3

GENE–ENVIRONMENT INTERPLAY EXPLAINED

Introduction

Chapter 2 discussed behavioral genetic research, where samples of siblings are analyzed to decompose phenotypic variance into genetic and environmental components. This line of research might leave the impression that genes and the environment are independent from each other and work in relative isolation. This is not always the case, and the separation of genetic effects from environmental effects is sometimes an artificial bifurcation that does not adequately capture reality.[1] Instead, biosocial research has shown that genes and the environment are sometimes mutually reinforcing and codependent. Accordingly, phenotypic variance, including variance in antisocial phenotypes, can be created by the intersection of genetic and environmental factors, a phenomenon that has come to be known as gene–environment interplay. This chapter will discuss three main types of gene–environment interplay—gene X environment (GxE) interactions, gene X environment correlations (rGE), and epigenetics—and examine how each one is linked to antisocial phenotypes.

GxE Interactions

Exposure to the same environments often produces a wide range of heterogeneous responses. Children exposed to neglectful and abusive environments, for example, are at risk for displaying antisocial behaviors later in life, but most abused children will mature into prosocial adults. Adolescents living in crime-ridden, impoverished neighborhoods

are at risk for being arrested for serious violent offenses, but most will never have contact with the criminal justice system. Some parents, despite being loving and caring, will raise offspring who ultimately turn out to be criminal, while most children who are raised by detached, unresponsive parents will never be arrested for a crime. Even siblings raised in the same household turn out quite differently despite being exposed to many of the same environments. One child, for instance, may lead a life of crime, while their sibling may become a successful businessperson. Why do we see time and again the same environments produce very different outcomes? This is a particularly pressing question that is difficult for purely environmental explanations to answer. After all, if the environment is so powerful, we should see people exposed to the same environmental stimuli display very similar responses.

The concept of GxE interaction, however, can shed some much-needed insight into why people do not always respond to the same environments in the same way. At the heart of GxEs lies the fact that all people have their own unique genotypes, and these unique genotypes produce different genetic predispositions. These predispositions, in turn, are responsible for creating differential susceptibilities to the same environments. A health-related example will help to make this point clearer. Smoking cigarettes is a major environmental risk factor for developing lung cancer, but not all people who smoke will be diagnosed with lung cancer. So, why are some smokers resilient to lung cancer, while others are susceptible? The answer appears to be found in genotype. Alleles of some single-nucleotide polymorphisms (SNPs) have been found to affect the odds of developing lung cancer, where smokers who possess certain alleles for these SNPs are at greater risk for developing lung cancer than smokers who do not carry these alleles.[2] It is the combination of environmental risk (e.g., smoking cigarettes) and genetic risk (e.g., having certain alleles), which leads to differential outcomes (e.g., developing or not developing lung cancer). Keep in mind that although a person might have the genetic predisposition for developing lung cancer (i.e., genetic risk), if they are never smoke cigarettes (i.e., environmental risk), then their odds of developing lung cancer are on par with persons lacking the genetic predisposition. In this scenario, both genetic risk and environmental risk contribute—though perhaps to varying degree—to the development of lung cancer.

This same logic can be applied to antisocial phenotypes to understand why exposure to criminogenic environments will not inevitably lead to crime and why genetic risk will also not inevitably lead to crime. It appears as though genotype structures differential responses to environments, meaning that criminogenic environments have their strongest effect when they are paired with a genotype that is susceptible to antisocial phenotypes.

Remove the vulnerable genotype and replace it with a not-so-vulnerable genotype, and the effect of the criminogenic environment will not be nearly as strong. Conversely, take someone with a vulnerable genotype, remove them from a high-risk environment and place them in a low-risk environment, and the effect of genotype will either evaporate or not be as strong. With this background, we now we are in position to state a formal definition of GxEs: the effect of the environment depends on the presence of genotype, and the effect of genotype depends on the presence of the environment. From a GxE perspective, it is easy to see why the same environments produce different outcomes—because some genotypes are more sensitive to the environment than are other genotypes.

Figure 3.1 provides a graphical depiction of GxEs. The left-hand circle in the figure represents genetic risk, while the right-hand circle represents environmental risk. The overlap between the two circles represents people who have both genetic risk and environmental risk for antisocial phenotypes, while the nonoverlapping areas of the circle represent people who have only genetic risk or only environmental risk. As can be seen, antisocial phenotypes are most likely to surface for people who have both risk factors—precisely what is meant by GxEs.

Some of the earliest research that attempted to test for GxEs on antisocial phenotypes used samples that consisted of adopted children. By using an adoption-based research design (see Chapter 2), researchers are able to compare the adoptee to the biological parent

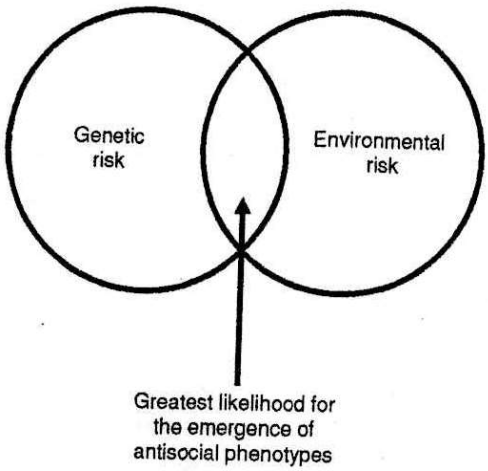

FIGURE 3.1 Depiction of gene X environment interactions in the production of antisocial phenotypes.

and to the adoptive parent. Genetic risk is considered to be present when the biological parent is arrested, and environmental risk is considered to be present when the adoptive parent was arrested. The results of adoption-based studies have revealed that adoptees who have a biological parent who was arrested *and* an adoptive parent who was arrested are at greatest risk for becoming criminal.[3] These findings provided initial support for the role of GxEs in the development of antisocial phenotypes.

Additional evidence for GxEs has also come from studies conducted by behavioral geneticists, where they calculate heritability estimates for people who are exposed to different environments. For example, perhaps a research team was interested in determining whether there was an interaction between genetic factors and being reared by abusive parents in the prediction of antisocial behavior. To answer this question, the sample would be divided into two groups: one group would consist of persons who were reared by abusive parents, and the other group would consist of persons who were not raised by abusive parents. Heritability estimates would then be calculated separately for each group. Evidence in support of a GxE would be garnered if the heritability estimates were significantly greater for one group (e.g., the group of people who were raised by abusive parents) than for the other group (e.g., the group of people who were not raised by abusive parents). Behavioral genetic research designs have been important in highlighting the importance of GxEs in human phenotypes, but there is a drawback to this line of research: genetic risk is modeled as a latent factor, meaning that no information is provided about the specific genes that are implicated in the GxE.

