1= Time one; T2= Time two. †p<.07; *p<.05; **p<.01.

Table 3

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Twin Age	948	67	146	95.13	10.72
DRD2	736	-.50	.50	-.13	.48
DRD4	831	-.50	.50	-.20	.46
Prosocial Behavior (Parent Report, Time 1)	922	0	2.00	1.34	.36
Prosocial Behavior (Parent Report, Time 2)	739	0	2.00	1.39	.38
Positive Parenting (Parent Report, Time 1)	922	-1.41	.69	.00	.36
Negative Parenting (Parent Report, Time 1)	922	-2.04	1.95	.00	.70
Positive Parenting (Parent Report, Time 2)	410	-3.12	2.68	.00	1.04
Negative Parenting (Parent Report, Time 2)	411	-3.76	3.64	.00	.90
Positive Parenting (Twin Report, Time 2)	721	-2.41	1.59	.00	.62
Negative Parenting (Twin Report, Time 2)	721	-1.87	2.13	.00	.68

Table 4

Regression Analyses on Child Prosocial Behavior at T1

Child Prosocial Behavior (T1)	*Unstandardized β*	*Standardized β*	*SE*	*p*
DRD2	-.02	-.03	.05	.49
Positive Parenting (Parent Report, Time 1)	.28	.30	.04	.001**
Positive Parenting (Parent Report, Time 1) X DRD2	-.02	-.01	.05	.83
DRD2	-.03	-.05	.05	.34
Negative Parenting (Parent Report, Time 1)	-.01	-.03	.04	.53
Negative Parenting (Parent Report, Time 1) X DRD2	-.01	-.01	.05	.91
DRD4	-.03	-.04	.04	.29
Positive Parenting (Parent Report, Time 1)	.28	.30	.04	.001**
Positive Parenting (Parent Report, Time 1) X DRD4	.02	.01	.04	.80
DRD4	-.04	-.05	.04	.19
Negative Parenting (Parent Report, Time 1)	-.01	-.01	.04	.78
Negative Parenting (Parent Report, Time 1) X DRD4	.08	.08	.04	.04*
CGPI	-.02	-.04	.04	.32
Positive Parenting (Parent Report, Time 1)	.28	.30	.04	.001**
Positive Parenting (Parent Report, Time 1) X CGPI	.01	.01	.04	.80
CGPI	-.02	-.04	.04	.32
Negative Parenting (Parent Report, Time 1)	.01	.02	.05	.63
Negative Parenting (Parent Report, Time 1) X CGPI	.06	.09	.04	.02*

Note: †$p<.07$; *$p<.05$; **$p<.01$.

Table 5

Regression Analyses on Prosocial Behavior at T2

Child Prosocial Behavior (T2)	*Unstandardized β*	*Standardized β*	*SE*	*p*
DRD2	-.03	-.03	.04	.47
Positive Parenting (Parent Report, T1)	.28	.28	.05	.001**
Positive Parenting (Parent Report, T1) X DRD2	.01	.01	.05	.90
DRD2	-.01	-.02	.04	.69
Negative Parenting (Parent Report, T1)	-.03	-.05	.04	.25
Negative Parenting (Parent Report, T1) X DRD2	-.02	-.02	.04	.71
DRD2	-.002	-.002	.04	.96
Positive Parenting (Parent Report, T2)	.04	.13	.07	.07†
Positive Parenting (Parent Report, T2) X DRD2	-.01	-.02	.05	.73
DRD2	.02	.02	.05	.64
Negative Parenting (Parent Report, T2)	-.03	-.07	.06	.27
Negative Parenting (Parent Report, T2) X DRD2	.09	.11	.06	.05*
DRD2	-.01	-.01	.04	.88
Positive Parenting (Twin Report, T2)	.07	.13	.04	.001**
Positive Parenting (Twin Report, T2) X DRD2	.001	.001	.04	.98
DRD2	-.01	-.02	.04	.69
Negative Parenting (Twin Report, T2)	-.07	-.13	.04	.002*
Negative Parenting (Twin Report, T2) X DRD2	.08	.07	.04	.09
DRD4	-.04	-.05	.04	.14
Positive Parenting (Parent Report, T1)	.26	.26	.05	.001**
Positive Parenting (Parent Report, T1) X DRD4	.001	.001	.04	.99
DRD4	-.05	-.07	.04	.08
Negative Parenting (Parent Report, T1)	-.02	-.03	.05	.46

Negative Parenting (Parent Report, T1) X DRD4	.03	.03	.04	.42
DRD4	-.05	-.07	.04	.08
Positive Parenting (Parent Report, T2)	.12	.14	.07	.07†
Positive Parenting (Parent Report, T2) X DRD4	-.04	-.05	.06	.36
DRD4	-.06	-.08	.04	.08
Negative Parenting (Parent Report, T2)	-.03	-.07	.07	.28
Negative Parenting (Parent Report, T2) X DRD4	.02	.02	.06	.74
DRD4	-.04	-.05	.04	.18
Positive Parenting (Twin Report, T2)	.08	.14	.04	.001**
Positive Parenting (Twin Report, T2) X DRD4	.04	.04	.04	.29
DRD4	-.05	-.06	.04	.12
Negative Parenting (Twin Report, T2)	-.07	-.13	.04	.001**
Negative Parenting (Twin Report, T2) X DRD4	.06	.06	.04	.18
CGPI	-.06	-.12	.04	.01*
Positive Parenting (Parent Report, T1)	.26	.26	.05	.001**
Positive Parenting (Parent Report, T1) X CGPI	-.04	-.03	.05	.53
CGPI	-.06	-.11	.05	.02*
Negative Parenting (Parent Report, T1)	-.01	-.01	.05	.78
Negative Parenting (Parent Report, T1) X CGPI	.02	.02	.05	.68
CGPI	-.05	-.10	.05	.04*
Positive Parenting (Parent Report, T2)	.04	.13	.07	.07†
Positive Parenting (Parent Report, T2) X CGPI	-.02	-.04	.06	.48
CGPI	-.06	-.10	.05	.03*
Negative Parenting (Parent Report, T2)	-.02	-.06	.06	.38
Negative Parenting (Parent Report, T2) X CGPI	.03	.05	.06	.45

