Family Structure, Parenting, Genes and the Co-development of Behavioral Problems

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Abstract:

Child behavioral problems co-occur at a higher rate than would be expected by chance, but little is known about different classes of individuals based on the development of more than one domain or how the *co-development* relates to family structure and parenting or genes. The present study uses identified groups based on the co-development of behavioral problems in children ages 3-9 and examines how these trajectory groups are associated with family structure and parenting prior to age 3 in the Fragile Families and Child Wellbeing study. We also include serotonergic and dopaminergic pathway genes known to be related to behavioral problems and sensitivity to environmental influence. We find that being in one of the three groups: 1) a low symptoms class, 2) a decreasing symptoms (from 3-9) class, and 3) a severe symptoms class for internalizing and externalizing (and anxiety and depression) is strongly associated with family structure and parenting. Further genes appear to only play a significant role among the severe symptoms group, and when included lead to 50% larger parenting and family structure effects.

The long term consequences of childhood behavioral problems (CBP) are well documented and involve a wide range of negative outcomes in adulthood, including lower educational attainment (McLeod and Fettes 2007), higher rates of mental adult illness and criminal behavior (Fergusson, Horwood, and Ridder 2007; Knoester 2003; Mannuzza, Klein and Moulton 2008; Reef et al 2010), persistent anti-social behavior (Bongers et al 2008; Moffitt 1993; Simonoff et al 2004), substance abuse (Fergusson, Horwood, and Ridder 2005), and poor relationship quality (Knoester 2003). An important consideration in this work, however, is that children are the product of continuous, reciprocal interactions between the child and the environment (Cicchetti, 1984; Sameroff, 2010; Sameroff, 2000; Sroufe & Rutter, 1984). Children's internalizing reactions (e.g., feelings of anxiety, depression) as well as their externalizing reactions (e.g., aggressive and rule-breaking behavior) in relation to their environments are thus dynamic processes that unfolds over time as trajectories (Masten & Cicchetti, 2010; Sameroff, 2010). Application of the developmental and life course perspectives has given rise to several studies on the development of psychosocial and wellbeing domains in many fields. For example in sociology, demography and developmental psychology, a large body of research shows that family instability and harsh parenting is positively associated with CBP (Brown 2006; Cavanagh, Crissey and Raley 2008; Cavanagh and Huston 2006; Cherlin et al. 1991; Fomby and Cherlin 2007; Hao and Xie 2002; Manning and Lamb 2003; McKnight and Loper 2002; McLanahan and Sandefur 1994; Osborne and McLanahan 2007; Seltzer 1994; Wu and Thomson 2001). Similarly a large body of literature in developmental psychology, biology, and public health finds that genetic markers in the dopaminergic (Miczek et al. 2002; Young et al 2002; Benjamin, Ebstein, & Belmaker, 2002; Schmidt et.al., 2002) and serotoninergic systems (Fox et al 2005) are associated with CBP.

However rarely are the multiple processes studied jointly (Cicchetti & Rogosch, 2002; Rutter & Sroufe, 2000). Psychological disorders and CBP co-occur at a much higher rate than would be expected by chance (Angold, et al., 1999). For example, youth with depression are 8.2 times more likely to be diagnosed with an anxiety disorder, and youth with a conduct disorder are 6.6 times more likely to be diagnosed with depression (Angold, et al., 1999). Because of high rates of co-occurrence and

comorbidity, focusing on a single symptom domain (e.g., anxiety, aggression, internalizing, or externalizing, etc.), as many studies do, may underestimate the influence of factors that are related to larger underlying processes—like genetics and family environment. One way to obtain a more nuanced and comprehensive understanding of CBP then is to investigate how domains co-develop, or change concurrently, and how the co-development of different aspects of CBP may differ across groups of individuals, but few studies have done this.

In this paper we argue that by modeling the co-development of different domains of CBP we can better measure underlying process of children's socio-emotional development. Further we argue that greater integration of the biological and social science literatures improves our understanding of children's socio-emotional development and long term health and wellbeing. By using classes, or groups, determined by parallel-process growth mixture models of CBP we extend the literature in 3 important ways. First, we document the extent to which the family environment, namely family structure and harsh parenting, is associated with the co-development of 3 CBP domains: 1) internalizing and externalizing behaviors, 2) depression and anxiety, and 3) aggression and rule-breaking. Second we document the extent to which serotonergic and dopaminergic genes are associated with being in different classes of co-development of the 3 sets of CBP. Finally, third, we document the extent to which genes and family environment interplay to influence the co-development of CBP. To accomplish this work we use data from the first 5 waves of the Fragile Families and Child Wellbeing Study (FFCWS).