In the past decade, researchers have moved away from modeling genetic risk as a latent factor and have begun to examine the effects that measured genetic polymorphisms have on behavioral phenotypes in the presence and absence of certain environmental stimuli. For example, suppose we were interested in examining whether a hypothetical gene, say Gene B, was associated with criminal offending. Suppose further that we also were interested in examining whether the effect of this gene varied depending on whether the person lived in a disadvantaged area or a nondisadvantaged area. Pretend that we found that Gene B was associated with criminal offending for people living in disadvantaged areas, but the effect of Gene B was not associated with criminal offending for people living in nondisadvantaged areas. Such a finding would be supportive of a GxE because the effect of Gene B was confined to persons residing in disadvantaged areas. This is the same type of analyses that researchers have used to test for GxEs in the production of antisocial phenotypes.[4]

Avshalom Caspi and his colleagues conducted the first study to detect a GxE between a measured gene and a measured environment on a behavioral phenotype.[5] They were interested in determining why childhood maltreatment produced antisocial behavior in some children, but not in others. They hypothesized that a polymorphism in the promoter region of the monoamine oxidase A (*MAOA*) gene (i.e., the gene that produces the enzyme, MAOA, which breaks down neurotransmitters) would affect their response to childhood maltreatment. Different alleles of the *MAOA* gene have been linked to the production of differential activity levels of MAOA. One group of *MAOA* alleles codes for the production of high MAOA activity, while another group of *MAOA* alleles codes for the production of low MAOA activity. Caspi and his research team hypothesized that alleles that code for the production of low MAOA activity would be associated with displaying antisocial phenotypes. But there was a catch: they hypothesized that the effect of *MAOA* on antisocial phenotypes would only be observed for males who had been maltreated as a child; in other words, the *MAOA* gene would have no effect on antisocial phenotypes for nonabused males.

The reason that the effect of *MAOA* was thought to affect males but not females is because the *MAOA* gene is located on the X chromosome. Remember that males have one X chromosome, while females have two X chromosomes. As a result, males have only one copy of the *MAOA* gene, while females have two copies. What this means is that if males inherit an allele that codes for the production of low MAOA activity, they do not have a "backup" copy to compensate for it. Females, in contrast, have two copies so even if they inherit an allele that codes for the production of low MAOA activity they have a "backup" copy that may code for the production of high MAOA activity.

Caspi et al. tested their hypothesis by analyzing data drawn from the Dunedin Multidisciplinary Health and Development Study. The results of their statistical models revealed that *MAOA* did not have a significant direct effect on the antisocial phenotype measures. However, the analyses did reveal that alleles that coded for the production of low MAOA activity increased antisocial phenotypes for males who had been maltreated as children. In other words, there was a GxE between *MAOA* and childhood maltreatment, where the effect of *MAOA* only surfaced for maltreated males. The effect was relatively staggering: although only 12% of males from this sample had the low MAOA activity genotype *and* had been maltreated, they accounted for 44% of all violent convictions and 85% of them displayed antisocial phenotypes.

A number of follow-up studies have since been conducted to determine whether the GxE between *MAOA* and maltreatment would be observed in different samples (i.e., to ensure that the findings could be replicated and were not due to a chance finding). The results from some of these studies have upheld the *MAOA* X maltreatment interaction,[6] but other studies have failed to find support for this GxE.[7] These divergent findings spawned Julia Kim-Cohen and her associates to conduct a meta-analysis of studies testing the *MAOA* X maltreatment interaction.[8] The results of this meta-analysis revealed that across five independent studies, the GxE between *MAOA* and maltreatment was a statistically significant predictor of antisocial phenotypes. Kim-Cohen and colleagues concluded by stating that "These findings provide the strongest evidence to date suggesting that the *MAOA* gene influences vulnerability to environmental stress, and that this biological process can be initiated early in life."[9]

Researchers have also tested for GxEs that involve genes other than *MAOA* and that involve environments other than maltreatment. The results garnered from these studies have provided even more support for the importance of GxEs in the etiology of antisocial phenotypes. Table 3.1 summarizes some of the studies that have detected statistically significant GxEs on antisocial phenotypes. The format of this table is relatively straightforward: the far left-hand column contains the polymorphism (i.e., the G in the GxE) that was studied, the middle column contains the environment (i.e., the E in the GxE), and the right-hand column contains the phenotypic outcome that was predicted by the GxE. In some situations, there was more than one environment that interacted with the polymorphism. As a result, each environment is numbered (for each polymorphism) and so too is each phenotypic outcome. The numbers can then be matched together to determine the phenotypic outcome that was predicted by the GxE. For example, look at *DAT1*. We can see that *DAT1* interacted with alcoholic father (environment #1) to predict alcohol problems (phenotypic outcome #1). Similarly, we also see that *DAT1* interacted with delinquent peers (environment #2) to predict number of police contacts and violence (phenotypic outcome #2), and *DAT1* also interacted with family adversity (environment #3) to predict attention deficit hyperactivity disorder (ADHD) (phenotypic outcome #3).

It should also be noted that not all research shows that genetic effects are more powerful in high-risk as opposed to low-risk environments. Kevin Beaver and his colleagues, for example, examined the effect of *DRD2* on adolescent victimization and found that the A1 allele increased victimization, but only among white males who had relatively few delinquent peers; there was no effect of *DRD2* on victimization for white males who were exposed to a lot of delinquent friends.[10] Other studies have also detected stronger genetic effects in low-risk rather than high-risk environments.[11]

TABLE 3.1 The effects of some gene X environment interactions on antisocial phenotypes

POLYMORPHISM	ENVIRONMENT(S)	PHENOTYPIC OUTCOME
DAT1	1. Alcoholic father	1. Alcohol problems[63]
	2. Delinquent peers	2. Number of police contacts; violence[64]
	3. Family adversity	3. ADHD[65]
DRD2	1. Delinquent peers	1. Victimization[66]
	2. Religiosity	2. Violent delinquency[67]
	3. Family risk	3. Early-onset offending[68]
	4. Marital status	4. Desistance from delinquency[69]
	5. Marital stability	5. Childhood ADHD[70]
	6. Criminal father	6. Antisocial phenotypes[71]
DRD4	1. Marital status	1. Desistance from delinquency[72]
	2. Maternal insensitivity	2. Externalizing behaviors[73]
5HTTLPR	1. Delinquent peers	1. Number of police contacts[74]
	2. Antisocial parents	2. Externalizing behaviors[75]
	3. Socioeconomic status	3. Psychopathic traits[76]
	4. Adverse childhood events	4. Antisocial personality disorder[77]
COMT	1. Birth weight	1. Early-onset antisocial behavior[78]
MAOA	1. Maltreatment	1. Antisocial phenotypes; conduct disorder[79]
	2. Neuropsychological deficits	2. Delinquency; low self-control[80]
	3. Marital status	3. Desistance from delinquency[81]
	4. Perceived prejudice	4. Criminal arrests[82]