CGPI	-.06	-.10	.05	.02*
Positive Parenting (Twin Report, T2)	.08	.14	.04	.001**
Positive Parenting (Twin Report, T2) X CGPI	.02	.03	.05	.57
CGPI	-.06	-.11	.05	.02*
Negative Parenting (Twin Report, T2)	-.06	-.12	.04	.004*
Negative Parenting (Twin Report, T2) X CGPI	.06	.08	.05	.08

Note: T1=Time one; T2= Time two. †p<.07; *p<.05; **p<.001

FIGURES

Chapter One

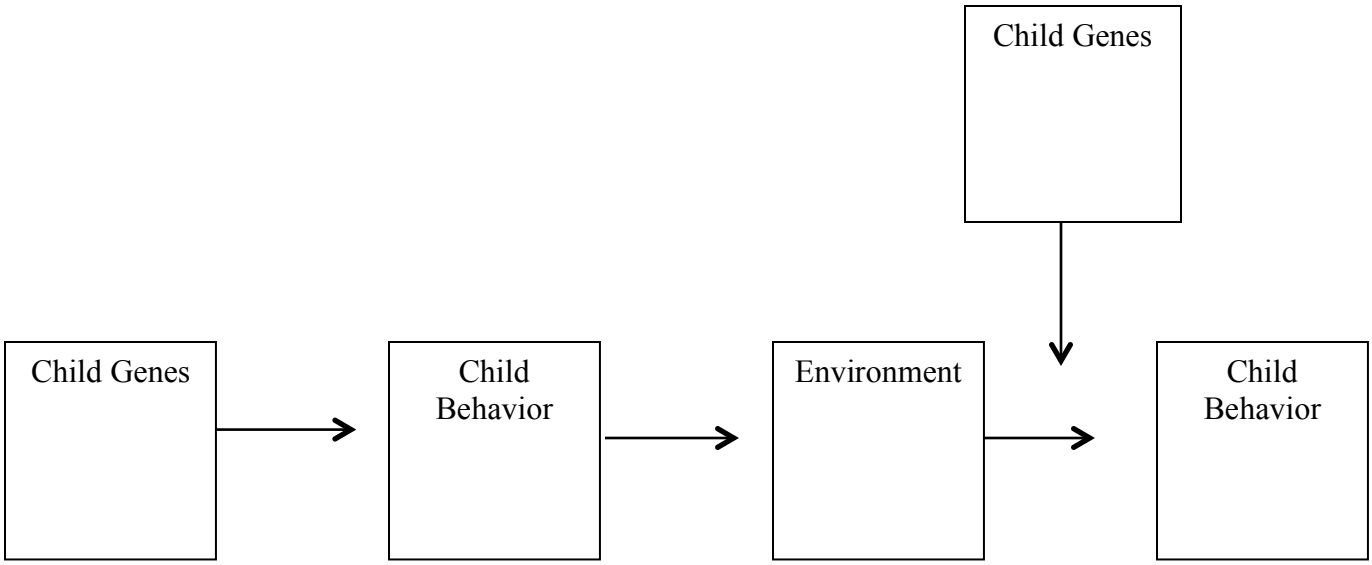
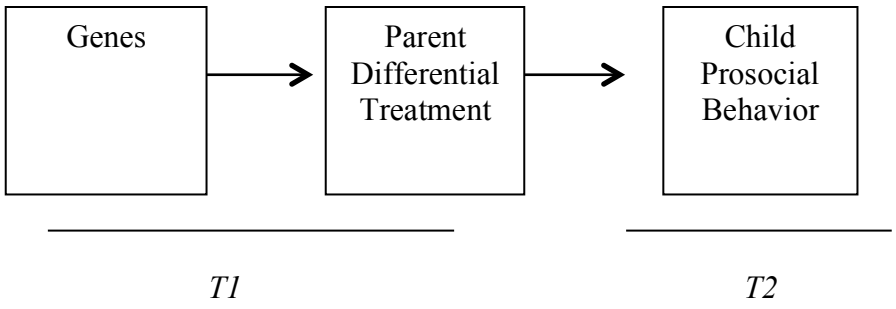


Figure1. Mechanisms of Genes-Environment Interplay in Child Development.

Socially-mediated Path



Evocative Path

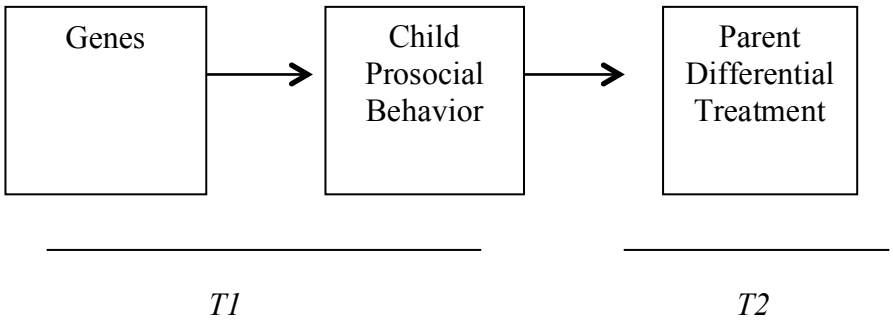


*Figure 2.*Gene-Environment Correlations: Socially-mediated and Evocative Path.

