Interplay between genetic and environmental influences on the development of aggressive antisocial behavior during childhood and adolescence

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*CITATION:*

Vitaro, F., Brendgen, M., & Tremblay, R. E. (2017). Interplay between genetic and environmental influences on the development of aggressive antisocial behavior during childhood and adolescence. Dans P. Sturmey (Ed.), The Wiley Handbook of Violence and Aggression, Vol.1, Chapter 22. Hoboken, NJ: Wiley.

**Abstract**

For both the perpetrators and their victims, aggressive antisocial behavior during childhood and adolescence is related to concurrent and later adjustment problems, including violent and criminal behavior. Quantitative (i.e., behavioral) genetic studies showed that aggressive antisocial behavior, as well as related risk factors such as negative parenting, are subject to both genetic and environmental influences. In this chapter, we present evidence from genetically-informed studies regarding the additive and interactive role of genetic and environmental factors (in particular, negative parenting) in the development of aggressive antisocial behavior during childhood and adolescence.  We also explore epigenetic mechanisms that may explain the role of environmental factors such as negative parenting in fostering the expression of youngsters' genetic liability for aggressive antisocial behavior. Implications for prevention and for future research are discussed.  
  
Key words: aggression, antisocial behavior, negative parenting, behavioral genetic studies, quantitative genetic studies, gene-environment correlation, gene-environment interaction  
  
  
**Brief biography**:  Frank Vitaro is full professor at the University of Montreal. He is also director of the Research Unit on Children's Adjustment Problems and Senior Researcher at the Sainte-Justine Hospital Research Centre. His research addresses: (a) the interplay between genetic and environmental factors, notably peers and parents, in the development of externalized problems such as delinquency, substance use and gambling, and (b) the use of prevention programs involving peers and parents to mitigate the development of externalized problems and, by the same token, test developmental models. Frank Vitaro has published over 350 articles and 50 books or book chapters, including Peers and Delinquency: A Genetically Informed, Developmentally Sensitive Perspective (2015).

Antisocial behavior during childhood and adolescence is an important risk factor for later serious and persistent adjustment problems, including violent and criminal behavior ([Nagin & Tremblay, 1999](#_ENREF_28)). It is also linked to a number of concurrent negative outcomes, both for the perpetrators (ex., social sanctions) and for the victims (ex., pain, humiliation, and fear). Two types of antisocial behavior have been reported in the literature: aggressive and non-aggressive. Aggressive antisocial behavior refers to behaviors such as aggression, personal violence, and destruction of property, whereas non-aggressive antisocial behavior refers to behaviors such as theft, lying, cheating, and rule breaking. Although correlated (*r* between .4 and .6), the two types of antisocial behavior are associated with partly different risk factors ([Burt, 2009](#_ENREF_6)). Aggressive and non-aggressive antisocial behaviors also demonstrate important developmental differences. Aggressive antisocial behavior is typically highest during early childhood and tends to decrease thereafter for most, but not all, children ([Tremblay, 2003](#_ENREF_40)). In contrast, non-aggressive antisocial behavior tends to increase from childhood to adolescence. These almost opposite developmental patterns suggest that we should distinguish between aggressive and non-aggressive behavior. The focus of this chapter is on aggressive antisocial behavior, but at times we expanded the literature review to include non-aggressive antisocial behavior, as many authors did not distinguish between aggressive and non-aggressive antisocial behavior problems.

Traditionally, aggressive antisocial behavior has been examined mostly from an environment-focused behavioral perspective. This perspective has provided important insights about the potential role of social experiences, most notably negative parenting (i.e., harsh discipline, criticism, conflict, parental rejection), in the development of aggressive antisocial behavior ([Patterson, 1982](#_ENREF_30)). At the same time, behavioral (i.e., quantitative) genetic studies showed that aggressive antisocial behavior, like most aspects of human development, is subject to genetic influences ([Moffitt, 2005](#_ENREF_26)). In consequence, a complete picture of the development of aggressive behavior requires the integration of both environmental and genetic perspectives.

Behavioral genetic studies have also shown that many environmental factors are themselves partly under genetic influence. Ignoring this evidence may contribute to a biased view of the role of these factors. In addition, genetic and environmental factors may not operate independently, but interactively. Specifically, exposure to environmental factors may influence the expression of genetic liability through epigenetic mechanisms that may be best examined in the context of genetically informed studies that also include specific environmental factors. In sum, behavioral genetic studies represent strong quasi-experimental designs to investigate the role of environmental factors and their interplay with genetic dispositions ([Moffitt, 2005](#_ENREF_26)).

The goal of this chapter is fourfold: 1- to present evidence from a quantitative (i.e., behavioral) genetic perspective regarding the role of genetic and environmental influences on the development of aggressive antisocial behavior during childhood and adolescence; 2- to examine the role of environmental factors, specifically negative parenting, in the context of genetically informed or genetically controlled studies; 3- to explore epigenetic mechanisms that may explain the role of negative parenting in regard to the expression of genetic liability towards aggressive antisocial behavior; 4- to draw a number of implications for prevention and for future research. Of note, although this chapter stresses the importance of genetic influences on aggressive antisocial behavior, it is important to keep in mind that its main goal is to examine how environmental factors such as negative parenting may work together with genetic influences in explaining aggressive antisocial behavior. Of course, a vast array of environmental factors such as the peer group, the school context or the neighborhood may be relevant to examine in this context. Due to space limitations, however, we focus on negative parenting as an illustration of the possible interplay between environmental and genetic factors.

