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Genetic and Environmental Influences on Behavior: Capturing All the Interplay

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Basic quantitative genetic models of human behavioral variation have made clear that individual differences in behavior cannot be understood without acknowledging the importance of genetic influences. Yet these basic models estimate average, population-level genetic and environmental influences, obscuring differences that might exist within the population and masking systematic transactions between specific genetic and environmental influences. This article discusses a newer, more sophisticated and powerful quantitative genetic model that articulates these transactions. Results from this model highlight the ways in which the gene–environment interaction and correlation are intertwined. They can be used to integrate findings from quantitative and molecular genetic studies and to understand the roles of genetic influences and social forces in manifested behaviors, even when DNA sequence variation is not relevant.

Keywords: genetic influences, environmental influences, gene–environment interplay, gene–environment correlation, income–health gradient

> Harry unwrapped his chocolate frog and picked up the card. It showed a man's face. He wore half-moon glasses, had a long, crooked nose, and flowing silver hair, beard, and mustache. Underneath the picture was the name Albus Dumbledore.. . . Harry [looked at the picture again] and saw, to his astonishment, that Dumbledore's face had disappeared.
>
> 'He's gone!'
>
> 'Well, you can't expect him to hang around all day,' said Ron. 'He'll be back.. . .'
>
> '. . .But in, you know, the Muggle world, people just stay put in photos.'
>
> 'Do they? What, they don't move at all?' Ron sounded amazed. 'Weird!' (Rowling, 1997, p. 103)

The question of how nature and nurture contribute to the manifestation of behavior has been a source of fascination from time immemorial. Though there have been extremists who have believed that either the genetic influences of nature or the environmental influences of nurture predominate, most students of the question have recognized that both are important and neither is deterministic. It is only now, however, that we are coming to understand that genetic and environmental influences are rarely independent and static like subjects in Muggle photos. Instead, like subjects in photos in Harry Potter's world of wizards, they transact or interplay with each other, sometimes strongly present, other times asleep or even absent. This article discusses a newer, more sophisticated and powerful quantitative genetic model that makes it possible to define and quantify how these transactions are intertwined for particular variables. Results from this model can be used to integrate findings from quantitative and molecular genetic studies and to understand the roles of genetic influences and social forces in manifested behaviors, regardless of whether DNA sequence variation is relevant. Results from the model also suggest ways of understanding the paradoxical observation of the pervasiveness of genetic influences and the relative absence of consistent main effects of specific genetic polymorphisms.

Behavioral scientists are beginning to realize that genetic differences among individuals are commonly associated with differential sensitivities to the environments to which the individuals are exposed and that genetic differences among individuals are also commonly associated with differences in environmental exposure. That is, any given environment may have different effects on individuals who differ genetically, and genetic differences among individuals may create differences in the environments to which individuals are exposed. A simple Muggle camera will not do: We need a wizard's camera that can capture all of this interplay. Like Harry, however, who knows that a Muggle photo is a static representation of a dynamic situation, we are aware of the nature of the interplay in concept, but the prospect of actually capturing it is still surprising. The purpose of this article is to draw us into the wizard's world, where seeing it displayed is ordinary. There are at least two well-known dynamic concepts to consider.

First, there is the gene–environment interaction (G × E) or the association between differential environmental effects and genetic differences. A well-understood example involves the recessive alleles for phenylketonuria (PKU). These alleles prevent metabolism of phenylalanine, an enzyme commonly found in food. In children with two copies of these alleles, the metabolic products of unprocessed phenylalanine build up and damage the developing brain. Phenylalanine has no harmful effects on children who carry

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at least one copy of an allele that enables metabolism of phenylalanine, and the brain damage associated with PKU can be prevented through modification of the diet to eliminate foods containing phenylalanine. Second, there is the gene–environment correlation (r_{GE}) or the association between genetic differences and differential environmental exposure. A commonly used example is intellectual enrichment for children. Brighter parents pass their genes for intelligence on to their children and may also provide them with more intellectually stimulating home environments. They may do this both because they are expressing their own intellectual interests to their children and because they are responding to their children's expression of intellectual interests, reinforcing their further development and expression in the children.