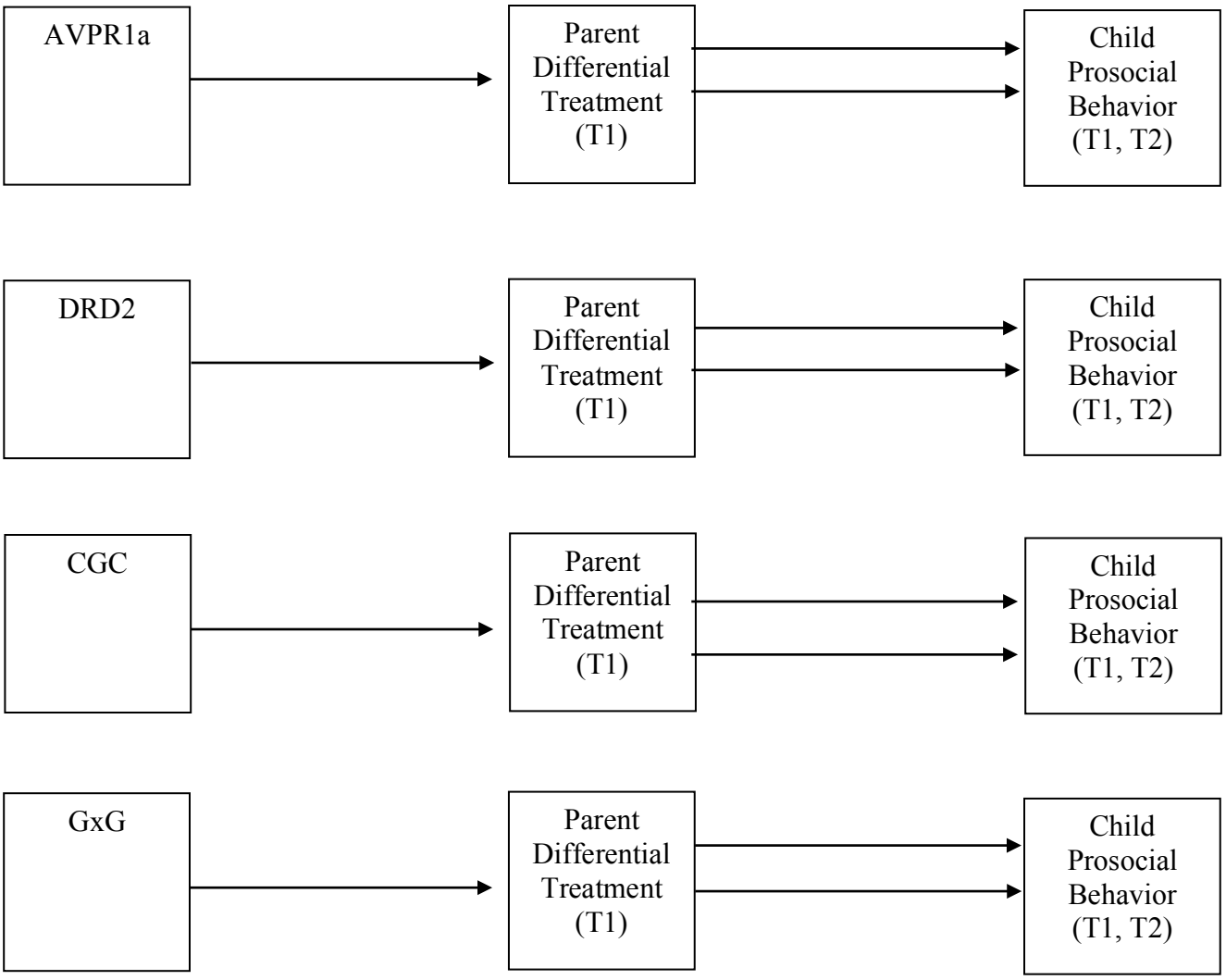


Figure 3. Series of Proposed Socially-Mediated Analyses. AVPR1a= Child arginine vasopressin receptor 1a gene; DRD2= Child dopamine receptor D2 gene; CGC= Cumulative genetic composite; GxG= Gene-by-gene interaction.