One of the most common explanations to these seemingly counterintuitive findings is known as the "social push" hypothesis.[12] According to this explanation, without exposure to criminogenic environments, individuals will be most affected by their genetic predispositions. In contrast, youth who are reared in environments that promote

antisocial behaviors will be affected more by the environment (that is pushing them toward delinquency) than they will be by genetic factors. Take, for instance, the study by Beaver and associates showing that *DRD2* did not have an effect on victimization for respondents with a relatively high number of delinquent peers. It is quite obvious that being in constant, daily contact with delinquent peers increases the odds of being victimized regardless of individual characteristics, including genotype. In different situations, where a person is not exposed to delinquent peers as frequently, other factors are more likely to come into play (e.g., their temperament) and these other factors—many of which are genetically influenced—ultimately affect the chances of being victimized.

Although findings creep up from time to time that are in accordance with the social push hypothesis, most of the time findings reveal that genetic effects are strongest when they are paired with adverse environmental factors. Until recently, the explanation employed to account for this finding was the diathesis–stress model.[13] Under this explanation, people with genetic predispositions for antisocial phenotypes would only display that phenotype if they encountered a disadvantaged or criminogenic environment. The environment would act as a "trigger" for the genetic predisposition to surface. If the environmental risk factor was missing, then the genetic potential would never be realized. The diathesis–stress model has been used to help explain not just antisocial outcomes, but numerous types of psychopathologies.[14]

Relatively recently, however, another explanation has been advanced to explain GxEs, wherein genetic effects are strongest in the presence of criminogenic environments. This explanation—known as the differential susceptibility model—has been developed by Jay Belsky.[15] According to this explanation, the alleles for certain genetic polymorphisms should not be viewed as "risk alleles," but rather as "plasticity alleles." These plasticity alleles indicate how malleable each person is; the more plasticity alleles that a person possesses, the more susceptible they are to the environment (both "good" environments and "bad" environments). One of the unique contributions of this explanation is that "plasticity alleles" work in a better-or-for-worse manner. What this means is that persons who possess a greater number of plasticity alleles will turn out the "best" when they are exposed to positive environments, but they are the same people who will turn out the "worst" when they are exposed to negative environments.

Belsky's differential susceptibility hypothesis has sparked a great deal of research trying to determine whether the diathesis–stress model or the differential susceptibility model is better at explaining GxEs.[16] Unfortunately, most studies published prior to the advancement of the diathesis–stress model are unable are not able to delineate between the two models because most GxE research views genetic polymorphisms as risk factors, focuses only on

negative environments, and studies only maladaptive phenotypes. Both explanations would make identical predictions in that the greater the number of risk or plasticity alleles, the more likely antisocial outcomes will surface in the presence of negative environments. The unique predictions would unfold when examining the association between the risk or plasticity alleles in the presence of a positive environment when predicting prosocial outcomes. According to the diathesis–stress model, risk alleles should not interact with positive environments to predict prosocial outcomes. In contrast, the diathesis–stress model would predict that plasticity alleles should interact with positive environments to predict prosocial outcomes.

Since Belsky's argument was first advanced, an emerging body of research has examined the efficacy of both the differential susceptibility and the diathesis–stress models. The results have been mixed, with some research showing support of the differential susceptibility model,[17] some research showing support for the diathesis–stress model,[18] and some research providing support for both perspectives.[19] As a result, much more research is needed to uncover the various ways in which these two models might be involved in contributing to the development of antisocial phenotypes.

GxEs have offered some much-needed insight into the understanding of behaviors and to the explanation of behavioral patterns that cannot be accounted for by purely environmental explanations. At the same time, however, sociological criminologists (and others) have tended not to hold GxE research to the same standard of science as they hold other lines of biosocial research. As James Lee and Matt McGue explain:

> There is a general recognition that GxE are not met with the same skepticism as findings from other areas of behavioral genetics. Over the past 15 years, there has been a consequent explosion of published GxE research in psychology. Unfortunately, much of this research has been susceptible to the same limitations with which other areas of psychology are struggling—small samples, ad hoc analytical decisions, multiple model tests, etc. And the result? GxE research has a rather poor record of replicability, leading to calls for its claims to meet the same standards of proof that have been established in other areas of genetics.[20]

This quote captures quite accurately how sociological criminologists frequently view findings from biosocial research. They are quick to point out all of the limitations of twin-based research, adoption studies, and molecular genetic association studies, but they overlook the fact that many of the same criticisms leveled against these research designs are applicable to GxE research. Moreover, the replication problems with genetic association studies are just as applicable—and perhaps more so—to GxE research as they are to candidate gene studies. Scholars, therefore, need to view GxE studies with caution,

particularly if they are focusing on novel GxEs that have not been replicated. Conducting replication studies and employing some of the safeguards that have been used in molecular genetic association studies (e.g., using two independent samples for novel GxEs) are some of the ways to help deal with issues related to nonreplication with GxEs.

Among sociological criminologists, moreover, there is an emerging belief that genetic influences only have their effects when they are part of a GxE; that, however, is not the case. There is now a significant amount of research showing that genes can have additive and independent effects on explaining phenotypic variance. While genetic effects sometimes are absorbed within GxEs, genetic effects are also frequently detected independent of GxEs. Failure to recognize the consistent finding that genes can operate independent of the environment has led some criminologists to the erroneous belief that GxEs are the only way that genes can have effects on antisocial behaviors. This is more a political statement than one that is grounded in the literature and thus limits our ability to truly understand the complex ways in which genes and the environment work together and work in isolation to produce criminal and antisocial behaviors.