Growth Mixture Models of Psychological Symptom Domains Examined Separately

A handful of child and adolescent studies used growth mixture modeling to examine internalizing (Proctor, et al., 2010; Sterba, et al., 2007), and its components of anxiety (Broeren, et al., 2013; Crocetti, et al., 2009; Duchesne, et al., 2010; Feng, et al., 2008; Marmorstein, et al., 2010) and depression (Marmorstein, et al., 2010; Yaroslavsky, et al., 2013). A few middle childhood and adolescent studies examined externalizing (Latendresse, et al., 2011; Proctor, et al., 2010; Silver, et al., 2010); more studies, almost all starting in late childhood/adolescence, examined a component of externalizing, aggression (e.g., Cote, et al., 2006; for reviews, see Jennings & Reingle, 2012; Shaw, et al., 2012). These studies that

only examined one symptom domain at a time (internalizing, anxiety, depression, externalizing and aggression separately) generally found a large normative group characterized by low levels of symptoms as well as a smaller severe class characterized by high stable or increasing symptoms, but varied in the number of intermediate classes. Often, studies found one intermediate class characterized by initially high symptoms that decreased over time and/or an additional intermediate class characterized by initially low symptoms that increased, although this was not always the case. In aggression, for example, one study found no intermediate classes (a total of two classes, low and high) (Petras, et al., 2011).

Only two studies examined the joint probabilities of being in different combinations of internalizing and externalizing classes. The first study examined adolescents in middle school and the first year of high school (Chen & Simons-Morton, 2009). They found that among boys and girls with the highest level of conduct problems, few experienced the highest level of depression symptoms, but among boys with the highest levels of depression symptoms, a large proportion (42%) experienced the highest levels of conduct problems (Chen & Simons-Morton, 2009). This was not true for girls, however; only 10% of the girls with the highest levels of depression symptoms experienced the highest level of conduct problems (Chen & Simons-Morton, 2009). A second study identified internalizing and externalizing classes separately for toddlerhood through late childhood, and then calculated the joint probability of being in both types of classes (Fanti & Henrich, 2010). This study, however, had to discard 4 potential combinations of classes because of low probabilities that the individuals assigned to that group actually belonged in that group (Fanti & Henrich, 2010). This method of calculating the joint probabilities is a fruitful starting place. However, because this method is constrained to combinations of internalizing and externalizing classes that have already been identified in separate, single class models, there is less flexibility to allow groups based on simultaneous examination of internalizing and externalizing to emerge. A more data-driven approach, such as parallel process growth mixture modeling, could allow for greater validity in classifying individuals based on simultaneous consideration of growth factors.

Consistent with a person-centered approach emphasized (Cicchetti, 1984; Sameroff, 2000; Sroufe & Rutter, 1984), using parallel process growth mixture modeling as the statistical tool (Greenbaum &

Dedrick, 2007; Wu, et al., 2010), researchers can sort individuals into groups based on changes in more than one symptom domain simultaneously (e.g., anxiety and depression, internalizing and externalizing, or aggression and rule-breaking). This approach can identify subgroups that would otherwise be obscured by looking at a single time point (i.e., some individuals who have low levels of symptoms at an early age may stay low, but others who start low may increase over time). Also, examining domains concurrently as parallel processes, instead of simply averaging or summing the symptom domains, is advantageous because it allows researchers to distinguish whether individuals have moderate levels in both symptom domains versus high levels in just one symptom domain and low in the other.

Only one study used this parallel process growth mixture modeling approach to examine the co-development of psychological symptom domains in a youth sample, investigating internalizing and externalizing (Hinnant & El-Sheikh, 2013). This study focused on a later period in childhood, ages 8 to 11. The authors identified three classes based on the co-development of internalizing and externalizing. The normative, largest class was characterized by low, decreasing internalizing and externalizing; an intermediate class was characterized by moderate levels of internalizing and low levels of externalizing; and a severe class was characterized by high, stable levels of internalizing and high, increasing levels of externalizing (Hinnant & El-Sheikh, 2013).

Family Structure and Parenting in Relation to Childhood Behavioral Problems Trajectory Groups

Beyond classifying individuals based on the co-development of symptoms, it is also important to investigate how developmental patterns of environmental factors, such as family structure and parenting, contribute to the co-development of symptom domains, in order to have a fuller picture of how these processes unfold over time. Unfortunately, but not surprisingly considering the sparse literature cited above, we can find no documentation of the effects of family structure or parenting on the co-development of CBPs. However, a large body of empirical evidence finds that family structure and parenting is associated with CBP, beginning in early childhood and extending through adolescence and into adulthood (Brown 2006; Cavanagh, Crissey and Raley 2008; Cavanagh and Huston 2006; Cherlin et al. 1991; Fomby and Cherlin 2007; Hao and Xie 2002; Manning and Lamb 2003; McKnight and Loper

2002; Osborne and McLanahan 2007; Seltzer 1994; Wu and Martinson 1993; Wu and Thomson 2001). Family structure (and changes in that structure) are often tied to different levels of stress and resources which result in wellbeing differences for children (George, 1989, 1993; Holmes and Rahe 1967; Rutter 1983).