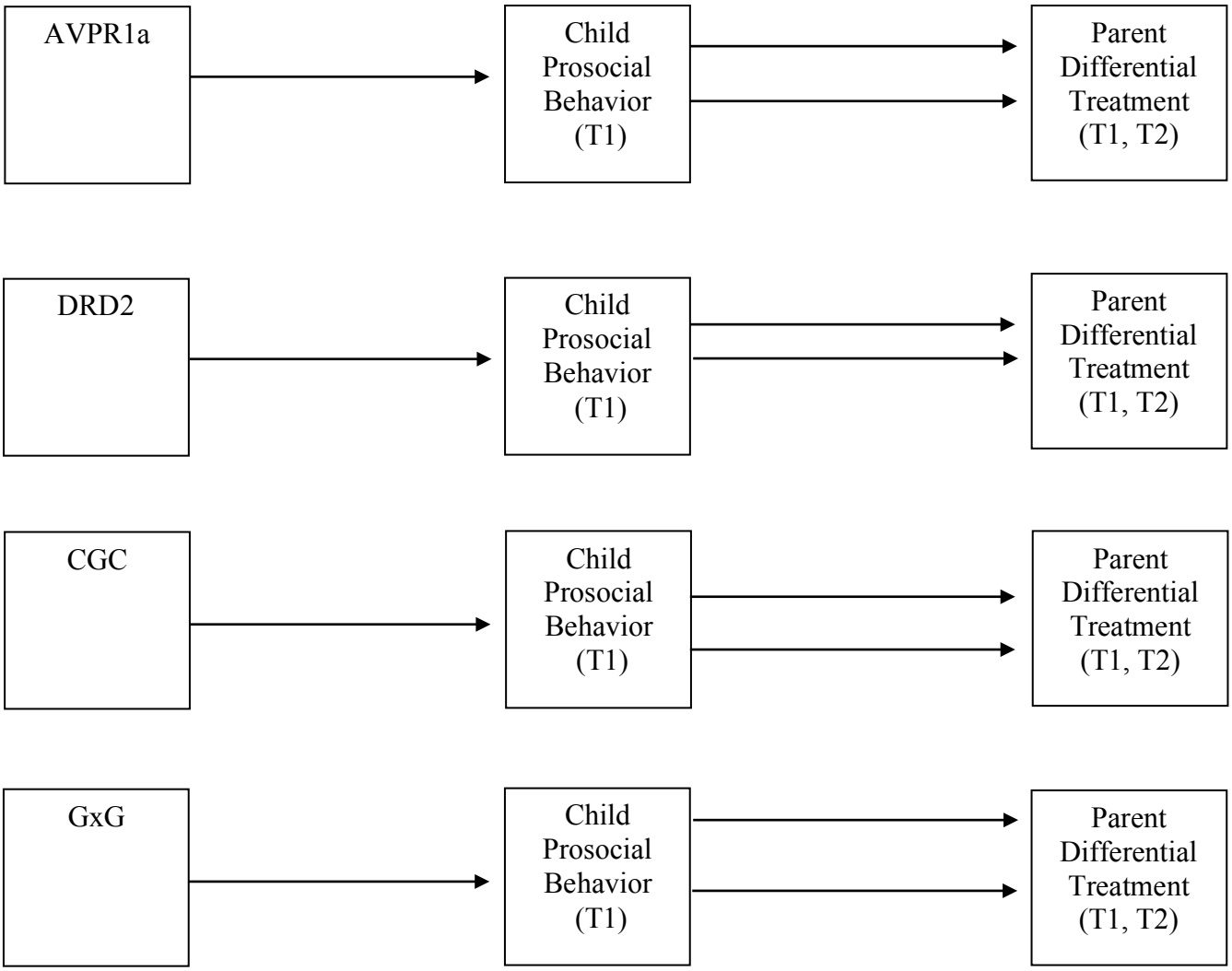


Figure 4. Series of Proposed Evocative Analyses: AVPR1a= Child arginine vasopressin receptor 1a gene; DRD2= Child dopamine receptor D2 gene; CGC= Cumulative genetic composite; CPS= Child Prosocial Behavior at T1; PDT (T1)= Parental differential treatment at T1; PDT (T2)= Parental differential treatment at T2.

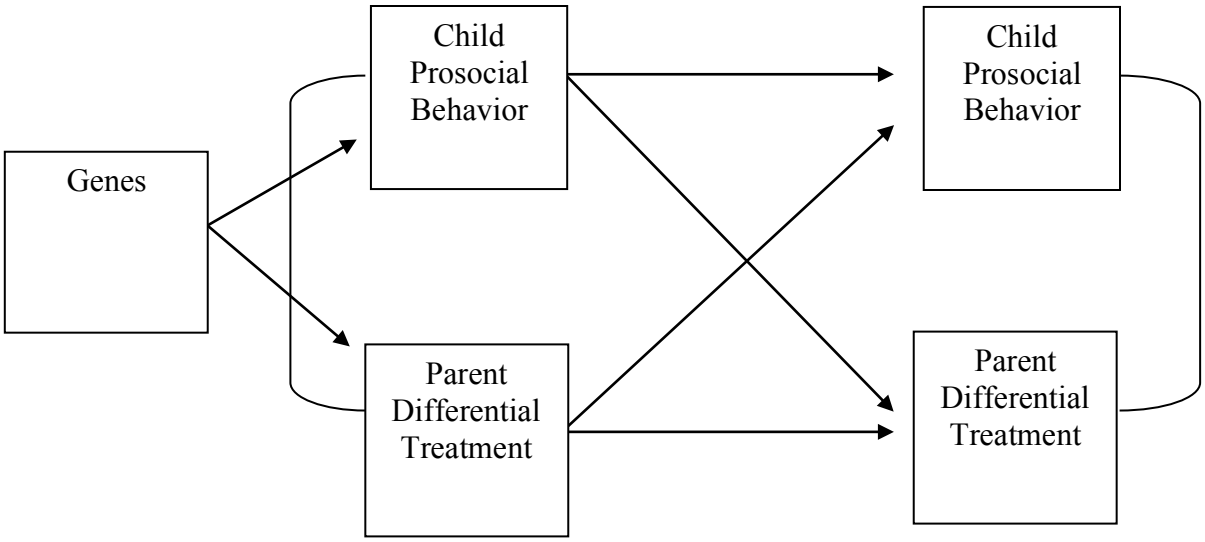


Figure 5. Conceptual Model: Cross-Lagged rGE Model.