Gene X Environment Correlations

rGE is the second type of gene–environment interplay. Where GxEs refer to the processes by which genes and the environment combine to produce phenotypic variance, rGEs capture the processes by which genotype structures differential exposure to environments.[21] This is a foreign concept to most criminologists because environmental measures are assumed to be purely social and not influenced by genetic factors. It seems somewhat odd to think that an environment could be due, in part, to genetic factors, but this is exactly what a line of quantitative research has revealed. Virtually every environment, from parental socialization to peer interactions, is partially influenced by genetic factors.[22] Below we will explore how genes and environment are correlated, but for now realize that there is reason to believe that rGEs may be more common than GxEs.[23] Lisabeth DiLalla added to this when she opined that "These correlations [rGEs] probably occur with most of the behaviors that we study, but they are extremely difficult to measure."[24] Before moving into a discussion of the literature bearing on rGEs, let us first discuss the three different types of rGEs: passive rGE, evocative rGE, and active rGE.

Passive rGEs are the result of biological parents passing along genotype and an environment to their children. Figure 3.2 shows that since genotype and the rearing environment are derived from the same source (i.e., parents), the two will be correlated

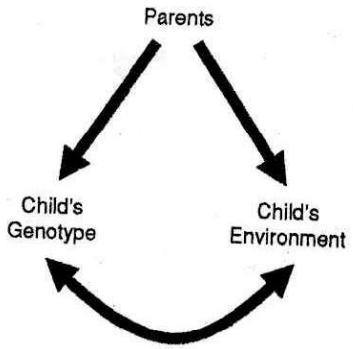

FIGURE 3.2 Portrayal of a passive gene X environment correlation.

(as the double-headed arrow reveals). For example, suppose a child is born to two parents, both of whom are highly aggressive and antisocial. This child is at risk for being raised in an abusive and neglectful environment and, at the same time, at risk for inheriting genetic predispositions for antisocial phenotypes. The end result is that the child's environment (i.e., abuse and neglect) is correlated with genetic tendencies (i.e., genetic tendencies for displaying antisocial phenotypes).

Evocative rGEs arise from genotype eliciting certain reactions from the environment and these reactions are positively correlated with genetic predisposition. Of course, genotype does not directly elicit reactions from the environment. Instead, and as Figure 3.3 depicts, genes influence the environment indirectly via phenotypes. The environmental reaction, which is a response to the phenotype, is then correlated with genotype (as depicted with the double-headed arrow). For example, suppose that a child has been diagnosed with conduct disorder (CD), a disorder that has been shown to be highly heritable.[25] Conduct disordered children are likely to evoke harsh discipline from their parents and they are also likely to be rejected by their same-age peers. As a result, the child's genetic predispositions (e.g., genetic factors for CD) are positively correlated with the environment (e.g., harsh discipline and peer rejection). Evocative rGEs probably can explain part of the reason why people with antisocial propensities tend to have difficulties in many spheres of their lives, such as relationship problems, employment and educational problems, economic problems, and so on.

Active rGEs refer to the integral role that genotype plays in the selection of environments that are compatible with genetic tendencies and that allow optimal genetic expression. Figure 3.4 contains a representation of an active rGE and shows that genotype

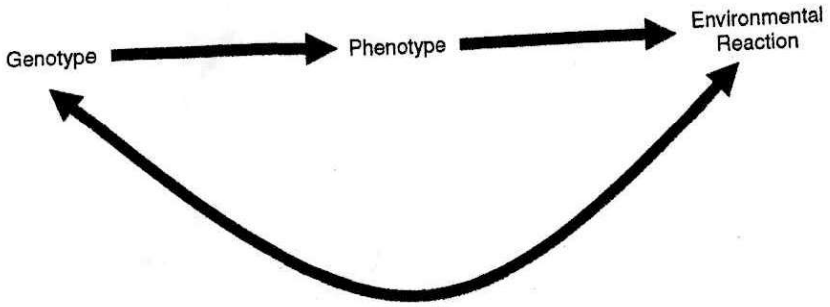

FIGURE 3.3 Portrayal of an evocative gene X environment correlation.

will influence the choice and selection of one environment over another.[26] Why do musically inclined youths join the choir? Why do athletically talented adolescents play sports? Why do quiet and reserved adults veer away from loud, boisterous parties? Part of the reason is because genetically influenced traits (e.g., being a good singer, being a good athlete, and being shy) propel people toward or away from certain environments. In this way, genotype plays an active role in carving out niches that are compatible with genetic predispositions.

The formation of peer groups is also partially a function of rGEs. Some adolescents, for example, prefer to associate with delinquent peers, others prefer to associate with athletes, and still others prefer to associate with band members. How are these friendship networks formed? This is obviously a complex question, but we do know that peers tend to befriend other peers who share similar talents, interests, and beliefs—all of which are partially influenced by genetic factors. When a person chooses another friend on the basis of shared traits (which are genetically influenced), they are really choosing other friends

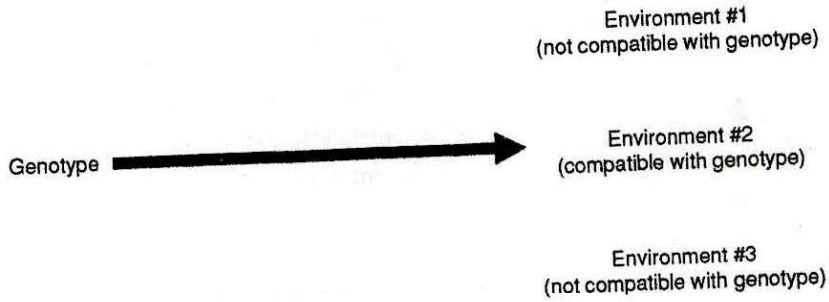

FIGURE 3.4 Depiction of an active gene X environment correlation.

on the basis of genetic factors. This necessarily translates into meaning that genotype is centrally involved in the formation of peer groups.

A criminological example with delinquent peers will help to make the concept of active rGE clearer. One of the strongest correlates to adolescent delinquency is affiliating with antisocial friends. There is debate among criminologists over whether contact with antisocial peers causes delinquency or whether delinquents seek out other delinquents to befriend. The evidence seems to indicate that both processes are at work, but it is the latter process—where delinquents befriend other delinquents—that can be explained by active rGEs. Why?—because we know that antisocial phenotypes are genetically influenced and we also know that delinquent peers befriend other delinquent peers. Consequentially, the genetic factors that are partially responsible for antisocial behavior are the same genetic factors that are driving delinquent youths to befriend each other.