A QUICK PRIMER TO GENETICALLY INFORMED STUDIES

Behavioral genetic studies use two types of designs: the twin design and the adoptee design. Since most studies reported in this chapter rest on the twin design, more will be said about this specific design. Behavioral genetic studies estimate the relative strength of genetic and environmental influences on a phenotype (i.e., an observable behavior or trait such as aggressive antisocial behavior) by examining the similarity of family members with varying degrees of genetic relatedness in regard to that phenotype in a specific population. The classical twin genetic design rests on the comparison of identical (i.e., monozygotic, MZ) and fraternal (i.e., dizygotic, DZ) twin pairs who are raised together. In this design, the genetic and environmental variance associated with a given phenotype is decomposed by comparing the within pair similarity of MZ twins, who share 100% of their genes, to the within pair similarity of same-sex DZ twins, who only share on average 50% of their genes. The underlying assumption of behavioral genetic studies is that inter-individual differences in a phenotype can be decomposed into three different sources of variance: *additive (or non-additive) genetic factors*, *shared environmental factors*, and *non-shared environmental factors*. In the classical twin design, *genetic* influences are indicated when the phenotypic similarity (i.e., the within-pair correlation) of MZ twin pairs is greater than the phenotypic similarity of DZ twin pairs. Shared environment refers to environmental factors ― both inside and outside of the family ― that siblings are jointly exposed to and that make them similar to each other (e.g., neighborhood crime level, family SES, parental mental health problems). *Shared environmental* influences are indicated when MZ pairs as well as DZ twin pairs are similar to each other and, in addition, the degree of similarity between DZ twins is comparable to that of MZ twins. Non-shared environmental factors refer to experiences within the family or outside the family that make siblings different from each other. *Non-shared environmental* influences are indicated by the extent to which even MZ twins, who are genetically identical and are raised in the same family, are different from each other (i.e., the degree to which the within-pair correlation is less than 1). It is also important to note that: 1- non-shared environmental effects include measurement error; 2- genetic effects do not only index direct genetic effects but also interaction effects between genes and between genetic and shared or non-shared environmental factors. Therefore, both genetic and non-shared environmental factors may be inflated relative to shared environmental factors.

Quantitative genetic studies help determine whether genetic influences are involved, but these genetic influences remain unmeasured. They represent the sum across many genes and many alleles (i.e., genetic polymorphisms), but no specific gene or allele is identified. In contrast, molecular genetic studies identify specific genes and specific alleles that are associated with a specific phenotype. Molecular and quantitative genetic studies are thus complementary. Space limitation prohibits the coverage of molecular genetic studies within the scope of this chapter, except for a brief overview of epigenetic studies on aggressive antisocial behavior.

GENETIC AND ENVIRONMENTAL INFLUENCES ON AGGRESSIVE ANTISOCIAL BEHAVIOR

**Gene-Environment Correlations and the Role of Negative Parenting**

Summarizing 103 twin and adoption studies, Burt ([2009](#_ENREF_6)) concluded that between 40% and 60% of the variance of aggressive antisocial behavior during childhood and adolescence is explained by genetic factors, whereas non-shared environmental factors explain the rest. In comparison, around 50% of the variance of non-aggressive antisocial behavior is under genetic influence according to Burt’s review. The remaining variance of non-aggressive antisocial behavior is mostly (i.e., at around 35%) explained by non-shared environmental factors, and to a smaller extent (i.e., at around 15%) by shared environmental influences. Does this mean that the environment plays only a minor role with respect to the development or the expression of aggressive behavior? This question is important in light of evidence showing that environmental experiences might themselves be influenced by children’s or adolescents’ genetic makeup, a phenomenon commonly referred to as a gene-environment correlation (or rGE). To illustrate, around 40% of the variance in parents’ negativity is explained by genetic factors, although variation may occur depending on the identity of the informant or other methodological features ([see Klahr & Burt, 2014](#_ENREF_32)). Two types of rGE may be especially relevant with respect to the link between youngsters’ antisocial behavior and negative parenting ([Plomin et al., 1977](#_ENREF_33)): *Passive* rGE (children and parents share genes that put the child at risk for aggression and predispose the parents to use negative parenting) and *evocative* rGE (children with a genetic risk for aggression elicit negative parenting).