Similarly, harsh parenting, which includes physical assault (e.g., hitting) as well as psychological aggression (e.g., threatening to hit the child) by the parent or caregiver, plays a major role in the development of CBP (for reviews, see Cicchetti & Toth, 1995; McCrory, et al., 2012; Oswald, et al., 2010). Harsh parenting is particularly relevant because during early developmental stages (early childhood to middle childhood), parents are the major external influence on the child and the home is the primary environment for the child. At this age, children have yet to undergo the social shifts that occur in adolescence where peers grow in importance and parents become a less prominent factor in development (Steinberg & Morris, 2001). Relating trajectories of harsh parenting to symptom co-development therefore captures a potentially major influence on symptoms during this crucial developmental period.

Genes in Relation to Childhood Behavioral Problems Trajectory Groups

A well-established literature examines genetic influences on many anti-social behaviors including CBP (Moffitt 2005). This research began by looking at correlations within and between families via twin and adoption studies (Rhee and Waldman 2002). However, with the increasing availability of molecular biological markers (i.e. specific gene variants), researchers have begun to explore the specific biological pathways that influence a wide range of behaviors. Most of this research has centered on the role of several monoamine neurotransmitter systems; for the purposes of this paper we focus on two of the most prominent systems: dopamine and serotonin. We should note that both systems are influenced by scores of genes, and each gene may have several markers (many of them highly correlated with each other), which has led to an enormous expansion of the literature. Further confusing the literature is that most genes appear to have small influences on a wide range of behaviors, suggesting an underlying processes that is not accounted for when examining each behavior separately.

Dopamine is a neurotransmitter, a chemical that transmits signals in between the nerve cells (neurons) of the brain. Of primary interest here are the functions of dopamine neurons located in a part of the brain called the ventral tegmental area (VTA) that help regulate thought, movement, attention, motivation and learning (Ungless, Magill and Bolam 2004; Brischoux, Chakraborty, Brierley, and Ungless 2009). VTA dopamine neurons become activated when something good or bad happens. If the event is pleasurable then dopamine is released leading to greater focus and motivation to continue the activity; if it is painful, dopamine levels are lowered, resulting in less focus and less desire to continue the activity. Those with higher levels of dopamine typically have less attention and greater thrill seeking—which, depending on several other factors, can result in higher rates of externalizing behavior and lower internalizing behavior (Zald et al 2008; Miczek et al. 2002; Young et al 2002; Benjamin, Ebstein, & Belmaker, 2002; Schmidt, Fox, & Rubin, 2002; Bakermans-Kranenburg and van IJzendoorn 2006; Guo, Roettger and Shih 2007).

Serotonin is also a neurotransmitter that helps to regulate the cognitive functions of memory, mood and learning. However, in contrast to the dopaminergic system, the serotonergic system does not have as strong a connection for externalizing behaviors, but rather for internalizing behaviors such as depression, anxiety and being withdrawn (Uher and McGuffin 2010; Williams et al 2003). Primarily it is hypothesized to work on externalizing behaviors by inhibiting all social actions, thereby lowering externalizing behaviors (Fox et al 2005). However, neither serotonin nor dopamine have been shown to be related to the co-development of CBP—despite strong theory that they are more likely to influence the co-occurrence of these behaviors over independent changes.

Gene-Environment Interactions and Biological Susceptibility

Studies of human molecular genetics and social environment interactions (GxE) have increased dramatically during the past decade. Most of these studies rely on the classic diathesis-stress model that treats genetic variations and environments as being either “risky” or “protective” (Belsky and Pluess 2009). According to this view individuals have a vulnerability in their temperament—which may be a result of genetics or some other physiological process—that makes them more likely to be unfavorably

influenced by a stressful environment or event. Thus, when the person with the negative temperament is placed in a negative environment they experience negative outcomes, while nearly everyone else is assumed to have similar, more favorable outcomes.