A body of research has examined rGEs on a wide array of environments. The most common way of testing for rGEs is by employing environmental measures as dependent variables. Heritability estimates are then calculated for these environments in the same way that heritability is calculated for behavioral phenotypes (see Chapter 2). In this case, it is possible to calculate, for example, the percentage of variance in an environment that is accounted for by genetic factors. rGEs are detected when the environment is found to be at least partially heritable. Once again, these types of studies model heritability as a latent factor, which tells us nothing about the particular genes that might be involved in the rGE or even which type of rGE (i.e., passive, evocative, or active) might be at play. Recent rGE research has overcome this first limitation and examined whether certain genetic polymorphisms explain a significant amount of variance in environmental measures. Below we will review both of these lines of literature, but let us begin with the results garnered from behavioral genetic research and then we will move into a discussion of the molecular genetic studies that have tested for rGEs.

There are simply too many behavioral genetic studies that have examined the heritability to environmental measures to discuss and summarize all of them individually here. A review of the behavioral genetic literature by Kenneth Kendler and Jessica Baker, however, provides a thorough overview of the findings in respect to rGEs and will be the basis for our discussion.[27] Kendler and Baker reviewed 55 studies that had estimated the heritability of different environments. They divided the studies into different groupings based on the type of environment that was being examined. Four of these groupings are of particular relevance to criminological research: parenting behaviors, family environment, peer interactions, and stressful life events.

Parental socialization occupies a fundamental position within criminological scholarship. Almost every single criminological theory includes some aspect of parenting behaviors and most empirical-based research includes measures of parental socialization. Rarely, however, do criminologists entertain the idea that the parenting measures are genetically influenced. A line of behavioral genetic research has explored this possibility, and Kendler and Baker's review examined 19 of them. These studies estimated the genetic basis to dimensions of the parent–child relationship including maternal and paternal warmth, maternal and paternal negativity, maternal and paternal control, and maternal and paternal monitoring. The studies revealed moderate heritabilities for these parenting environments with heritability estimates ranging between .12 and .37. Kendler and Baker also examined the heritability of family environments that extended beyond parenting behaviors. The environments that fell into this category included measures such as family cohesion, family conflict, and family control. Once again, they found that the average heritabilities for these environments ranged between .18 and .30.

The next group of studies that were included in the review examined the heritability of peer interactions. Peer networks are of utmost importance to some of the major criminological theories, especially social learning theory, but criminologists have been slow to examine the heritability of peer groups. Kendler and Baker's review included six studies that examined the genetics of peer interaction and overall they reported that the average heritability across studies was .21. It should be pointed out, however, that these studies indexed various dimensions of peer relationships, not necessarily contact with antisocial peers. There have been a number of studies conducted that estimate the heritability of delinquent peer exposure. The results from most of the studies have revealed heritability estimates of about .40 or higher,[28] although it should be noted that at least one sample revealed a heritability estimate of only .03.[29]

Finally, Kendler and Baker reviewed the studies that had examined the heritability of stressful life events. Stressful life events have been linked to various maladaptive outcomes, but within criminology, Robert Agnew's general strain theory focuses on different sources of strain, including stressful events, and how they facilitate antisocial behaviors.[30] Agnew's theory has accrued a good deal of empirical support,[31] but again, criminologists typically ignore the genetic underpinnings to stressful situations. A total of 10 studies examining the heritability of stressful life events were included in the review,

and the heritability estimates ranged between .24 and .47, with an average weighted heritability that was equal to .28.

The above evidence appears to indicate beyond a shadow of doubt that most environments are genetically influenced, or in the words of Kendler and Baker, "Genetic influences on measures of the environment are pervasive in extent and modest to moderate in impact."[32] Based on these findings, a wave of research has begun to identify the precise genes that are associated with differential exposure to various environments. A small but ever-expanding body of research has explored this issue and the results have revealed that genes involved in neurotransmission are correlated with different environments, including criminogenic environments.

The first study to report an rGE between a measured gene and a measured environment was conducted by Danielle Dick and her colleagues.[33] In this study, they were interested in examining the associations among marital status, alcohol dependence, and the *GABRA2* gene (a gene that is involved in the transmission of the inhibitory neurotransmitter, GABA). The results of their analysis revealed that *GABRA2* was related to alcohol dependence. Most importantly was that *GABRA2* was also linked with marital status, where a SNP in *GABRA2* was associated with the odds of being married. This latter finding was the direct evidence of an rGE, most likely an active rGE.

Marital status has taken on great importance for life-course criminologists, where research has shown that offenders who marry are more likely to desist from crime than are offenders who remain single.[34] Although marriage is known to be a nonrandom event where people choose to marry or not to marry (i.e., an active rGE), criminologists have never taken into consideration the role that genetic factors play in the decision to marry.[35] As with most criminological research, standard social science methodologies (SSSMs) are employed to examine the relationship between marital status and desistance, which leaves open the possibility that the marriage–desistance association is spurious, owing to unmeasured genetic factors.

The family environment has also been of interest to researchers conducting molecular genetic studies testing for rGEs. For example, Michael Lucht and his colleagues examined whether a polymorphism in the *DRD2* gene was associated with negative paternal parenting.[36] The results of their study indicated an empirical link between alleles of the *DRD2* gene and negative paternal parenting, where certain alleles corresponded to more paternal rejection. Another study, conducted by Kevin Beaver et al. also reported a link

between dopaminergic genes and parenting behaviors.[37] More specifically, they examined the association between *DAT1*, *DRD2*, and *DRD4* and maternal negativity, paternal negativity, and childhood maltreatment. The results of their analysis revealed that *DRD2* was related to maternal negativity, paternal negativity, and childhood maltreatment, while *DAT1* was associated with maternal negativity. *DRD4* was unrelated to all of the parenting measures.

The results of these two studies could be interpreted as support for evocative rGEs, where children are equipped with genotypes that elicit certain responses from the environment—in this case, the environment would be parental socialization. The dopaminergic genes that were found to be involved in rGEs have also been found to confer an increased risk to developing antisocial phenotypes such as ADHD and delinquency (see Chapter 2). Children and adolescents displaying these antisocial phenotypes, in turn, are likely to be difficult to manage and evoke harsh discipline and punishment from their parents. The findings could also be interpreted as support for passive rGEs, where parents who are excessively negative, harsh, and neglectful pass on genotypes that make their offspring difficult and taxing. The research designs employed by Lucht et al. and Beaver et al., however, make it nearly impossible to disentangle evocative rGEs from passive rGEs. As a side note, adoption-based research designs are extremely powerful when trying to figure out what type of rGE is at play.[38]