The importance of genetic influences on negative parenting becomes even more evident in light of findings that they stem at least in part from the same genetic factors that influence aggressive behavior in the offspring. There are indeed a number of studies showing that negative parenting and child/adolescent aggressive (and non-aggressive) antisocial behavior may become spuriously related through common genetic factors. Some of these studies used standard bivariate genetic modeling while others used another simple but powerful design to determine the overlap between genetic influences related to negative parenting and children’s aggressive antisocial behavior. This alternative design (known as the cross-twin, cross-phenotype design) involves two steps: first, twin’s 1 aggressive behavior is correlated with twin’s 2 negative parenting, and vice-versa; second, the correlations between twin’s 1 negative parenting and twin’s 2 aggressive behavior among MZ pairs and same-sex DZ pairs are compared; if the correlation is higher among MZ pairs than among same-sex DZ pairs, then this indicates that genetic factors underlying both negative parenting and the offspring’s aggression explain at least part of the association between these two variables. To illustrate, Jaffee et al. ([2004](#_ENREF_20)) examined the overlap in genetic influences on two forms of negative parenting, i.e., corporal punishment considered in the normative range (ex., spanking), and physical maltreatment, considered more extreme (ex., sexual abuse). Using the cross-twin, cross-phenotype design, Jaffee et al. found that almost all of the correlation between parental corporal punishment and children’s aggressive behavior was accounted for by children’s genetic relatedness. Interestingly, however, children’s genes did not account for the correlation between physical maltreatment and children’s aggression, suggesting that more extreme forms of negative parenting may not result from rGE.

Other studies examining the overlap in genetic influences linked to children’s aggressive behavior and their experience of negative parenting used the Children of Twins design [COT]. The COT uses the contrast in genetic relatedness of MZ and DZ twins who are parents to estimate the influence of parents’ genes and environments on their parenting, their children’s behavior, and the association between parenting and children’s behavior. Findings from studies that used a COT design suggest that parents’ genes partially explain the associations between negative parenting and their adolescents’ aggressive behavior problems, likely through passive rGE ([D'Onofrio et al., 2007](#_ENREF_12); [Silberg et., 2012](#_ENREF_39)).

Whereas the COT design is specifically useful for testing passive rGE, the Extended Children of Twins (ECOT) design enables disentangling between passive and evocative rGE by combining a sample of parents who are twins and their children with a sample of children who are twins and their parents ([Silberg & Eaves, 2004](#_ENREF_38)). Two studies have used the ECOT design to disentangle the contributions of passive rGE, evocative rGE, and direct environmental parenting influences on the association between negative parenting and child adjustment problems, both aggressive and non-aggressive. In the first study, Narusyte et al. ([2011](#_ENREF_29)), found that the association between maternal criticism and adolescent antisocial problems was explained by evocative rGE, whereas there was a direct environmental influence of paternal criticism on child antisocial problems. Using a larger sample with more fathers and a wider range of negative parenting (including negativity, conflict, and harsh discipline), Marceau et al. ([2013](#_ENREF_23)) showed that adolescents’ genetically influenced antisocial problems contributed to the evocative rGE underlying maternal and paternal negativity.

The findings of genetic influences on negative parenting and their overlap with genetic influences on aggressive behavior suggest that the “effects” attributed to these social experiences in past studies may have been, at least partially, spurious (i.e., explained by the children’s or adolescents’ genetic makeup). This question was addressed in a number of studies that explored the role of negative parenting while controlling for possible rGEs through the use of the MZ difference method. Since MZ twins share 100% of their genes (and the same family environment when raised together), any differences between the two twins are deemed to arise from non-shared environmental experiences. The MZ difference method thus affords a unique opportunity to examine the role of negative parenting (as a non-shared environmental experience), while controlling for rGE. This is achieved by correlating within-pair differences in a measured environment (e.g., negative parenting) with later within-pair differences in a measured behavior (e.g., twins’ aggressive behavior), while controlling for baseline differences in aggressive behavior and differences in other types of relevant environmental experiences ([see Vitaro et al., 2009, for a full description of the method](#_ENREF_43)). To illustrate, Caspi et al. ([2004](#_ENREF_10)), used within-pair differences in observer-rated maternal expressed emotion (i.e., negativity and warmth) to predict, both concurrently and longitudinally, within-pair differences in mother and teacher ratings of antisocial behavior in a sample of five-year old MZ pairs. Within-pair differences in maternal negativity and warmth were associated with current and later within-pair differences in antisocial behavior, even after accounting for possible confounders such as differences in neurological status as indexed through differences in birth weight. More specifically, the twin that received more negativity and less warmth than his-her co-twin became more antisocial over a two-year period than his-her co-twin. Two other longitudinal studies using the MZ-difference method reported similar results (Viding et al., 2009, from age 7 to age 9; Cecil et al., [2012](#_ENREF_11), from age 9 to age 12). In all these studies, the effect sizes between negative parenting and children’s aggressive or antisocial behavior tended to be more modest than in studies using one-child-per-family (i.e., around .10 compared to around .20), as this ought to be expected once the spurious effects of genetic factors are controlled. Nevertheless, negative parenting still seemed to have a significant effect on aggressive and non-aggressive behavior problems.