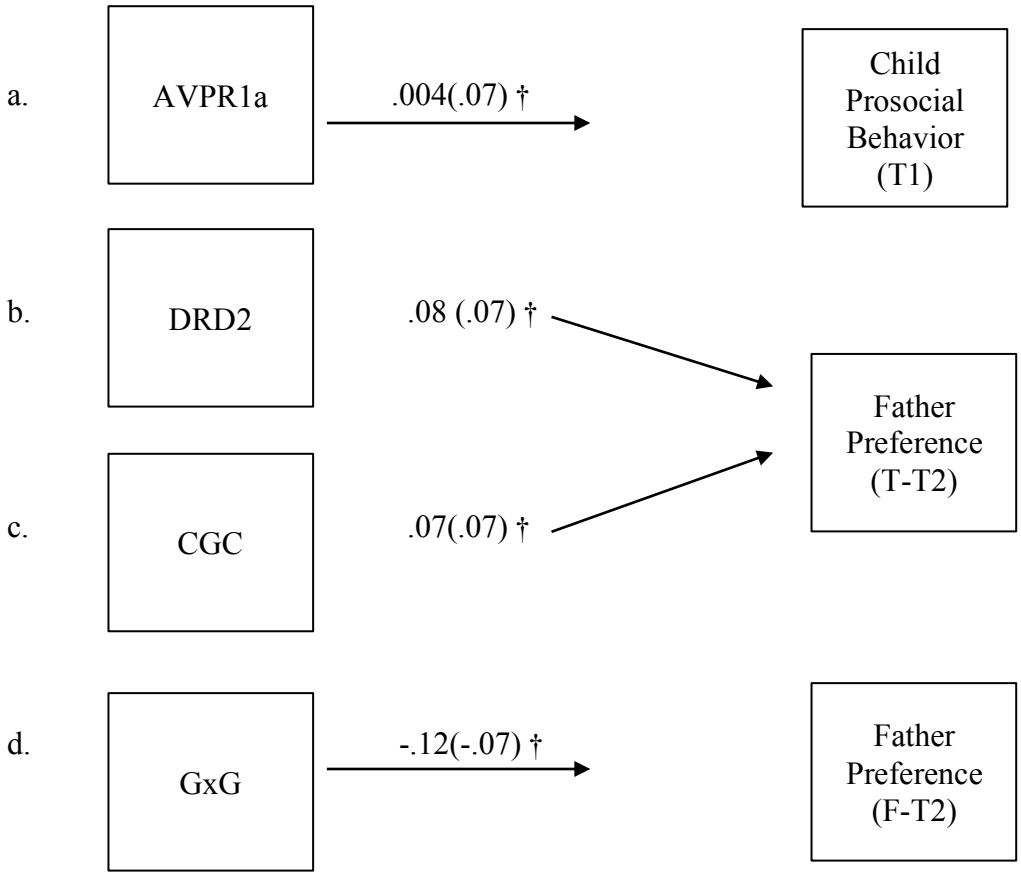


Figure 6. Genetic- Behavior and Gene-Environment Correlations. Numbers outside parenthesis are unstandardized coefficients; numbers inside parenthesis are standardized coefficients. All analyses included sex, age, and SES as covariates. †p<.07; *p<.05; **p<.01.

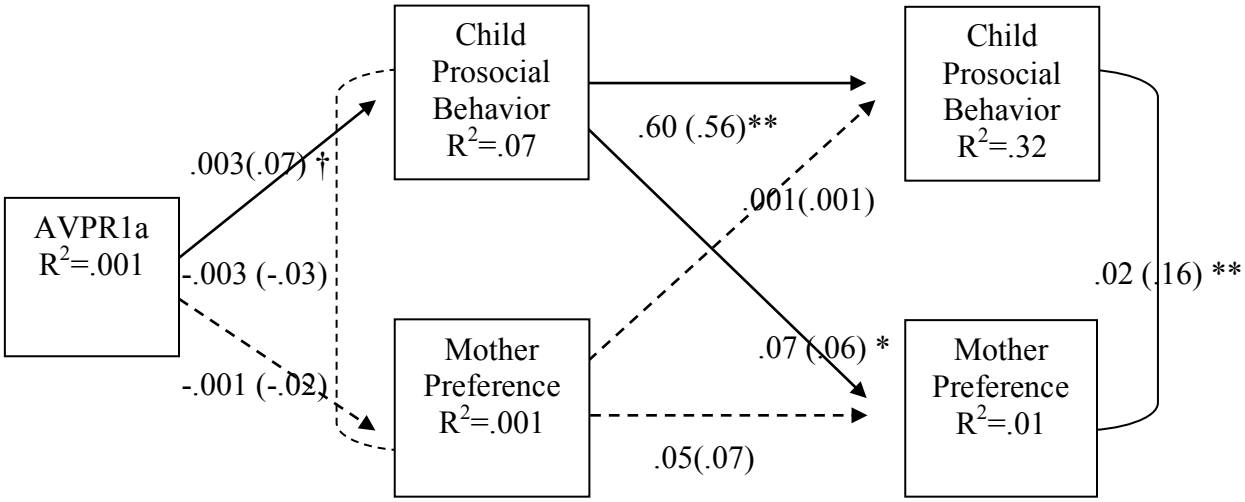


Figure 7. Cross Lagged Model: AVPR1a, Child Prosocial Behavior, and Mother Preference. Numbers outside parenthesis are unstandardized coefficients; numbers inside parenthesis are standardized coefficients. Solid lines indicate marginal or significant findings; dotted lines indicate non-significant findings. †p<.07; *p<.05; **p<.01.