The existence and importance of associations between genetic and environmental influences is consistent with the concept that natural selection governs the patterns of genetic influences within and across populations. Over time, genes that facilitate reproductive fitness in a given environment increase in frequency and ultimately reach fixation, whereas genes that impede reproductive fitness are gradually eliminated. Differences in response to the environment caused by genetic differences are the raw material for this process (Ridley, 2003). But the environment is not a unitary, constant set of circumstances, and individual efforts to seek or create environments compatible with their genetic endowments are fundamental to the process of evolution. There is a tendency to think of evolution as a long-drawn-out process that took place some time in the past, yet the day-to-day responses of individual organisms to the environment and the adaptation of the environment to those responses are the stuff of which evolution is made. Behavior takes place through genetic expression, yet genetic expression is dependent on the environment in which it takes place. Given the wealth of accumulated evidence for genetic influences on all other areas of biological, psychological, and behavioral functioning, it is extremely unlikely that there are no genetic influences on responsiveness to and selection of the environment. For these reasons, we should expect G × E and r_{GE} to be common and fundamental means of genetic and environmental transactions involving behavior, and identifying and measuring them and their effects should be a fundamental research goal.

Epidemiology is the study of the incidence, distribution, and control of diseases in the population. Focus is generally placed on identifying risk factors that contribute to the incidence and spread of diseases, which ultimately means understanding their etiologies. This approach can be applied to many issues in psychology that involve the study of patterns of behavior in the population. When behaviors are maladaptive or disruptive to social organization, the concept of disease may be relevant to this approach, regardless of whether the patterns of behavior meet some diagnostic disease category. The concept of disease, however, is not necessary to the use of an epidemiological approach to the study of behavior. What is necessary is the focus on distributional and etiological patterns at the level of the population. Given that all behaviors show both genetic and environmental influences, illuminating the role of gene–environment interplay in patterns of behavior is a crucial task in understanding those patterns. It is only through understanding this role that we will be able to develop constructive interventions to interrupt or prevent maladaptive or socially disruptive behavior patterns or to enhance socially constructive behavior patterns.

This emphasis on understanding patterns of behavior at the level of the population, without identification of involved individuals, is compatible with the use of both quantitative genetic and molecular genetic techniques as used in genetic epidemiology. Quantitative genetic techniques provide estimates of the relative magnitudes of omnibus genetic and environmental influences without the necessity of specifying the actual DNA sequences or environmental circumstances that provide those influences. These quantitative genetic techniques have been invaluable in demonstrating the existence of genetic influences on behavior. Yet the ways in which these techniques traditionally have been applied have been based on the assumption that genetic and environmental influences are independent, and, thus, they provide only a snapshot, still-life view of their relative magnitudes. The population forces identified by an epidemiological approach have their effects on individuals one at a time in a changing world, and distributional and epidemiological patterns have to reflect both the lack of independence between genetic and environmental influences and the fact that these influences may not be static across environments, population groups, or over time. Like wizards, we need a quantitative genetic snapshot view that provides some sense of the dynamic nature of the subject under study. A still-life Muggle photo will not do.

Two recent articles have dealt extensively with the role of gene–environment interplay in psychopathology (Moffitt, Caspi, & Rutter, 2006; Rutter, Moffitt, & Caspi, 2006), and their discussion is relevant to patterns of behavior in populations more generally. These articles have defined the following four forms of gene–environment interplay: variations in genetic influence according to environmental circumstances (quantitative), epigenetic programming (environmental effects on gene expression), G × E correlation (r_{GE}), and G × E between specific DNA sequences and specific measured environments. This article addresses the relations among quantitative G × E, r_{GE}, and G × E between specific DNA sequences and specific measured environments, with particular emphasis on the information provided by the quantitative genetic model of G × E and r_{GE}. To accomplish this, I use the classic epidemiological puzzle of the income–health gradient (Adler et al., 1994; Antonovsky, 1967; Marmot et al., 1991) as an example to illustrate the kinds of information provided by a quantitative genetic approach that explicitly recognizes the possibility of gene–environment interplay. The findings I describe are documented in detail in Johnson and Krueger (2005) and are based on data from the twin sample of the MacArthur Survey of Midlife Development in the United States (MIDUS; Kendler, Thornton, Gilman, & Kessler, 2000; Kessler, Gilman, Thornton, & Kendler, 2004). Many of the concepts I address are not new; they were discussed in the classic work of Jinks and Fulker (1970). They deserve fresh treatment, however, because of the explosion in quantitative and molecular genetic methodological power and knowledge in the nearly 40 years since that work was published.

