The Influence and Interplay of Family Instability and Genes on Children's Prosocial Behavior

by

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Abstract

This study examines whether the relationship between biological-parent relationship stability and children's prosocial behavior is moderated by child's genetic make-up. Based on biological susceptibility theory, we hypothesize that children with particular gene variants are more responsive to changes in family structure than children without such variants. Using data from the Fragile Families and Child Wellbeing Study, we find that the biological father entering a residential relationship with the mother increases prosocial behaviors, and when he exits it decreases prosocial behavior. We also find strong main effects for genetic markers of serotonergic system. Further, we find that genetic markers of the serotonergic and dopaminergic systems interact with biological-father residential change to influence trajectories in children's prosocial behaviors. Children with more reactive genotypes experience a greater benefit to their father entering the household than other children; they also experience a greater cost to their father exiting the household.

This paper examines the largely neglected area of research on prosocial, or positive, behaviors in childhood. Prosocial behavior in childhood is predictive of several important social outcomes such as civic commitment, attachment to the community, empathy, cooperation, volunteerism, and responsibility (Batson 2009; de Waal 2008; Eisenberg et al 2006; Flanagan et al 1998; Van Lange 2008). Yet, despite these important connections to social outcomes, these childhood behaviors have received substantially less attention than their "negative" counterparts such as externalizing, internalizing and attention problems. We attempt to address some of this gap by extending and uniting three areas of prosocial research: demographic, genetic and gene-environment interactions (GxE). More specifically we examine the extent to which a child's genetic makeup moderates the influence of family instability on childhood prosocial behavior.

In this paper we argue that greater integration of the biological and social science literatures improves our understanding of children's socio-emotional development and long term wellbeing. Specifically, we argue that the social science literature can enrich genetic studies by providing more socially theorized measures of the environment (in this case the family environment). Similarly, the genetics literature can add to social science studies by proving a biological explanation for why some children respond more strongly to family change than others.

Using growth curve models and newly collected genetic data from the Fragile Families and Child Wellbeing study (FFCW), we demonstrate several interrelated points: 1) biological fathers' moves into and out of the household are associated with children's prosocial behavior, with entrances increasing positive behavior and exits decreasing prosocial behavior; 2) measures of the both the dopaminergic and serotonergic systems are associated with levels of prosocial behavior and 3) the associations between family transitions (moves in and moves out) and prosocial behavior are moderated by variation in children's dopaminergic and serotonergic genes, with the number of "reactive" genetic variants intensifying the associations, for better and for worse.

Family Instability and Prosocial Behavior

Previous demographic research has typically found that family instability, and parental divorce in particular, is associated with children's socioemotional wellbeing, typically showing an increase in behavioral problems (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; Mitchell et al 2011a; Osborne and McLanahan 2007; Seltzer 1994; Waldfogel, Craigie and Brooks-Gunn 2010; Wu and Thomson 2001). However, almost none of this research has focused on prosocial outcomes. One exception is Lichter, Shanahan, and Gardner's (2002) work showing that the amount of time spent living in a "female-headed household" as a child is negatively associated with volunteering as an adolescent. However, this study was unable to examine changes in family structure, which more recent studies have utilized to examine family instability.

Attachment theory suggests that children who are not adequately attached to a parent are less likely to be empathetic of others, and may have lower levels of cooperation and trust, thus leading to fewer prosocial behaviors (DeWit, Embree, and DeWith 1999; Raskoff and Sundeen; Wiley and Carlin 1999). Further, social stress theory argues that family change itself is stressful, irrespective of the type of change, by triggering modifications in household composition, residential location, and economic resources—all of which are expected to interfere with parent-child relationships (George, 1989, 1993; Holmes and Rahe 1967; Rutter 1983). However, we might also expect that the entrance of a biological father to actually reduce the stress of the change (compared to the entrance of a social father) and thus may actually improve parent-child attachment and positive social learning. The reason for this is because the biological father is more likely than a social father to share resources with their child, less likely to compete with the child for the mothers' attention, and more likely to have been in the child's life since birth. In fact, two studies have recently shown that the entrance of a biological father is associated with declines in material hardship, increases in the quality of parenting, and decreases in externalizing behavior (Mitchell et al 2011a ; Osborne, Berger, Magnuson Forthcoming).