More recently, researchers have proposed a 'genetic plasticity' or 'biological susceptibility' model, which posits that some genotypes are highly susceptible to environmental influences (both positive and negative), whereas others are not (Belsky and Pluess 2009; Boyce and Ellis 2005; Ellis and Boyce 2008; Belsky et al 2009). This model implies a cross-over effect, with those who have greater genetic susceptibility experiencing more negative outcomes than others when the environment is 'unfavorable' and more positive outcomes when the environment is 'favorable' (Mitchell et al 2011; Mitchell et al 2013). This model is often referred to as the "orchid-dandelion hypothesis," to highlight the fact that some genotypes (orchids) are highly susceptible to environmental influence whereas others (dandelions) are not. Due to the novelty of the biological susceptibility model there is little guidance in how to determine the reactivity of a genetic variant or polymorphism. To date most studies have taken genetic markers that were formerly classified as "risky" and reclassified them as "reactive" (Belsky et al 2009; Belsky 2011; Mitchell et al 2011; Mitchell et al 2013).

Recent GxE work has shown a strong possibility of an interaction between dopaminergic and serotinergic genes and parenting for CBP. A recent meta-analysis found that although children (under age 10) with typically defined "risky" dopamine genetic markers had higher levels of externalizing behavior in negative parenting environments, they also had lower levels of externalizing behavior in more supportive parenting environments (compared to children without these genetic variants; Bakermans-Kraneburg and Ijzendoorn 2011). One study even found experimental evidence where toddlers with a reactive dopamine receptor D4 gene (DRD4) genotype were more affected by experimentally induced changes in parenting than children without the DRD4 variant (Bakermans-Kranenburg et al. 2008). Finally another paper showed that family structure instability was differentially associated with externalizing behavior trajectories based on dopaminergic and serotonergic genes. However, none of these have looked at the interaction of family environment and genes for the co-occurrence of CBP.

Methods

Participants

Data were from the Fragile Families and Child Wellbeing Study (Reichman, et al., 2001), which follows a large, representative cohort of predominantly low-income children born in 20 large cities in the United States between 1998 and 2000. Families were recruited to participate at the hospital after the focal child's birth. The present study used data from mother or other primary caregiver in-home interviews at ages 3, 5, and 9 of the child from 18 of the 20 cities. Data from the 18 cities included in the present study are nationally representative when weighted. Of a total 4688 families recruited to participate, 4192 completed the harsh parenting measure (Conflict Tactics subscales Psychological Aggression and Physical Assault) and 4397 completed the CBP domains measure (Child Behavior Checklist) for at least one of the three time points (ages 3, 5, and 9); these data were included in the analyses. Participant characteristics are shown in Table 1.

Measures

Child Behavioral Problems

Psychological symptom domains (internalizing, externalizing, anxiety, depression, aggression and rule-breaking) were assessed using the parent-report form of the Child Behavior Checklist (CBCL). The CBCL/2-3 version (Achenbach, 1992) was collected at age 3, CBCL/4-18 (Achenbach, 1991) at age 5, and CBCL/6-18 (Achenbach & Rescorla, 2001) at age 9. Although different versions of the CBCL are given across ages, the constructs that they measure are similar across versions. Moreover, the CBCL/2-3 version contains modifications of the questions for very young children in order to measure symptom domains in a developmentally appropriate manner.

"Depression" symptoms were operationalized using the withdrawn (CBCL/2-3 and 4-18) and withdrawn/depressed (CBCL/6-18) subscales. Internal consistencies for Depression were alpha = .66, .59, and .70 for age 3, 5, and 9 in our sample. "Anxiety" was measured using the anxious/depressed subscales across all three versions (Cronbach's alphas = .63, .68, and .78). "Internalizing" was comprised of the combination of the Anxiety and Depression subscales (Cronbach's alpha = .75, .76, and .84). To be

consistent with the CBCL/2-3 and CBCL/4-18, the somatic complaints subscale was not included with Anxiety and Depression when calculating Internalizing for CBCL/6-18.

"Aggression" was operationalized as the aggressive subscale across all versions (Cronbach's alphas = .86, .85, .89). The destructive (CBCL/2-3), delinquent (CBCL/4-18), and rule-breaking (CBCL/6-18) subscales represented "Rule-breaking" (Cronbach's alphas = .65, .49, and .77). At age 5, three items from the delinquent subscale ("Thinks about sex too much", "Truancy, skips school", and "Uses alcohol or drugs for non-medical purposes") were omitted because they are not very applicable to very young children. "Externalizing" was comprised of the Aggression and Rule-breaking subscales (Cronbach's alphas = .88, .87, .91). Mean item scores were calculated to represent each subscale, and thus all subscales ranged from 0 to 2. The questions that were used to calculate each scale at each time point are listed in Supplemental Methods.