There are, however, exceptions to this overall concordant picture. Thus, Hou et al. ([2013](#_ENREF_18)) did not find longitudinal links between within-pair differences in parent hostility and changes in externalizing problems (i.e., a combination of aggressive and non-aggressive antisocial behaviors) from age 14 to age 16. Similarly, Burt et al. ([2006](#_ENREF_7)) did not find longitudinal links between within-pair differences in the level of conflict between mother and adolescent and changes in behavior problems from age 11 to age 14 or from age 14 to age 17 when examining the full sample of 486 MZ twin pairs. Longitudinal links were found only for the most discordant cases with respect to mother-adolescent conflict, and only from age 11 to age 14. One feature that distinguishes the Burt et al. and the Hou et al. studies from studies that found significant longitudinal associations between parenting and antisocial behavior is their use of a cross-lagged design, controlling for both the continuity of their behavioral outcome, i.e., antisocial behavior, and the stability of their environmental predictor, i.e., maternal negativity/parent hostility. Another distinguishing feature between genetically-controlled studies that found longitudinal links between parenting and those that did not is the age of the participants. Studies that found longitudinal links used children, whereas those that did not used adolescents. It is thus possible that negative parenting may exert a direct environmental influence on youngsters’ antisocial behavior problems more during childhood than during adolescence, net of possible rGE. However, no study directly compared the results using the same sample, the same measures, and the same design at two or more developmental periods.

**Moderating Role of Environmental Experiences**

Negative parenting may exert its influence on aggressive antisocial behavior not only directly, net of genetic influences, but also by modulating the expression of a genetic disposition for aggressive behavior. This mechanism is known as a gene environment interaction (GxE). GxE may arise through two types of processes ([Brendgen, 2012](#_ENREF_5)): 1- Parenting may exacerbate the expression of a genetic liability for aggressive behavior according to a *facilitation process* ([also known as a contextual triggering process, which is similar to a diathesis-stress model; Shanahan & Hofer, 2005](#_ENREF_37)); in this case a liability for aggressive behavior would be expressed only, or more so, when parenting is poor; 2- in contrast, poor parenting could diminish or mitigate the expression of a genetic liability toward aggressive behavior in accordance with a *suppression process* ([also known as a social control process; Shanahan & Hofer, 2005](#_ENREF_37)). According to this perspective, even individuals at low genetic risk may resort to aggression if they are exposed to negative environments.

Using a mixed (i.e., twin, siblings and non-siblings) design, Feinberg et al. ([2007](#_ENREF_14)) found that genetic influences on antisocial behavior (a combination of aggressive and non-aggressive behaviors) increased as parental negativity increased. This moderating effect of parental negativity applied to antisocial behavior but not to depressive symptoms. Other studies also found that general family dysfunction or parental maltreatment exacerbated the expression of genetic risk associated with antisocial behavior ([Button et al., 2005](#_ENREF_8); [Jaffee et al., 2005](#_ENREF_19)). Finally, Cadoret et al. ([1995](#_ENREF_9)) used an adoption design in which adopted offspring who were separated at birth from biological parents with documented antisocial personality disorder were followed up as adults. These adoptees were compared with controls whose biological parents showed no psychopathology. Results revealed that only adoptees with biological parents with antisocial personality *and* an adverse adoptive environment (defined as adoptive parents who had marital problems, were divorced, were separated, or had anxiety conditions, depression, substance abuse and/or dependence, or legal problems) manifested increased conduct problems in adolescence. Although not specifically documented, it is possible that the moderating effect of the family environment operated through parenting.

Overall, the above studies support a facilitation GxE process in the interplay between negative parenting and youngsters’ genetic liability towards antisocial behavior: At low levels of negative parenting, the child’s genetic liability is not outwardly expressed or at least less so. However, at high levels of negative parenting, genetically at risk children may react with outbursts of anger and opposition. This is often the case when children with a difficult temperament (i.e., an endophenotypic marker of genetic liability) are exposed to negative parenting. A spiraling coercive cycle may result from such encounters, as Patterson and his colleagues described some years ago ([Patterson et al., 1992](#_ENREF_31)). Such coercive style, in turn, results in low parent-child bonding and risk of exposure to a cascade of other personal (i.e., information processing schemes favorable to aggression) and interpersonal (i.e., affiliation with deviant peers and poor schooling) outcomes ([Dodge & Pettit, 2003](#_ENREF_13)).

In sum, genes influence not only our behavior but also our social environment (in line with rGE). Conversely, environmental experiences such as negative parenting influence behavior directly (at least during childhood) or indirectly via its effect on genetic expression (in line with GxE). We now turn to a recent methodological approach that investigates one of the putative biological mechanisms responsible for the moderating role of the environment on gene expression, i.e., epigenetics.

THE CONTRIBUTION OF EPIGENETICS TO THE STUDY OF AGGRESSION

Epigenetic studies focus specifically on the biological effects of the environment on gene expression. To understand epigenetic effects it is important to understand that genes have to be “turned on” to have any form of impact, and this “turning on” mechanism is largely due to environmental signals. One of the mechanisms that turns genes on and off is DNA methylation ([Tremblay & Szyf, 2010](#_ENREF_41)). The environmental signals that methylate and demethylate genes are chemical signals that come from a large variety of sources, including what we eat and drink as well as how our brain reacts to environmental stimuli such as fearful or joyful events.