Genes and Prosocial Behavior

Most studies of prosocial behavior have relied on twin designs[1], which have shown that up to 50% of the variation in prosocial behavior is associated with genetic characteristics (Knafo et al 2008). Interestingly, these genetic effects appear to increase in importance as the child ages (Knafo and Israel 2009). More recently, a few studies have shown the influence of specific genetic markers on prosocial behavior (Bachner-Melman et al 2005; Knafo, Israel and Ebstein 2011; Knafo et al 2008; Israel et al 2009; DiLalla, Elam and Smolen 2009). However, only two of these found a result in children (Knafo, Israel and Ebstein 2011; DiLalla, Elam and Smolen 2009). Nevertheless, two systems are theoretically interesting are the dopaminergic and serotonergic systems.

The dopamine system may be particularly interesting because 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 may lead to variations in sensitivity to attachment to and learning from a parent. This also suggests a possible sensitivity to changes in parental availability. Interestingly, the two studies that found a

[1] It is important to note that many social scientists balk at the strong assumptions required to estimate heritability (e.g. no assortative mating) and the fact that the genetic variance component includes not only genetic main effects but any gene-environment effects as well (Freese and Shostak 2009).

genetic effect in children both utilized the same genetic marker on the dopamine D4 receptor (DRD4) (Knafo, Israel and Ebstein 2011; DiLalla, Elam and Smolen 2009).

Genes that regulate the serotonin signalling system are also potential targets for research in the prosocial behavior. Serotonin is also a neurotransmitter that helps to regulate the cognitive functions of memory, mood and learning. The serotonergic system has a strong a connection with internalizing behaviors such as depression, anxiety and being withdrawn (Uher and McGuffin 2010; Williams et al 2003). These behaviors are almost polar opposites of prosocial behavior that requires connections to others. Thus, even more than dopamine, we might expect a large main effect of serotonin markers. Serotonin is hypothesized to work by inhibiting all social actions, thereby lowering prosocial behaviors (Chiao 2011). To date we have found no studies test the influence of serotonergic system genes on children's prosocial behavior.

Gene-environment Interactions and Prosocial Behavior

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 2011b). 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. However, even among all these studies the focus has still primarily been on negative behavioral outcomes such as externalizing, internalizing, depression, and delinquency. However, the biological susceptibility model also suggests that these interactions should work for positive outcomes as well. Thus we provide a rare examination of a positive outcome even within the biological susceptibility literature.

We found only example of a GxE study on prosocial behaviors. In a study of Isreali twins, Knafo, Israel and Ebstein (2011) found that although there were no main effects of genes (i.e. one marker of the DRD4 gene) and parenting (i.e. mother's positivity) there was an interaction. Namely, those with at least one 7-repeat allele in the 3rd exon of the DRD4 gene experienced greater gains in prosocial ratings with increases in mother's positivity

than those with no 7-repeat alleles. However, this study also found that the children with at least one 7-repeat allele were also more responsive to mother's negative parenting—but such that more unexplained punishment resulted *higher* levels of prosocial behavior. Thus, while there is at least one example of the expected biological sensitivity, the results are still unclear. Further, this paper only utilized one marker of a large dopaminergic system, and no study has examined a GxE for prosocial behavior using serotonin markers.

DATA and METHODS

Sample

Our data are taken from the *Fragile Families and Child Wellbeing Study* (FFCWS). FFCWS is based on a stratified, multi-stage, probability sample of children born in large U.S. cities between September 1998 and September 2000, with an oversample of children born to unmarried parents (three-quarters unwed, one-quarter wed) (Reichman et al 2001). Because of the large oversample of non-marital births and the urban nature of the sample, the families in this sample may be at particular risk of union instability (Osborne and McLanahan 2007). This feature of the data affords us greater power to detect interactions with genes than an equally sized population of marital births. Baseline interviews with mothers and fathers were conducted within 48-hours of the child's birth, and subsequent interviews were conducted when the focal child was 1, 3, 5 and 9 years old. Prosocial behavior was reported in years 3, 5 and 9. Saliva DNA samples were taken at the age 9 follow-up, using the Oragene®DNA sample collection kit (DNA Genotek Inc, Ontario). We use data from all five waves and restrict the analysis to children where the father is known, with genetic information, and at least one measure of prosocial behavior. These restrictions result in a final sample of 2,823 children.