Group Trajectories[1]

To identify groups based on developmental trajectories of symptom domains and of harsh parenting, we used two forms of growth mixture modeling, parallel process growth mixture modeling and latent class growth analysis, with Mplus version 5.21 statistical software (Muthen & Muthen, 1998-2007). Growth mixture modeling is a person-centered analysis that allows identification of unobserved but distinct groups of individuals who have similar developmental trajectories (Muthen & Muthen, 2000). To identify groups of individuals who have similar trajectories of symptoms, we used parallel process growth mixture modeling, which assigns individuals to groups based on initial levels (intercepts) and changes (slopes) in multiple domains concurrently (Wu, et al., 2010). We ran separate models for the co-development of internalizing and externalizing, anxiety and depression, as well as aggression and rule-breaking. To determine groups of individuals with similar trajectories of harsh parenting, we used latent class growth analysis (Muthen & Muthen, 2000).

[1] The documentation of these groups is beyond the scope of this paper but is a companion paper (Wiggins et al 2013).

--Table 1 and Figure 1about here--

We found that the co-development of internalizing and externalizing is best described by three classes (see Table 1 and Figure 1 for more detail). The first class, IE-1, represents the normative trajectory of internalizing and externalizing over ages 3-9, encompassing 73% of the sample. This class is marked by initially low, declining levels of internalizing and initially medium, declining levels of externalizing. The next largest class (IE-2, 23%) has medium levels of internalizing that decrease over time and initially high but declining externalizing. The third class (IE-3, 4%), represents a subgroup of individuals that start out with medium levels of internalizing that increase over time and high, stable externalizing levels.

We similarly found a three-class model was accepted as best-fitting for the co-development of anxiety and depression. Normatively, individuals start with low levels of anxiety and depression that decrease from age 3 to 9 (AD-1, 82%). A second class of children start with high levels of anxiety and medium levels of depression, both of which decrease over time (AD-2, 14%). The third class (AD-3) is marked by initially medium levels of anxiety and depression (intermediate between the normative class (AD-1) and the second class (AD-2)) that *increase* over time.

A parallel process growth mixture model approach yielded only two classes for the concurrent development of aggression and rule-breaking behaviors. The two classes are characterized by similarly decreasing slopes and differentiated only by intercepts (one class has higher starting levels of aggression and rule-breaking than the other class).

--Table 2 about here--

Family Structure at Birth and until age 3

Family structure and the limited family structure instability between birth and age 3 is measured using data gathered at each wave from the mother on the current relationship status and past relationship history with the biological father (only a few new fathers entered in this time period, so we focus on the relationship with the biological father). Beginning with the relationship at birth we determined if the biological father was in a coresidential (i.e. cohabiting or married) relationship with the mother (52% coresidential: 24% married, 28% cohabiting). Then at the following wave, 1 year after the birth, we

utilized the same information to determine if the biological father and mother were in a coresidential relationship. Comparing that with the previous wave we then determined if the father exited the residential union, entered into a residential union with the mother, or did not change their residential status. Between each wave about 10-12% of children saw their father exit the residential relationship. Of course, since the time periods are unequal (1 year and 2 years), in fact we have higher rates of leaving earlier in the child's life. Similarly, about 10% of children see their father enter into a residential relationship with their mother in the first year after birth, but then then about 6% in the next two years (by age 3). For mothers who missed a wave and responded to a later wave, we utilized the relationship histories to determine when (if any) residential changes occurred.

Harsh Parenting

Harsh parenting was measured using the mean of the Psychological Aggression and Physical Assault subscales (10 items total) of the Parent-Child Conflict Tactics Scales at age 3. Both subscales were scored for annual chronicity with severity weights in accordance with the frequencies indicated by the response categories. The subscales were standardized to a 0 to 1 scale, indicating the proportion of possible total score (Straus, 2001; Straus, et al., 1998). The ten items from both subscales that comprised our harsh parenting measure have a Cronbach's alpha value of 0.74.

Genes

Serotonin[2] . Our measure of the serotonin systems comes from 4 genetic markers of 2 genes in the serotonin system. First, we use two markers of the most researched gene of this system, the serotonin transporter gene (5-HTT). This gene codes for the protein which recycles the serotonin from the synapses—in theory, allowing for greater responsiveness to the environment. Our two well-examined polymorphisms (or variants) of the serotonin transporter gene are: 1) a functional polymorphism (5-HTTLPR) in the 5' regulatory region and 2) a 17 base pair variable number tandem repeat (VNTR) in the second intron region (called STin2 VNTR). For the 5-HTTLPR polymorphism, the most common alleles

[2] Genotypes for both HTTLPR and STin2 were obtained by PCR followed by gel electrophoresis, while the dopamine an TPH genes were marked with an Illumina chip.