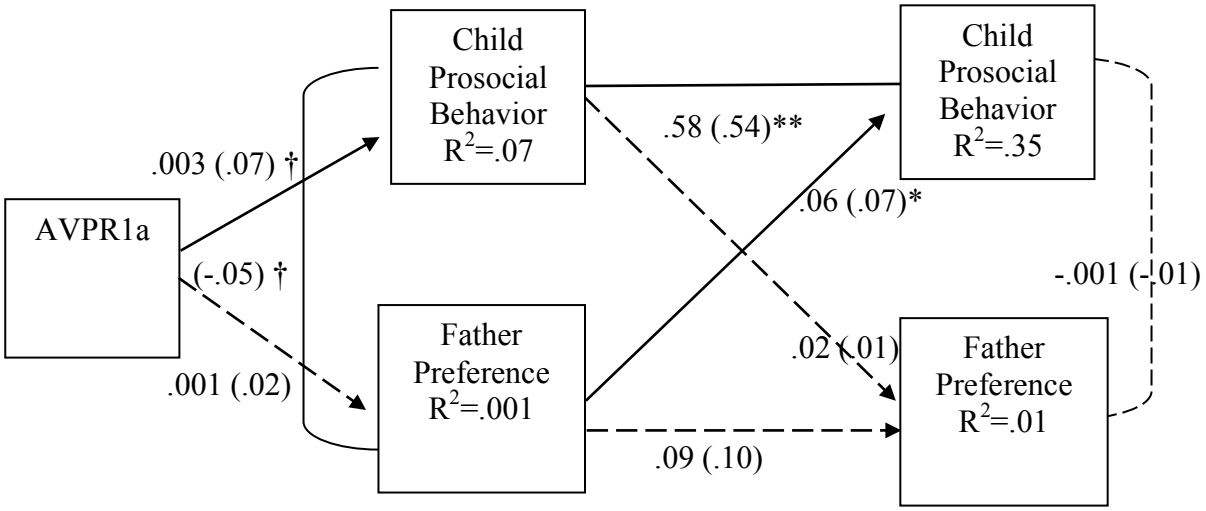


Figure 8. Cross Lagged Model: AVPR1a, Child Prosocial Behavior, and Father Preference. Numbers outside parenthesis are unstandardized coefficients; numbers inside parenthesis are standardized coefficients. Solid lines indicate marginal or significant findings; dotted lines indicate non-significant findings. †p<.07; *p<.05; **p<.01.