The classic epigenetic example for the effects of neglectful parenting on offspring’s behavior comes from an experimental study of maternal behaviour in rats which showed that rat pups insufficiently licked by their mothers in the days following birth (i.e., neglected) had reduced expression of the gene encoding the Glucocorticoid receptor in the hippocampus ([Weaver et al., 2006](#_ENREF_46)). The study further showed that this gene methylation effect had downstream effects on the hypothalamic–pituitary–adrenal axis (HPA) which regulates stress responses. A study of maternal separation at birth with mice also showed DNA methylation alterations associated with chronic hypersecretion of corticosterone, problems with stress coping and memory ([Murgatroyd et al., 2009](#_ENREF_27)). Similar results were also obtained with animals that are closer to humans from an evolutionary perspective. For example, important epigenetic differences were observed in blood and in brain cells when rhesus monkeys separated at birth from their mothers were compared to others that were brought up by their mothers ([Provençal et al., 2012](#_ENREF_35)).

Epigenetic mechanisms provide a concrete physiological explanation of the mechanisms by which genes and environments have impacts on the brain and on behavior. The main reason why epigenetic mechanisms are suspected to play a role in the development of behaviour problems is that they can program the genome at different time points during development and they can mediate the effect of genetic polymorphisms on phenotypic variations. Furthermore, DNA methylation can change over time and these changes can be used as markers of environmental effects during development. The epigenetic hypothesis thus provides a parsimonious and testable mechanism for the evaluation of, for example, negative parenting on aggressive behavior because we can test whether exposure to negative parenting has an impact on DNA methylation that is associated with the brain’s control of aggressive behavior. So far, however, this proposition has not been tested directly. However, a few epigenetic studies with humans tested the hypothesis that men and women with a chronic aggression problem have a DNA methylation profile that is different from similar individuals without a chronic aggression profile. Provençal, Suderman, Caramaschi et al. ([2013](#_ENREF_34)), used peripheral blood cells DNA from monocytes and T cells of young men with and without a chronic aggression trajectory during childhood and observed an association between childhood chronic aggression and DNA methylation in regulatory regions of cytokine and transcription factor genes. The cytokines were also shown to be repressed in the men with chronic aggression ([Provençal, Suderman, Vitaro, et al., 2013](#_ENREF_36)). Interestingly, one of these downregulated cytokines in men with chronic aggression, Interleukin-6 (IL-6), was previously shown to be involved in aggressive behaviour in mice ([Alleva et al., 1998](#_ENREF_1)). In humans, immunoregulators may influence brain circuitry and behaviors directly, or via interactions with other biological systems. Epigenetic changes in peripheral tissues may correlate to some extent with brain activity. For example, Wang et al. ([2012](#_ENREF_45)) found a significant association between chronic aggression during childhood and adult DNA methylation profiles in the *SLC6A4* gene promoter in peripheral blood DNA. Higher *SLC6A4* methylation was also associated with lower *in vivo* brain serotonin synthesis in the lateral left and right orbitofrontal cortex (OBFC). Interestingly, these specific brain regions were also shown to have lower serotonin synthesis in the subjects with higher aggressive behaviour during childhood ([Booij et al., 2010](#_ENREF_4)).

Links between DNA methylation and chronic aggressive behavior were also studied with a sample of girls. Guillemin et al. ([2014](#_ENREF_16)) observed DNA methylation signature associated with childhood CPA in women similar to those observed in men. For both males and females the same 31 gene promoters were significantly associated with chronic aggression. This almost perfect overlap between the functional categories in men and women provides further evidence that these methylation profiles --rather than confounding factors -- are at least partly associated with chronic aggression. Interestingly, specific genes involved in serotonin metabolism and HPA axis regulation, previously shown to be involved in aggression, were differentially methylated in women with chronic aggression during childhood. The difference between men and women for these genes may be explained in part by the fact that the HPA axis negative feedback control is more sensitive in females ([Keck et al., 2002](#_ENREF_21)).

In summary, young adult females and males with chronic aggression during childhood have epigenetic profiles that are different from non-aggressive individuals and these differences in epigenetic profiles correlate with brain serotonin synthesis differences that are also linked with chronic aggression. These correlations support the hypothesis that environmental factors early in life, such as negative parenting, may have epigenetic effects that impact brain development and behavior regulation. However, part of these effects could also be due to factors other than negative parenting or to the life style of chronic aggressors. To confirm the role of specific environmental experiences and their underlying epigenetic mechanisms, we will need longitudinal studies that start during pregnancy and follow individuals until adulthood with regular assessments of DNA methylation profiles, brain development and behavior. One powerful research design would be to follow a sample of MZ twins (hence capitalizing on the power of the MZ-difference method) from pregnancy onwards and integrate a host of measured environmental experiences, including negative parenting. Another powerful alternative would be an experimental design that includes a randomised preventive intervention aimed to improve negative parenting for at risk-families.

IMPLICATIONS FOR PREVENTION AND CONCLUDING COMMENTS

The studies reviewed in this chapter have significant implications for informing preventive interventions. First, the findings point to the importance of early prevention, when negative parenting seems to have most impact, net of rGE. During the early years, parents are relatively easy to engage in prevention programs that focus on parenting and their parenting skills are still malleable. Moreover, there are a number of preventive interventions with demonstrated effectiveness, including cost-effectiveness, that can improve family functioning and parenting ([McMahon & Pasalich, in press](#_ENREF_24)).