are the short (S) 14-repeat and long (L) 16-repeat of a 23 base pair incomplete repeat, but other less common repeats are also found in various populations. When compared to the L allele, the S allele of the 5-HTTLPR polymorphism has been shown to be associated with less efficient transcription rates—thus presumably increasing responsiveness to the environment (Heils et al 1996). For the STin2 polymorphism, the two most common alleles are the 10 and 12 repeat, and when compared to the 10 repeat allele, the 12 repeat allele has been shown to be associated with lower transcription efficiency—thereby increasing sensitivity to the environment (Hranilovic et al 2004). We also use two markers of the TPH2 gene related to the production of tryptophan, a metabolite of serotonin. That is, Tryptophan hydroxylase (TPH) is an enzyme involved in the initial step (and the rate-limiting step) in the biosynthesis of serotonin. The TPH2 gene is only expressed in the brain (Sakowski 2006), and also influences serotonin production (Walther 2003). It has also been shown to be related to depression, bipolar disorder and other mental health problems (Mossner 2006; Zhang 2005; Zhou 2005). We have two markers for the TPH2 gene. The first marker is rs4570625 and has a G (vs. A) allele that appears lower transcription rates. Similarly the second marker, rs1386494, has a T (vs. C) allele that lowers transcription rates (Porcelli 2010).

In combining the serotonergic system markers, recall that in all cases people have two copies of the gene (one from the father and one from the mother) so that three options are available: 2 homozygote genotypes (two copies of the same allele) and 1 heterozygote genotype (1 of each allele). Thus we create a measure of serotonin biological susceptibility to environmental influence by summing the number of low transcription alleles genes (5-HTTLPR-S, STin2-12, TPH2a-G, TPH2b-T). This results in a possible range of 0-8 alleles.

Dopamine. For dopamine we use one measure each for four different genes along the dopaminergic system. Like 5-HTT for serotonin, DAT1 (SLC6A3, 5p15.3) is the gene that codes the dopamine transporter protein that helps clear dopamine from the synapses (Bannon and Whitty 1995). Whereas the 5-HTT measures were length polymorphisms, the DAT1 marker (rs40184, intron 14) is measured as a SNP, where the C (vs. T) allele is associated with lower transcription of the DAT1 gene

(Heinz et al 2000). The genes DRD2 (Taq1a, 11q23) and DRD4 (11p15.5) both code for proteins controlling the dopamine receptors in the synapse (Noble et al. 1991). DRD2 is also a SNP with C and T as alleles, where the T allele is associated with low transcription for DRD2 (rs1800497). For DRD4 we utilize the 48bp VNTR in the 3rd exon. We code 6-10 repeats as "long" or 7R alleles (which make up 80% of long alleles) and call the short allele 4R because is constitutes 85% of the short (2R-5R) alleles. 7R alleles have less sensitivity to dopamine (Asghari et al 1995; Propper et al. 2007). Finally, Catechol-O-methyltransferase (COMT, 22q11.21) codes for a major enzyme involved in the inactivation of dopamine in the synaptic cleft, and the Met allele of the Val158 Met polymorphism (rs4680) is known to decrease COMT activity by coding the amino acid methionine instead of valine (Lachman et al., 1996). To create a measure of reactivity we summed the homozygote low transcription genotypes (the C allele for DAT1, 7R for DRD4, the T allele for DRD2, and Met allele for COMT) to generate a score of dopaminergic reactivity from 0-8. We argue that using multiple genetic markers along the same biological pathway (for both serotonin and dopamine) improves measurement. We center the genetic measures on the median category to aide in interpretation of effects. The correlation between the serotonin and dopamine scores is 0.03, suggesting they are essentially independent.

Controls

Studies have found that the association between instability and child well-being is stronger for Whites than for Blacks (Fomby and Cherlin 2007; Wu and Thompson, 2001). Also due to differences in genotypes by race, we control for race (and later stratify by race) to address what geneticists call population stratification—that due to ancestry, race/ethnic allele frequencies differ substantially and then any significant behavioral differences will appear related. With respect to education and income, research suggests that mothers with more material and socioemotional resources are better able to cope with the uncertainty associated with partnership changes than mothers with fewer resources (Cooper et al 2009; Carlson and McLanahan 2006).We also control for mother's age, child's birthweight and child's birth order, all of which are known to influence externalizing trajectories (Miner and Clarke-Stewart 2008). We mean center all the controls to make for easier interpretation of the intercept and slope.