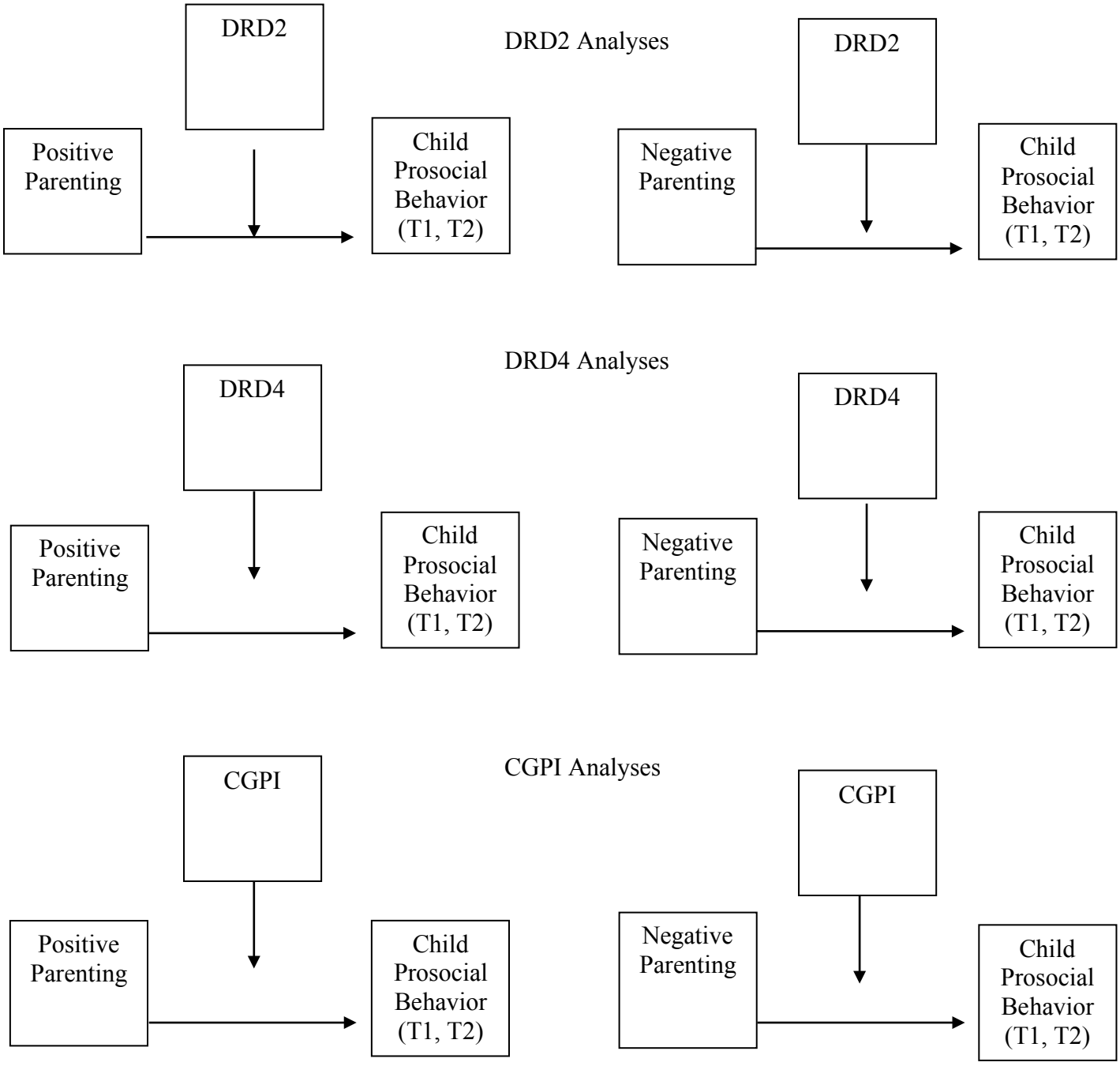


Figure 9. Series of Moderation Analyses. T1=Time one; T2= Time two.

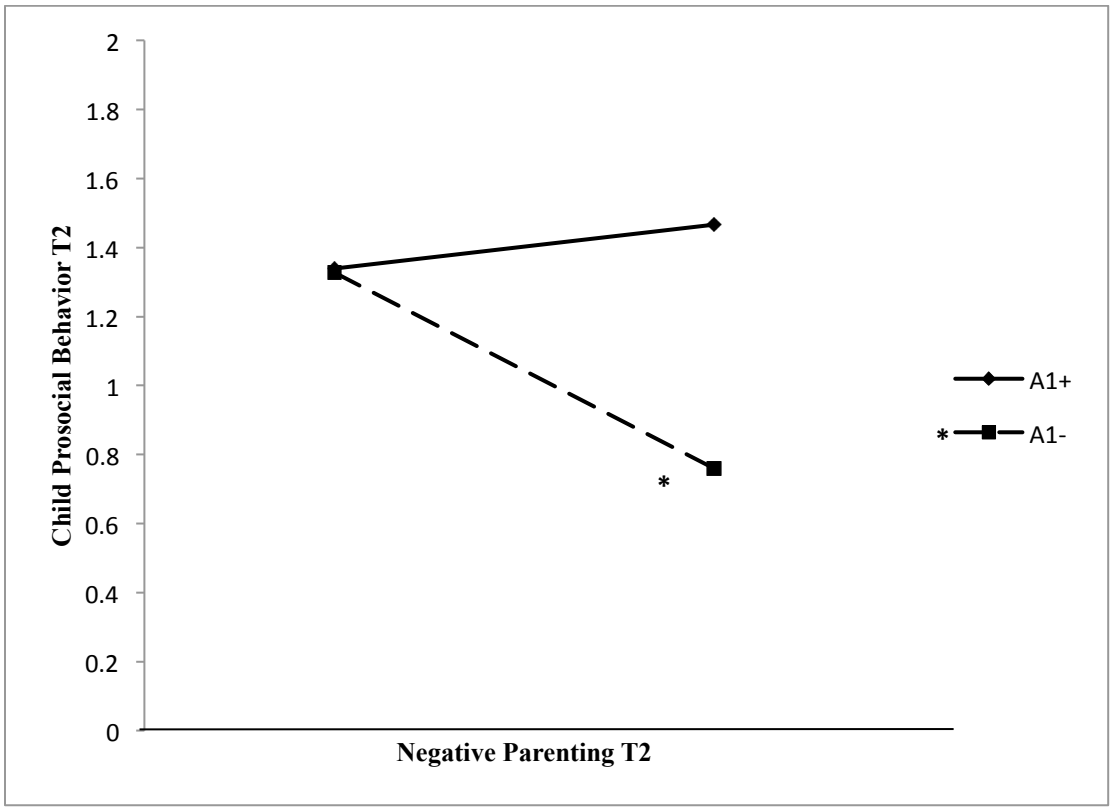


Figure 10. Gene-Environment Interaction: Negative Parenting at T2, DRD2, and Child Prosocial Behavior. * $p < .05$