The second implication points to the ongoing debate about targeted prevention vs universal prevention ([Vitaro & Tremblay, 2008](#_ENREF_44)). The relatively consistent findings of GxE across different studies suggest that preventive intervention should prioritize children who have both a risk-conferring genotype and risk-conferring family experiences (i.e., negative parenting). This does not mean that children who are only at genetic or environmental risk, or not at all at risk, cannot benefit from preventive interventions. However, given limited resources, providing interventions to a large number of children who do not (absolutely) require them, may result is reduced cost-effectiveness. More importantly, it can result in insufficient interventions for children at elevated risk ([Vitaro & Tremblay, 2008](#_ENREF_44)).

The third implication concerns the evaluation of preventive interventions. Studies that do not consider the child’s genetic profile as a possible moderator of the impact of a preventive intervention may fail to detect significant intervention effects. However, it is not always possible to determine genetic liability of an individual child without precise genotyping. Alternatively, baseline levels of the child’s aggressive behavior might serve as a proximal phenotypic indicator of genetic risk. Parents’ history of violence and antisocial behavior could serve a similar purpose. So far, most preventive programs targeting aggressive children indeed report modest main effects, but moderate effects for the most aggressive children ([McMahon & Pasalich, in press](#_ENREF_24); [Vitaro & Tremblay, 2008](#_ENREF_44)). Moderate effects, however, suggest that targeting parents only may not be sufficient. Multi-modal, multi-target prevention programs that include parent management training as well as social skills training with the child and interventions in the daycare or school setting may be most effective for aggressive children.

Finally, although male children are more at risk of aggressive (and non-aggressive) antisocial behavior, we believe that prevention studies need to include both female and male children. Indeed, findings from cross-fostering and epigenetic studies suggest that environmental effects are transmitted inter-generationally -- and most notably from mothers to daughters ([Meaney, 2001](#_ENREF_25)). Thus, if maternal lifestyle (eating, drinking, smoking, stress, depression) during pregnancy has epigenetic effects on the daughter’s brain development and functioning, the daughter is likely to have a similar life style during her own pregnancies ([Gluckman et al., 2009](#_ENREF_15)). Consequently, preventive interventions that support at-risk females from pregnancy onwards should help them be better adjusted and provide a better environment (intra and post uterine) for their offspring, both girls and boys. Of course, such efforts should complement, not replace, the current practice of targeting (mostly) boys in youth-focused individual interventions to prevent aggression and violence, since they are the most at-risk in the short term ([Archer & Côté, 2005](#_ENREF_2)).

References

Alleva, E., Cirulli, F., Bianchi, M., Bondiolotti, G. P., Chiarotti, F., De Acetis, L., & Panerai, A. E. (1998). Behavioural characterization of interleukin-6 overexpressing or deficient mice during agonistic encounters. *European Journal of Neuroscience, 10*(12), 3664-3672. doi: 10.1046/j.1460-9568.1998.00377.x

Archer, J., & Côté, S. (2005). Sex differences in aggressive behavior: A developmental and evolutionary perspective. In R. E. Tremblay, W. W. Hartup, & J. Archer (Eds.), *Developmental origins of aggression* (pp. 425-443). New York, NY: Guilford Press.

Booij, L., Tremblay, R. E., Leyton, M., Séguin, J. R., Vitaro, F., Gravel, P., Perreau-Linck, E., Lévesque, M. L., Durand, F., Diksic, M., Turecki, G., & Benkelfat, C. (2010). Brain serotonin synthesis in adult males characterized by physical aggression during childhood: A 21-year longitudinal study. *PLoS One, 5*(6), 1-9 (e11255).

Brendgen, M. (2012). Genetics and peer relations: A review. *Journal of Research on Adolescence, 22*(3), 419-437. doi: 10.1111/j.1532-7795.2012.00798.x

Burt, S. A. (2009). Are there meaningful etiological differences within antisocial behavior? Results of a meta-analysis. *Clinical Psychology Review, 29*(2), 163-178. doi: 10.1016/j.cpr.2008.12.004

Burt, S. A., McGue, M., Iacono, W. G., & Krueger, R. F. (2006). Differential parent-child relationships and adolescent externalizing symptoms: Cross-lagged analyses within a monozygotic twin differences design. *Developmental Psychology, 42*(6), 1289-1298. doi: 10.1037/0012-1649.42.6.1289

Button, T. M. M., Scourfield, J., Martin, N., Purcell, S., & McGuffin, P. (2005). Family dysfunction interacts with genes in the causation of antisocial symptoms. *Behavior Genetics, 35*(2), 115-120. doi: 10.1007/s10519-004-0826-y

Cadoret, R. J., Yates, W. R., Troughton, E., Woodworth, G., & Stewart, M. A. (1995). Genetic-environmental interaction in the genesis of aggressivity and conduct disorders. *Archives of General Psychiatry, 52*(11), 916-924.