Another layer of complexity to the model is that gender is often found to be a strong moderator of family instability and socio-emotional health. Although we expect boys and girls to have similar levels of exposure to family instability, there is some evidence that boys are more negatively affected by family instability (Bongers et al 2004; Cavanagh et al. 2008; Hetherington, Cox and Cox 1985). One reason for expecting boys to respond more negatively to family disruption is that the presence of a male role model may be more important for boys' identity (Allison and Furstenberg 1989). Following a divorce, boys tend to exhibit more externalizing problems than girls (Demo and Acock 1988; Entwisle, Alexander and Olson, 1997). Also, post-divorce mother-son relationships are significantly worse than comparable mother-daughter relationships (Hetherington et al. 1985). There is also evidence that boys are more sensitive than girls to a variety of changes that often occur during family transitions, such as parental conflict, parental employment, finances, and residential moves (Davies and Lindsay 2001; Kling, Ludwig and Katz 2005). Therefore we not only control for sex, but examine different models by sex.

Analysis Plan

Because the outcomes are groups of co-developing trajectories, we utilize multinomial logistic regression to examine the odds of being in one group compared to the largest, normative group for the internalizing and externalizing and anxiety and depression analyses. For the aggression and rule breaking analyses we use logistic regression because there are only two groups. We first run a model with controls, followed by a model with family structure and parenting. Parenting and family structure are tested separately and jointly. The next set of models add the genetic measures, first separately and then jointly. Finally the third set allows for an interaction between the genes and the family environments (all done separately).

Results

Although we have not run all the models yet we have several results (not in tables):

Effects of family structure

Being in a coresidential relationship decreases the odds of being in the non-normative trajectory group for all three CBP analyses. Among coresidential relationships being married reduces the odds of

being in the severe trajectory group for the internalizing and externalizing analysis. A similar, but smaller effect of marriage is seen in the internalizing and externalizing analysis.

Main effects of parenting

Harsh parenting is positively associated with being in the non-normative trajectory in all analyses and has an additionally strong effect on being in the severe trajectories.

Main effects of genes

Both serotonin and dopamine only help distinguish between the severe trajectory group and the other groups. This suggests that genes really only play a major role for those extreme CBP trajectories. Interestingly including genes increased the effects of family structure and parenting by about 50% .

Gene-environment interactions

This is the least finished set of analyses, but currently we see that in the internalizing and externalizing analyses there appears to an interaction such that for people with the most sensitive alleles family structure and parenting plays a larger role in determining trajectory group. That is among those children with the most sensitive alleles family environment appears to be more predicitive of trajectory group compared to children with fewer sensitive alleles.

"Preliminary" Discussion

To summarize, this study used parallel process growth mixture model to examine the co-development of child behavioral problems for children ages 3 to 9. The use of co-development or co-occurance is important because it relaxes the more common assumption that these are CBL are independent. We find that this allows for a more complete examination of socio-emotional development. We do find that family structure and parenting a significant determinants of co-development trajectories. Further, we find that genes are significant predictors of being the severe trajectories—implying that genes may be more responsible for those severe CBL compared to more normative or even high initial, but declining trajectories. The addition of genes appears to increase the strength of family environmental effects. Finally, there is some evidence that these genes are also interact with the family environment to influence CBP trajectories.

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Class		Parallel Process		Parallel Process		Parallel Process	
		Internal	External	Anxiety	Depress	Aggress	Rule-Br
1	Intercept	0.222	0.462	0.279	0.163	0.662	0.438
	Slope	***-0.018***	***-0.058***	***-0.026***	***-0.008***	***-0.068***	***-0.056***
	N	3209		**3596**		4397	
2	Intercept	0.531	0.965	0.711	0.605		
	Slope	***-0.049***	***-0.116***	***-0.082***	***-0.055***		
	N	1019		**602**			
3	Intercept	0.441	0.844	0.521	0.371		
	Slope	***0.047***	*-0.022*	***0.035***	***0.062***		
	N	169		**199**			
4	Intercept						
	Slope						
	N						

Table 1. Intercepts, slopes, and class size for optimum models for each process. Mean intercepts and slopes estimated for each class, as well as number of individuals (N) assigned to each class based on their most likely class membership. Internal = internalizing, External = externalizing, Depress = depression, Aggress = aggression, Rule-Br = rule-breaking. Bold font indicates slopes are significantly different from zero, $p < .05$. *Parallel process parameters for aggression and rule breaking not shown*.

N		4398
Race/Ethnicity		
	Black	48.3%
	Hispanic	27.0%
	White	21.1%
	Other	3.6%
Gender of focal child (% female)		47.5%
Family structure at birth		
	Single mother	48.2%
	Married couple	24.2%
	Cohabitating couple	27.5%
Mother's education		
	Less than high school	33.9%
	High school or equivalent	30.9%
	Some college/tech school	24.5%
	College or graduate school	10.6%
Mother's age (M, SD in years)		25.2 (6.03)

Table 2. Sample characteristics. Reported by mother at child's birth. N = number of participants who completed the harsh parenting or CBCL measures at any time point and thus were included in our study. Note: Nine individuals missing data on race/ethnicity, four missing data on mother's education.