To ensure that readers can interpret the example I use, the current article begins with some background information about the income–health gradient. I then introduce a quantitative genetic model that includes provision for gene–environment interplay and show how the existence of quantitative G × E implies the existence of corresponding kinds of r_{GE} by using the income–health gradient as an example. From there, I describe how the gene–

environment interplay model can be used to operationalize the investigation of the involvement of socially selective and causative forces in the manifestation of associations between environmental risk factors and outcomes, again with special focus on the income–health gradient as an example. I then show how information about G × E between specific DNA sequences and specific measured environments fits within the context of this model and how opposing environmental forces and imprecise measurement may complicate identification of underlying patterns of association. I conclude with a discussion of how investigating the nature of gene–environment interplay makes possible the articulation of new and specific research questions that should illuminate difficult issues in understanding patterns of behavior.

The Income–Health Gradient

The *income–health gradient* is the name given to the robust association between income and physical health. The same general phenomenon is sometimes called the *SES–health gradient*, when education and job status are combined with measurement of income. People with greater financial resources tend to have better physical health. The association is well established throughout history. It transcends national boundaries, existing in wealthy and developing nations alike (Adler et al., 1994; Antonovsky, 1967). It also transcends political systems. In particular, it transcends systems of health care delivery and is observed in countries with socialized medicine and national health care as well as in countries with free-market systems (Adler & Snibbe, 2003). It may seem obvious that people in severe poverty might have poorer physical health because of the effects of poor nutrition, crowded and dirty living conditions, and inadequate medical care. The association, however, exists across the income range. Those in the highest income levels have better health than those just below them, just as those just above the poverty line have better health than those actually in poverty (Marmot et al., 1991). The association also transcends disease categories, including mental health, applying to almost all known medical conditions (Adler & Snibbe, 2003). Historically, in the few cases of diseases that have been more prevalent among the wealthy than among the poor, the situation has reversed with growth in knowledge of the etiology of the disease. Gout, heart disease, and lung and breast cancer are examples of this (Gottfredson, 2004).

Adler et al. (1994) examined possible explanations for the association. First, they addressed the possibility that the relation is the result of common underlying genetic influences. If this were the case, they claimed, physical size or intelligence, for example, could contribute directly to both income and physical health, resulting in a spurious association between them. Adler et al. noted, however, that the association between job status and health persists after adjustment for height and body mass index (Marmot et al., 1991) and that intellectual capacity does not appear to be reliably linked to health. Thus they deemed this explanation for the association unlikely. By implication at least, Adler et al. rejected the behavioral implications of this possibility. That is, if genetically influenced traits like intelligence and personality were to contribute to both occupational development and health maintenance behaviors or to both behaviors that confer health risks and difficulties in maintaining income, it would be more difficult to think of the association as socially driven. This is because it would be likely that the association would involve expression of some single volitional trait, such as personal control. This possibility is known as *social selection* in the psychopathology literature. Though research subsequent to Adler et al. (1994) has made clear that substantive associations between intellectual capacity and physical morbidity and mortality do exist (e.g., Deary, Whiteman, Starr, Whalley, & Fox, 2004; Gottfredson, 2004), the social selection explanation for the income–health gradient has not been actively pursued.