Caspi, A., Moffitt, T. E., Morgan, J., Rutter, M., Taylor, A., Arseneault, L., Tully, L., Jacobs, C., Kim-Cohen, J., & Polo-Tomas, M. (2004). Maternal expressed emotion predicts children's antisocial behavior problems: Using monozygotic-twin differences to identify environmental effects on behavioral development. *Developmental Psychology, 40*(2), 149-161. doi: 10.1037/0012-1649.40.20.149

Cecil, C. A. M., Barker, E. D., Jaffee, S. R., & Viding, E. (2012). Association between maladaptive parenting and child self-control over time: cross-lagged study using a monozygotic twin difference design. *British Journal of Psychiatry, 201*(4), 291-297. doi: 10.1192/bjp.bp.111.107581

D'Onofrio, B. M., Slutske, W. S., Turkheimer, E., Emery, R. E., Harden, K. P., Heath, A. C., Madden, P. A. F., & Martin, N. G. (2007). Intergenerational transmission of childhood conduct problems - A children of twins study. *Archives of General Psychiatry, 64*(7), 820-829. doi: 10.1001/archpsyc.64.7.820

Dodge, K. A., & Pettit, G. S. (2003). A biopsychosocial model of the development of chronic conduct problems in adolescence. *Developmental Psychology, 39*(2), 349-371.

Feinberg, M. E., Button, T. M. M., Neiderhiser, J. M., Reiss, D., & Hetherington, E. M. (2007). Parenting and adolescent antisocial behavior and depression - Evidence of genotype x parenting environment interaction. *Archives of General Psychiatry, 64*(4), 457-465. doi: 10.1001/archpsyc.64.4.457

Gluckman, P. D., Hanson, M. A., Bateson, P., Beedle, A. S., Law, C. M., Bhutta, Z. A., Anokhin, K. V., Bougneres, P., Chandak, G. R., Dasgupta, P., Smith, G. D., Ellison, P. T., Forrester, T. E., Gilbert, S. F., Jablonka, E., Kaplan, H., Prentice, A. M., Simpson, S. J., Uauy, R., & West-Eberhard, M. J. (2009). Towards a new developmental synthesis: Adaptive developmental plasticity and human disease. *Lancet, 373*(9675), 1654-1657.

Guillemin, C., Provençal, N., Suderman, M., Côté, S. M., Vitaro, F., Hallett, M., Tremblay, R. E., & Szyf, M. (2014). DNA methylation signature of childhood chronic physical aggression in T cells of both men and women. *PLoS One, 9*(1), 1-16 (e86822). doi: 10.1371/journal.pone.0086822

Hou, J. Q., Chen, Z. Y., Natsuaki, M. N., Li, X. Y., Yang, X. D., Zhang, J., & Zhang, J. X. (2013). A longitudinal investigation of the associations among parenting, deviant peer affiliation, and externalizing behaviors: A monozygotic twin differences design. *Twin Research and Human Genetics, 16*(3), 698-706. doi: 10.1017/thg.2013.24

Jaffee, S. R., Caspi, A., Moffitt, T. E., Dodge, K. A., Rutter, M., Taylor, A., & Tully, L. A. (2005). Nature X nurture: Genetic vulnerabilities interact with physical maltreatment to promote conduct problems. *Development and Psychopathology, 17*, 67-84.

Jaffee, S. R., Caspi, A., Moffitt, T. E., Polo-Tomas, M., Price, T. S., & Taylor, A. (2004). The limits of child effects: Evidence for genetically mediated child effects on corporal punishment but not on physical maltreatment. *Developmental Psychology, 40*(6), 1047-1058. doi: 10.1037/0012-1649.40.6.1047

Keck, M. E., Wigger, A., Welt, T., Muller, M. B., Gesing, A., Reul, J., Holsboer, F., Landgraf, R., & Neumann, I. D. (2002). Vasopressin mediates the response of the combined dexamethasone/CRH test in hyper-anxious rats: Implications for pathogenesis of affective disorders. *Neuropsychopharmacology, 26*(1), 94-105. doi: 10.1016/s0893-133x(01)00351-7

Klahr, A. M., & Burt, S. A. (2014). Elucidating the etiology of individual differences in parenting: A meta-analysis of behavioral genetic research. *Psychological Bulletin, 140*(2), 544-586. doi: 10.1037/a0034205

Marceau, K., Horwitz, B. N., Narusyte, J., Ganiban, J. M., Spotts, E. L., Reiss, D., & Neiderhiser, J. M. (2013). Gene-environment correlation underlying the association between parental negativity and adolescent externalizing problems. *Child Development, 84*(6), 2031-2046. doi: 10.1111/cdev.12094

McMahon, R. J., & Pasalich, D. (in press). Family-based interventions for young children with conduct problems as a means of delinquency prevention. In W. M. Craig, D. J. Pepler, & J. Cummings (Eds.), *Creating healthy relationships to prevent bullying: Get the tools to take action (PREVNet Series, Volume V)*. Ottawa, ON: National Printers.

Meaney, M. (2001). Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. *Annual Review of Neuroscience, 24*, 1161-1192.

Moffitt, T. E. (2005). The new look of behavioral genetics in developmental psychopathology: Gene-environment interplay in antisocial behaviors. *Psychological Bulletin, 131*(4), 533-554.

Murgatroyd, C., Patchev, A. V., Wu, Y., Micale, V., Bockmuhl, Y., Fischer, D., Holsboer, F., Wotjak, C. T., Almeida, O. F. X., & Spengler, D. (2009). Dynamic DNA methylation programs persistent adverse effects of early-life stress. *Nature Neuroscience, 12*(12), 1559-U1108. doi: 10.1038/nn.2436

Nagin, D., & Tremblay, R. E. (1999). Trajectories of boys' physical aggression, opposition, and hyperactivity on the path to physically violent and nonviolent juvenile delinquency. *Child Development, 70*(5), 1181-1196.