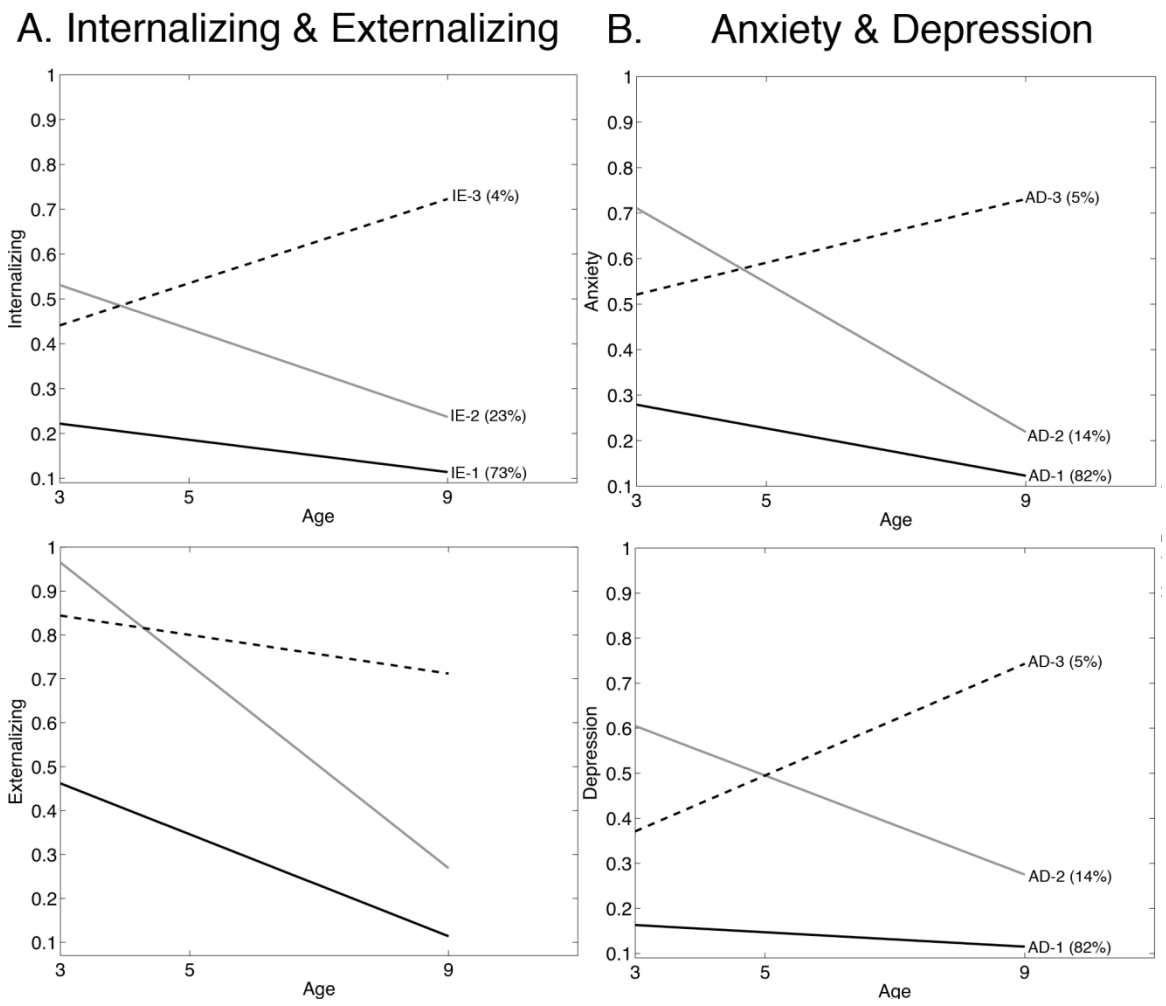

Figure 2. Estimated growth trajectories for each class. In the three models:

A. Internalizing and externalizing parallel process growth mixture models. IE-1 = initially low, decreasing internalizing and initially medium, decreasing externalizing, IE-2 = initially medium, decreasing internalizing and initially high, decreasing externalizing, IE-3 = initially medium, increasing internalizing and high, stable externalizing.

B. Anxiety and depression parallel process growth mixture models. AD-1 = initially low, decreasing anxiety and depression, AD-2 = initially high, decreasing anxiety and initially medium, decreasing depression, AD-3 = initially medium, increasing anxiety and depression.

C: Aggression and Rule Breaking not shown