Another study carried out by Lee Butcher and Robert Plomin employed a genome-wide scan to examine the association between 41 SNPs and a measure of family chaos.[39] The results of their study failed to detect any significant associations (beyond those that would have occurred by chance) between the SNPs and family chaos. However, Butcher and Plomin did not interpret these findings as evidence against rGEs. As they explained:

> The evidence for the heritability of measures of the family environment such as family chaos is persuasive, which implies that differences in DNA sequence are ultimately responsible for the heritability. It is likely that the DNA differences responsible for this heritability have such small or subtle effects that even more powerful strategies will be needed to detect them. Identifying genes associated with environmental measures will be worth the effort because they will foster research on an active model of experience in which individuals select, modify, and create environments on the basis of their genetic proclivities. In other

words, genetic effects on behavior do not stop at the skin—genetic effects need to be considered in relation to an 'extended phenotype' that includes effects on individuals' environments.[40]

One other study to detect an rGE was published by Kevin Beaver and his colleagues.[41] They were interested in examining whether alleles of a polymorphism in the *DAT1* gene were associated with differential exposure to delinquent peers. They analyzed data from the Add Health and found that *DAT1* was predictive of delinquent peers for male adolescents. This finding provided the first empirical evidence linking a genetic polymorphism to the formation of delinquent peer groups, an example of an active rGE. What was also of particular interest in this study was that the effect of *DAT1* on delinquent peers was only observed for males from high-risk families, not for males from low-risk families. This latter finding represents a GxE because the genetic effect (i.e., the effect of *DAT1*) was observed in one environment (i.e., high-risk families), but not in the other (i.e., low-risk families).

Research by Beaver et al. revealed that GxEs and rGEs can both be working simultaneously to create phenotypic variance. In fact, GxEs and rGEs are probably linked together in most phenotypes, which are studied. To see how this is possible, let's revisit the three types of rGEs. First, and as Figure 3.5 shows, passive rGEs equip children with a genotype and with environment, both of which are likely to be correlated. But note that since genotype and environment are correlated, children will often be hit with a "double whammy" where they receive genetic risk and environmental risk. When both risk factors are present, then interactions between the two are likely to occur, which, in turn, may produce antisocial phenotypes.

Figure 3.6 shows the dual effect of GxEs and evocative rGEs in the creation of phenotypic variance. Remember that with evocative rGEs, genotype is partially responsible for producing phenotypes and these phenotypes in turn elicit responses from the environment. For example, imagine a child with a genotype that produces serious violence during early adolescence. This youth, because of antisocial behaviors, has problems at school and is eventually expelled. In short, the youth's genotype was responsible for school failure, including the expulsion (i.e., an environmental reaction to behavior), which underscores the logic of evocative rGEs. Being expelled from school likely places the antisocial youth in environments where there is no supervision and where they may hang out with other youths who have also been expelled. As a result, the adolescent will be in

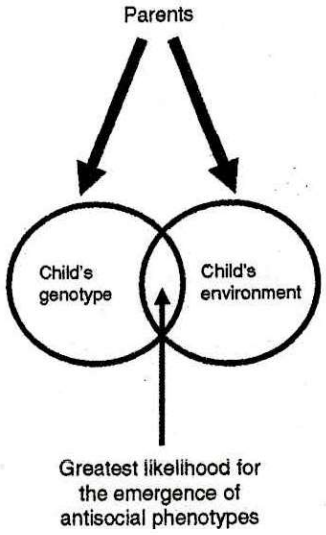

FIGURE 3.5 Dual effects of gene X environment interactions and passive gene X environment correlations in the creation of phenotypic variance.

a criminogenic environment, one that is likely to interact with genotype to produce even more antisocial phenotypes.

FInally, Figure 3.7 depicts the dual effects of GxEs and active rGEs. Remember that with active rGEs genotype is partially responsible for nudging a person into environments that allow genetic expression. Chronic offenders, for example, are likely to select criminogenic environments such as gangs and high-crime neighborhoods. Once in these

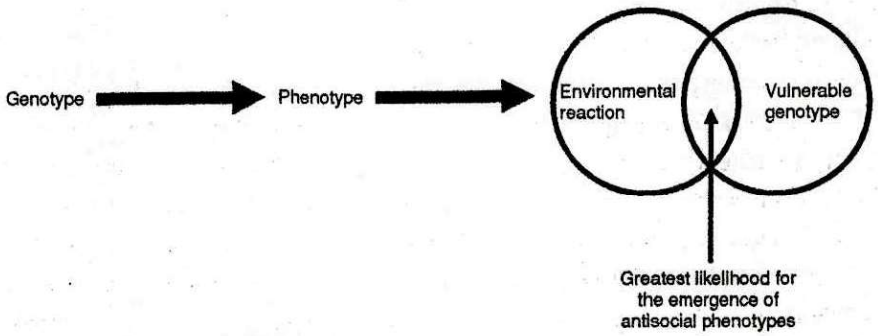

FIGURE 3.6 Dual effects of gene X environment interactions and evocative gene X environment correlations in the creation of phenotypic variance.

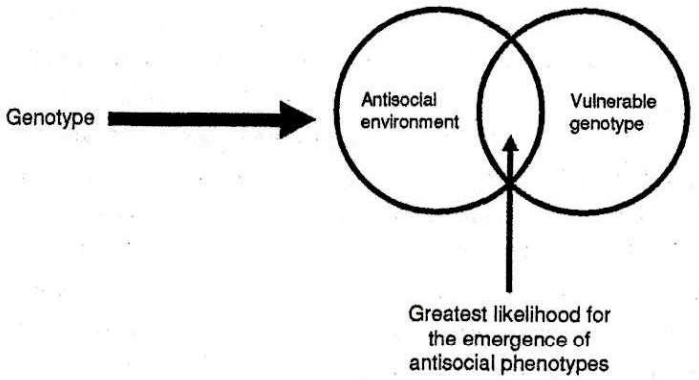

FIGURE 3.7 The dual effects of gene X environment interactions and active gene X environment correlations in the creation of phenotypic variance.

criminogenic environments, the person's genotype is likely to interact with the environment to produce antisocial phenotypes. The important point to bear in mind is that GxEs and rGEs are not mutually exclusive, but rather likely work simultaneously in the etiology of most human phenotypes including antisocial phenotypes.

Epigenetics

The human genome consists of all the genes contained on the 23 pairs of chromosomes. Although genes provide the necessary instructions for humans to form, develop, and live, they need additional information to tell them when and where to code for proteins. Remember that DNA is found in the nucleus of every cell except red blood cells. This means that the DNA found in kidney cells is the same DNA found in liver cells. What, then, separates kidney cells from liver cells and what separates all other cells from each other? The answer to this question is relatively straightforward: only those genes that are needed for the functioning of the kidney (liver) are expressed (meaning that they actually code for the production of proteins), while all of the other genes are silenced (meaning that they do not code for the production of proteins). How does the human genome know which genes should be expressed and which genes should be silenced? This information is not contained in DNA, but rather in the epigenome.