Narusyte, J., Neiderhiser, J. M., Andershed, A. K., D'Onofrio, B. M., Reiss, D., Spotts, E., Ganiban, J., & Lichtenstein, P. (2011). Parental criticism and externalizing behavior problems in adolescents: The role of environment and genotype- environment correlation. *Journal of Abnormal Psychology, 120*(2), 365-376. doi: 10.1037/a0021815

Patterson, G. R. (1982). *Coercive family process*. Eugene, OR: Castalia Press.

Patterson, G. R., Reid, J. B., & Dishion, T. J. (1992). *A social learning approach: IV. Antisocial boys*. Eugene, OR: Castalia Publishing Co.

Plomin, R., DeFries, J. C., & Loehlin, J. C. (1977). Genotype-environment interaction and correlation in the analysis of human behavior. *Psychological Bulletin, 84*(2), 309-322.

Provençal, N., Suderman, M. J., Caramaschi, D., Wang, D., Hallett, M., Vitaro, F., Tremblay, R. E., & Szyf, M. (2013). Differential DNA methylation regions in cytokine and transcription factor genomic Loci associate with childhood physical aggression. *PLoS One, 8*(8), 1-19 (e71691). doi: 10.1371/journal.pone.0071691

Provençal, N., Suderman, M. J., Guillemin, C., Massart, R., Ruggiero, A., Wang, D. S., Bennett, A. J., Pierre, P. J., Friedman, D. P., Côté, S. M., Hallett, M., Tremblay, R. E., Suomi, S. J., & Szyf, M. (2012). The Signature of Maternal Rearing in the Methylome in Rhesus Macaque Prefrontal Cortex and T Cells. *Journal of Neuroscience, 32*(44), 15626-15642. doi: 10.1523/jneurosci.1470-12.2012

Provençal, N., Suderman, M. J., Vitaro, F., Szyf, M., & Tremblay, R. E. (2013). Childhood chronic physical aggression associates with adult cytokine levels in plasma. *PLoS One, 8*(7), 1-7 (e69481). doi: 10.1371/journal.pone.0069481

Shanahan, M. J., & Hofer, S. M. (2005). Social context in gene-environment interactions: Retrospect and prospect. *Journals of Gerontology Series B-Psychological Sciences and Social Sciences, 60*(Special Issue 1), 65-76.

Silberg, J. L., & Eaves, L. J. (2004). Analysing the contributions of genes and parent-child interaction to childhood behavioural and emotional problems: A model for the children of twins. *Psychological Medicine, 34*(2), 347-356.

Silberg, J. L., Maes, H., & Eaves, L. J. (2012). Unraveling the effect of genes and environment in the transmission of parental antisocial behavior to children’s conduct disturbance, depression and hyperactivity. *Journal of Child Psychology and Psychiatry, 53*(6), 668-677. doi: 10.1111/j.1469-7610.2011.02494.x

Tremblay, R. E. (2003). Why socialization fails? The case of chronic physical aggression. In B. B. Lahey, T. E. Moffitt, & A. Caspi (Eds.), *Causes of conduct disorder and juvenile delinquency* (pp. 182-224). New York, NY: Guilford Publications.

Tremblay, R. E., & Szyf, M. (2010). Developmental origins of chronic physical aggression and epigenetics. *Epigenomics, 2*(4), 495-499. doi: 10.2217/epi.10.40

Viding, E., Fontaine, N. M. G., Oliver, B. R., & Plomin, R. (2009). Negative parental discipline, conduct problems and callous-unemotional traits" monozygotic twin differences study. *British Journal of Psychiatry, 195*(5), 414-419. doi: 10.1192/bjp.bp.108.061192

Vitaro, F., Brendgen, M., & Arseneault, L. (2009). The discordant MZ-twin method: One step closer to the holy grail of causality. *International Journal of Behavioral Development, 33*(4), 376-382. doi: 10.1177/0165025409340805

Vitaro, F., & Tremblay, R. E. (2008). Clarifying and maximizing the usefulness of targeted preventive interventions. In M. Rutter & J. Stevenson (Eds.), *Rutter's Child and Adolescent Psychiatry, 5th Edition* (pp. 989-1008). Oxford, United Kingdom: Blackwell Publishing.

Wang, D., Szyf, M., Benkelfat, C., Provençal, N., Turecki, G., Caramaschi, D., Côté, S. M., Vitaro, F., Tremblay, R. E., & Booij, L. (2012). Peripheral SLC6A4 DNA methylation is associated with in vivo measures of human brain serotonin synthesis and childhood physical aggression. *PLoS One, 7*(6), e39501. doi: 10.1371/journal.pone.0039501

Weaver, I. C. G., Meaney, M. J., & Szyf, M. (2006). Maternal care effects on the hippocampal transcriptome and anxiety-mediated behaviors in the offspring that are reversible in adulthood. *Proceedings of the National Academy of Sciences of the United States of America, 103*(9), 3480-3485. doi: 10.1073/pnas.0507526103