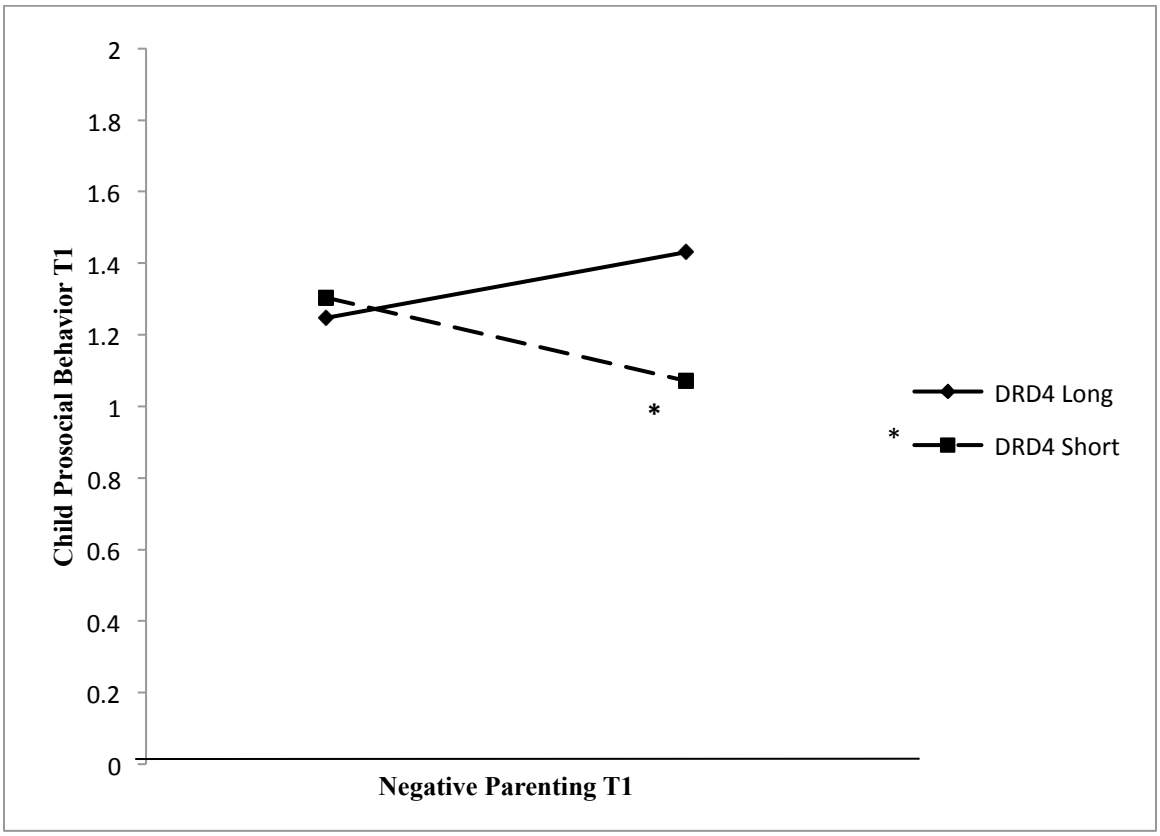


Figure 11. Gene-Environment Interaction: Negative Parenting at T1, DRD4, and Child Prosocial Behavior. * $p < .05$

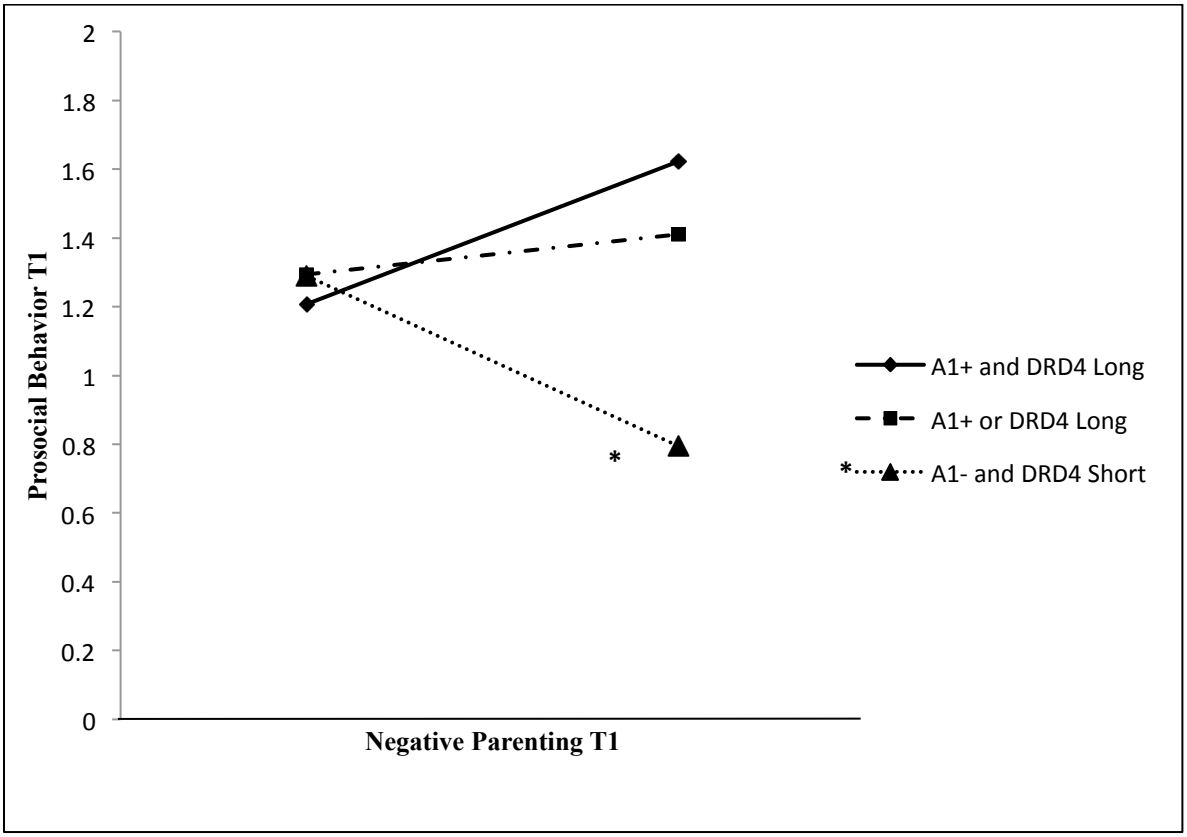


Figure 12. Gene-Environment Interaction: Negative Parenting at T1, CGPI, and Child Prosocial Behavior. * $p < .05$