Measures

Prosocial behaviors

We utilized 9-11 questions from the Adaptive Social Behavior Inventory to assess ratings of children's prosocial behavior (Hogan 1992). These measures were collected during the in-home portion of the interview when the child was 3, 5 and 9 years old. Each item consists of a 3-point Likert scale on which mothers reported whether their child's behavior is not true (0), sometimes or somewhat true (1), or often or very true (2). The scale consists of questions related to empathy, sociability, and confidence in interacting with others. We sum the items for each scale to form the prosocial index (year 3: 9 items, $\alpha = 0.80$, mean= 15.5, year 5: 11 items, $\alpha = 0.78$, mean= 18.3, year 9: 11 items $\alpha = 0.76$, mean= 17.4). Some items, while covering the same general concept, changed somewhat across waves to better measure the developmental changes in prosocial behaviors. However, the results were robust to using only the 7 items that remained consistent across all 3 waves. Substantive results of analyses were consistent between the raw and standardized scores.

Family Instability

The amount of instability is measured using data gathered at each wave from the mother on the current relationship status and past relationship history 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. 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, 2 years, 2 years, 4 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, then about 6% in the next two years, 4 % between ages 3 and 5 and finally another 4% between ages 5 and 9. Thus, by age 9 most families appear to have clearly defined their residential statuses with few residential changes between the biological parents still occurring. 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.

Genes

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 2011b). Normally these risky (now reactive) variants (polymorphisms) are the variants associated with lower transcriptional efficiency.

Serotonin[2] . Our measure of the serotonin systems comes from 5 genetic markers of 4 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 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).

[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.

We also use three markers of genes 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. TPH has 2 genes: TPH1 and TPH2. The TPH1 gene is be widely expressed in human tissues (Sakowski 2006). We employ the most examined marker of this gene, a single nucleotide polymorphism (SNP) at position 218 of TPH1 (rs1800532).This SNP has been reported to influence gene transcription, with the A (vs. C) allele being associated with decreased serotonin synthesis (Jonsson 1997). Although not yet found to be related to prosocial behavior, the A allele was found to be associated with lower mental health (Ham et al 2007). 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 (5-HTTLPR-S, STin2-12, TPH1-A, TPH2a-G, TPH2b-T) that ranges from 0 to 10 "reactive" genetic variants.

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). Both of these are also measured as SNPs where they either have a C or a T as well, where the C allele for DRD2 (rs1800497) and the T allele for DRD4 (rs1800955) are associated with lower transcription (Noble et al. 1997; 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 low transcription alleles (the C allele for DAT1 and DRD2 and the T allele for DRD4 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 (4 for serotonin and 3 for dopamine) to aide in interpretation of effects.

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 and child's birth order, which are known to influence prosocial behaviors (Knafo and Israel 2009; Lichter, Shanahan, and Gardner 2002). We mean center all the controls to make for easier interpretation of the intercept and slope.

Analytic Strategy

Because we are interested in capturing the dynamic aspect of family structure changes on prosocial behavior, we use latent growth curve modeling (Bollen and Curran 2006). This analytic strategy assumes that children differ in their initial level of prosocial behavior and that variance in subsequent trajectories vary by genes, father's residential status and the controls. A unique intercept (α), a linear, time-dependent slope (β), and some measurement error (ε) characterize each child's trajectory of prosocial behaviors. Thus, the level one equation is:

$$y_{it} = \alpha_i + \beta_i t + \varepsilon_{it} \quad (1),$$

and represents within-individual (i) change over time (t) since the first measure. To incorporate the time-varying changes in the biological father's entry or exit of a residential relationship with the mother on child's prosocial behavior we modify Equation 1 as follows:

$$y_{it} = \alpha_i + \beta_i t + \gamma_{tt'} w_{it'} + \varepsilon_{it} \quad (2),$$

where $\gamma_{tt'} w_{it'}$ represents the effect of each previous inter-wave time (t') entry or exit on prosocial behavior at time (t) for each ith individual. In other words, prosocial behavior at age 3 can be influenced by changes in father's residential status between waves 1 and 2 (ages 0 and 1) and waves 2 and 3 (ages 1 and 3). In addition to changes in father's residential status between ages 0-1 and 1-3, prosocial behaviors at age 5 can be influenced by changes in father's residential status between ages 3-5. Child's age 9 prosocial behaviors are similar to age 5, but have the additional influence of father's residential changes between ages 5-9. Each of the 18 (9 entry and 9 exit) $\gamma_{tt'}$ represents a perturbation from the latent prosocial trajectory caused by a change in father's residential status at structure at a specific point in time (Bollen and Curran 2006).