The epigenome consists of chemical markers that are situated along the strands of DNA. These chemical markers affect gene activity because they alter the ability of DNA to be duplicated onto RNA. Some of these chemical markers enhance gene activity, whereas

other chemical markers decrease or silence gene activity. Unlike the human genome that is immutable once formed, the chemical markers on the epigenome can actually be changed throughout life in response to the environment, and these epigenetic modifications can alter genetic expression. Since the epigenome partially controls the expression of the human genome, the epigenome is also partially responsible for producing phenotypes. Perhaps even more interesting is that these epigenetic modifications can be passed along from generation to generation.[42] This means that environmental stimuli can change a person's epigenome today and these epigenetic changes can be passed on to future generations.[43] If we return back to our original question where we asked what separates a liver cell from a kidney cell, it appears as though the answer is found in the epigenome, where chemical markers direct genes to be "switched on" or "turned off" depending on the particular cell.

Epigenetic mechanisms thus alter DNA activity without altering DNA sequences.[44] There are numerous different epigenetic processes, but we will focus on two: DNA methylation and histone acetylation. Let us begin by discussing DNA methylation. Remember that the epigenetic processes are partially responsible for why some genes are expressed in some cells (e.g., liver cells) but not in other cells (e.g., kidney cells). The silencing of genes is accomplished because an enzyme, called DNA methyltransferase, attaches a group of atoms, known as a methyl group (CH3), to the nucleotide cytosine (C in the genetic alphabet). But methylation is not likely to occur on all cytosine bases. There are blocks of DNA that are primarily made up of cytosine (C) bases and guanine (G) bases, and these dinucleiotide DNA sequences are referred to as CpG islands (the "p" indicates that the CG bases are held together by a phosphodiester bond). It is here, on cytosines on CpG islands, where methylation is most likely to occur. To understand why this is the case, it is important to note that certain sections of genes, known as promoter regions, act as switches that are able to turn genes "on" or "off" and CpG islands are located near those switches. These switches are turned on by special proteins called transcription factors. However, when a methyl group is attached to a cytosine base, the transcription factors are discouraged from turning the gene on. As a result, the transcription of DNA into RNA is prevented. If DNA cannot be transcribed into RNA, then the central dogma of biology does not occur. As a result, the protein specified by the particular gene will never be produced and that gene is turned "off" or silenced.[45] DNA methylation, in other words, is responsible for turning genes "off."

Histone acetylation is the second type of epigenetic process, which we will discuss. In order to understand this epigenetic process, it is first necessary to point out that if DNA was uncoiled and stretched out it would measure about 6 feet in length. DNA needs to be packaged very efficiently in order to fit into the nucleus of each cell. This is accomplished with the help of histones. Histones can be thought of as spools around which DNA is wound very tightly. The tighter the DNA is wound, the less likely genes are to be expressed. Think of this: transcription factors are needed in order for a gene to be transcribed into RNA. When DNA is tightly wound around histones, transcription factors are not as easily able to access genes. As a result, genes that are inaccessible to transcription factors are unable to be decoded into proteins.

Histone acetylation occurs when acetyltransferase enzymes tack a group of atoms, known as an acetyl group (CH_3CO), to the histone. This process loosens the DNA from the histone, which necessarily translates into transcription factors being able to access genes more readily. As a consequence of acetylation, genes are more likely to be turned "on" and expressed. Acetyl groups can be removed from histones via deacetylase enzymes, which results in the DNA becoming more tightly wound around the histone. And guess what this means? It means that genes are more likely to be turned "off" because transcription factors are less likely to be able to access the genes.

Let us recap four main points about epigenetics. First, epigenetic modifications can alter gene activity by turning genes "on" or "off." As a result, two people could have the exact same alleles for a gene, but due to epigenetic differences, the genes may be differentially expressed. Second, and as will be discussed in greater detail below, epigenetic modifications can occur in response to environments that are experienced from conception to death.[46] Diet and nutrition, smoking, and prenatal exposure to toxins are just a sampling of the many environments, which are thought to result in epigenetic alterations. The important point to remember is that the environment by way of altering the epigenome may actually be responsible for turning genes "on" and "off." Third, these epigenetic modifications can be inherited. This is a particularly fascinating finding because it means that the environment can change the epigenome and these changes can actually be passed across generations. Fourth, epigenetic modifications are reversible and thus are particularly attractive targets for different types of interventions for certain diseases such as cancer.[47]

So how do epigenetic modifications relate to human phenotypes, especially antisocial phenotypes? This is a difficult question to answer because no research has

directly examined the connection between epigenetics and criminal outcomes.[48] But, the existing research does seem to indicate that a wide range of environments—some of which are studied by criminologists—may be involved in altering the epigenome. In a ground-breaking study, Ian Weaver and his colleagues studied maternal nurturing among rats.[49] They divided mother rats into two groups: those that licked and groomed their newborn pups and that engaged in arched-back nursing (i.e., the high-nurturing group), and those that rejected their newborn pups (i.e., the low-nurturing group). The newborn pups were then placed into stressful environments to see how they would react. The pups from the high-nurturing group were relatively calm and responsive, while those from the low-nurturing group were skittish and not as adaptive.

These findings, while interesting, left unanswered whether the association between nurturing and behavior was due to genetic factors, environmental factors, or both. So, Weaver and associates then cross-fostered rats, where rat pups born to low-nurturing mothers and rat pups born to high-nurturing mothers were switched at birth. Cross-fostering is similar to the adoption-based research design and it helps to separate genetic from environmental effects. The cross-fostering experiment revealed that newborn pups resembled their "adoptive" mother more than their biological mother.