The second level of the growth model allows the random intercepts (α_i) and slopes (β_i) to be a function of variables that differ across individuals (i) but do not change across time (t). This level represents between-individual change over time. The level two equations are as follows:

$$\alpha_i = \alpha_0 + \alpha_1 \text{GENES}_i + \alpha_j \mathbf{X}_{ij} + u_i \quad (3)$$

$$\beta_i = \beta_0 + \beta_1 \text{GENES}_i + \beta_j \mathbf{X}_{ij} + v_i \quad (4)$$

For our purposes, genes have an effect on both the random intercept and the random slope. As well, there is a vector **X** of *j* number of controls that influence both the intercept and slope. The intercept and slope for each prosocial behavior are directly regressed on these characteristics to assess for potential group differences in the means of the growth factors.

Finally, to estimate the interaction between genes and time-varying family instability, we substitute equations 3 and 4 into equation 1 and add an interaction term ($\lambda_{tt'}$(GENES*$w_{it'}$):

$$y_{it} = \alpha_0 + \alpha_1 \text{GENES}_i + \alpha_j \mathbf{X}_{ij} + \beta_0 t + \beta_1 \text{GENES}_i t + \beta_j \mathbf{X}_{ij} t + \gamma_{tt'} w_{it'} + \lambda_{tt'}(\text{GENES} * w_{it'}) + u_i + v_i t + \varepsilon_{it} \quad (5),$$

where the 18 $\lambda_{tt'}$ represent the interactive effect of genes for the family instability in time t' on prosocial behaviors in time *t*. This interactive effect is a more parsimonious version of if we had made genes a time-varying covariate and interacted them with family instability at each wave (Li, Duncan, and Acock 2000).

We use a robust maximum likelihood estimator that accounts for clustering of observations (by hospital) and uses all available data, even if not all waves are present (Muthén and Muthén 2007). This technique has been shown to produce less biased results than listwise deletion and performs similar to multiple imputation methods (Schaefer and Graham 2002). All statistical tests referenced in the text are two-tailed. We evaluate model fit using the maximum likelihood ratio test statistic (χ^2), which, if significant, indicates poor fit (which is typical in large samples). We also use three other measures of fit: the root mean square error of approximation (RMSEA), the Comparative Fit Index (CFI) and Bayesian Crinterion Index (BIC). Convention dictates that RMSEA be below .05 and CFI close to 1.0 (Bollen and Curran 2006).

Using the methods above our analytic strategy is to proceed in 5 general steps. First, conditional on the control variables we examine the time-varying effects of family instability. Second, to model 1 we test the main effects of genes (both dopamine and serotonin) separately. The third step is to allow the time-varying intercepts to interact with genes. However, since we have no major theory suggesting that genes should interact differently over time we constrain all the entry interaction effects and all the exit interaction effects ($\lambda_{tt'}$ from equation 5) to be equal. Doing so allows us to test the hypothesis that genes make people differentially susceptible to environmental influences. Further, if father's entry and exit have different main effects, having interactions in different directions provides even further support that genes make someone more biologically susceptible to environmental influence. The fourth step is to free the constraints on the entry and exit interactive terms so that they are constrained to be equal for specific ages (i.e. all the interactions effecting age 5 are constrained to be equal), producing 6 interaction estimates. Again this allows for further examination of timing effects. As well, we test model fit of a model with no constraints on the interaction terms. Fifth, we provide a series of robustness checks of the model. We test for influential data points and skewed data, we run all models separately by race to rule out any effect of population stratification with genes, and we examine the possibility of gene-environment correlation (rGE).

Results

Based on the analyses we find:

1. Large, statistically significant effects of biological father entering the home on *increasing* prosocial behaviors.
2. Smaller, only marginally significant, effects of biological father exiting the home on *decreasing* prosocial behaviors.
3. A large, significant main effect of the number of "reactive" serotonin markers *decreasing* prosocial behavior
4. A small, insignificant main effect of the number of "reactive" dopamine markers *decreasing* prosocial behavior
5. Serotonin genes moderate the effect of family instability
    a. More reactive genetic markers have stronger *positive* effects of biological father entering on prosocial behaviors
    b. More reactive genetic markers have stronger *negative* effects of biological father exiting on prosocial behaviors
6. Dopamine genes moderate the effect of family instability only for entering
    a. More reactive genetic markers have stronger *positive* effects of biological father entering on prosocial behaviors
    b. More reactive genetic markers *do not* appear to have a stronger negative effects of biological father exiting on prosocial behaviors

We are currently conducting several variations of the models above to examine the difference in the GxE by age, robustness checks of outliers, differences by race and gender, and tests for gene-environment correlations using the mother's genetic information.