Most social scientists would have stopped there and concluded that these findings provided cold, hard evidence that socialization trumped genetics. Weaver et al., however, were cautious against making such a hasty conclusion and began to examine the methylation patterns of these rat pups. Their findings were striking: pups raised by high-nurturing mothers had less methylation of glucocorticoid receptor genes when compared to pups raised by low-nurturing mothers. Glucocorticoid receptors found in the hippocampus shape behavioral responses to stressful situations, and, in general, animals with less methylation of glucocorticoid receptor genes are better equipped to deal with stressful environments. Acetylation differences were also detected in genes associated with nerve growth in the hippocampus. These epigenetic differences emerged during the first week of life and persisted into adulthood. In some pups, Weaver and colleagues reversed the epigenetic patterns of the low-nurtured pups by administering a drug (trichostatin). Remarkably, the behavioral differences between low- and high-nurtured pups disappeared after the epigenetic patterns were equalized. In a follow-up study, this same research team identified more than 900 genes that were regulated by maternal care.[50]

These findings have direct bearing on criminology because most criminological theories identify nurturing and parental socialization as important factors implicated in the etiology of crime and delinquency. In a recent study, for example, Lee Ellis and his colleagues surveyed 1218 criminologists worldwide about what they thought causes crime.[51] Parenting- and family-level factors, such as an unstable family life and lack of supervision and monitoring, ranked near the top. And, as was discussed in Chapter 1, most criminologists interpret the relationship between parent-level factors and antisocial phenotypes as evidence in favor of socialization. The study conducted by Weaver et al. casts doubt on such a simplistic one-to-one relationship, and instead points to the likelihood that parents and other environments may exert their effects on antisocial phenotypes via changing the epigenome (see Figure 3.8). Criminologists have yet to take this idea seriously.

Studies using human samples have also detected epigenetic modifications by analyzing monozygotic (MZ) twin pairs. Even though MZ twins share 100% of their DNA, they often display divergent phenotypes. This is even true for genetically driven disorders such as schizophrenia and autism. One of the more dominant explanations for divergent outcomes between MZ twins is that they are exposed to different nonshared environments, and these nonshared environments may interact with genotype. If a pair of MZ twins is genetically predisposed to heart disease and one smokes but the other does not, then the smoker is much more likely to develop heart disease. From this example, it is relatively easy to see that exposure to different environments led to genetic susceptibilities being triggered in one twin but not the other.

Epigeneticists, however, have offered a new twist for why MZ twins may turn out differently. According to them, exposure to different environments may actually alter the epigenome and these alterations may cause certain genes to be differentially expressed, producing phenotypic differences.[52] Partial evidence in favor of this hypothesis was gathered by Mario Fraga and associates when they examined epigenetic differences in a sample of MZ twin pairs who were of different ages.[53] Younger MZ twin pairs had virtually identical epigenetic patterns. Older MZ twin

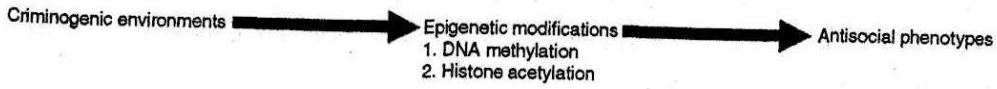

FIGURE 3.8 Possible interrelationships among criminogenic environments, epigenetic modifications, and antisocial phenotypes.

pairs, however, had 2.5 times as many epigenetic differences (as measured by DNA methylation patterns) as younger MZ twin pairs. These findings are particularly important because they indicate that, for one reason or another, epigenetic patterns change throughout the life course, and remember that these changes can affect gene expression.

The study by Fraga and colleagues was also important because it showed that MZ twins, although genetically identical, might have their genes differentially expressed because of epigenetic modifications that arise throughout life. These epigenetic differences *could* lead to phenotypic differences, but Fraga's research team did not directly examine this possibility. The findings of some studies have, however, revealed that epigenetic differences are linked to phenotypic differences. A study by Arturas Petronis and associates, for example, explored the relationship between epigenetic modifications and schizophrenia in two pairs of MZ twins.[54] One pair of twins was concordant for schizophrenia (i.e., both twins had developed schizophrenia) and the other pair was discordant for schizophrenia (i.e., one twin had developed schizophrenia and one twin had not developed schizophrenia). They analyzed epigenetic patterns on the *DRD2* gene in both sets of twins and their findings were truly amazing: the twin with schizophrenia (from the discordant twin pair) was epigenetically more similar to the two twins from the concordant twin pair (where both twins had schizophrenia) than they were to their own co-twin (who did not have schizophrenia). Additional studies have revealed that epigenetic modifications may be related to risk-taking behaviors,[55] ADHD,[56] childhood asthma,[57] autism and other neurodevelopmental disorders,[58] and bipolar disorder.[59]

A more recent study has added another layer of complexity to epigenetics and its relation to the genome.[60] In this study, Jason Gertz and his colleagues were interested, among other things, in examining whether genotype influences DNA methylation. The results of their analysis revealed that patterns of methylation are due, in part, to genetic factors. Other studies have reported findings that converge with these by showing that methylation across the genome is due, in part, to genetic influences.[61] Stated differently, results are emerging that consistently show that variation in epigenetic markers across people occurs because of variation in genotype (coded into the human genome). These findings underscore the dynamic and mutual interdependence among the genome, the epigenome, and the environment.

Whether the findings of epigenetic research could be extended to antisocial phenotypes remains unknown. Among criminologists, however, it has become fashionable to pontificate that epigenetics is central to explaining the links among, environments, genes, and antisocial behaviors. This excitement, however, should be tempered given that the study of epigenetics remains in its infancy. As the eminent behavioral scientist Terrie Moffitt and her coauthor explain:

> Many social scientists embrace the new epigenetics research because it has been billed as evidence that environment trumps genes. There is much excitement about this approach, which promises to capture a biological signature left behind by environmental adversity. However, our reading, and that of many biologically oriented scientists, is that epigenetics has been widely oversold, particularly in the media. Many of our expert epigenetics research colleagues are deeply embarrassed by the warm, uncritical response their work has attracted from social scientists.[62]

If real epigeneticists urge caution about the ability of epigenetics to explain complex human behaviors, then criminologists—who likely do not know as much about epigenetic processes and their application to human behavior—should follow in these footsteps and remain just as cautious about championing epigenetics as a key causal role in the genetic etiology of antisocial behaviors.

Summary

There is widespread recognition among biosocial criminologists that a complex arrangement of genetic and environmental factors frequently act in tandem to produce variance in antisocial phenotypes. The close nexus between genes and the environment has become known as gene–environment interplay, and there are three main types of gene–environment interplay. The first, GxE, occurs when genetic effects only surface when paired with certain environments or when environmental effects only surface when paired with certain genetic factors. The second, rGE, occurs when genotype and the environment are correlated. The last type of gene–environment interplay is epigenetics, where the expression of genes is altered without altering DNA sequences. It is likely that all three of these processes are involved—at varying degrees— in the creation of phenotypic variance including variance in antisocial phenotypes.