Alternatively, Adler et al. (1994) suggested that income influences biological functions that in turn affect health status. This possibility has become the focus of most subsequent research in this area. The basic conceptual framework for that research is that lower income is associated with increasing demands and decreasing resources for dealing with those demands (Adler & Snibbe, 2003). The mismatch between demands and resources at lower income levels creates both greater exposure to stress and greater psychological response to that stress. The resulting stress reactivity among individuals of lower income increases biological dysregulation, which, when chronic, may make these individuals more vulnerable to disease (Cannon, 1942; Dohrenwend, 2000; Dohrenwend, Shrout, Link, Skodol, & Martin, 1986; Gallo & Mathews, 2003). This possibility is known as *social causation* in the psychopathology literature.

McEwen (1998) has suggested a way to operationalize the notion of the presumed effects on physical health of chronic biological disregulation brought on by stress. He compiled a combination of indicators of these effects he termed *allostatic load*, including systolic and diastolic blood pressure, waist-to-hip ratio, HDL and LDL cholesterol, blood glycosylated hemoglobin (an indicator of glucose levels over the past 2–3 months), and the hormones cortisol, dehydroepiandrosterone, epinephrine, and norepinephrine. Allostatic load appears to increase with decreasing income among older adults and to be associated with general physical and cognitive decline, cardiac events, and mortality (e.g., Karlamangla, Singer, McEwen, Rowe, & Seeman, 2002; Singer & Ryff, 1999). The indicators involved in allostatic load as well as most of the common chronically debilitating physical health conditions, including heart disease, arthritis, many cancers, and diabetes, are generally acknowledged to be genetically influenced to some significant degree (e.g., Komaroff, 1999). As the income–health association tends to be strongest among these common chronic illnesses (Adler & Snibbe, 2003), it is clear that gene–environment interplay must be involved in some way in the association.

Data from humans and from studies of experimental animals suggest the manner of involvement. Genes for metabolic efficiency that enable adaptation to biologically stressful environments play a primary role in affecting lifespan and, by implication, health (Parsons, 2003). In the common fruit fly *Drosophila melanogaster*, for example, genetic variability for fitness, and especially mortality, increases in situations of high biological stress (Parsons, 2002). Tiret (2002) noted that genes for disease susceptibility also show amplified effects in the presence of triggering environmental risk factors. Possession of a specific gene in certain rats, for example, is associated with significantly greater adiposity, glucose intolerance, circulating leptin levels, and blood pressure during high-fat-diet feeding but not during normal-diet feeding (Pauzova et al., 2003). Genes associated with diabetes in humans have shown

similar effects (Weiss, Brown, Shuldiner, & Hagberg, 2002). These findings can be summarized as examples of the stress–diathesis model, in which environmental stressors transact with genetic vulnerabilities to produce illness and other decrements in well-being (Gottesman & Shields, 1972; Rosenthal & Kety, 1968). They can also be generalized to suggest that genetic influences on physical health problems increase with the increasing stress associated with decreasing income.

This was in fact the finding of Johnson and Krueger (2005) in a study based on data from the twin sample of the MIDUS. In that study, the model described in detail below was used to measure the effects of income on genetic and environmental variance in physical health. Results indicated that genetic variance in two measures of physical health, chronic illnesses and body mass index, decreased by roughly a factor or two across the range of income in the sample. This was true after adjustment for participants' levels of education and the presence or absence of health insurance coverage. Variance in both shared and nonshared environmental influences remained constant. The changes in genetic variance with income were associated with changes in the correlation between genetic influences on physical health and income as well: When income was high, the correlation between genetic influences on the two traits was high as well. When income was low, the correlation between genetic influences was also low. I use the results of the previous study as an example of how understanding gene–environment interplay can help us to understand the income–health gradient and, more generally, social processes of interest.

The Full Quantitative Gene–Environment Interplay Model

Figure 1 shows the standard, most common model of genetic and environmental influences on a measured phenotype or trait (e.g., physical health problems [HP]) for a single individual, who is usually, in most studies, one member of a twin pair (Jinks & Fulker, 1970). The parameter estimates shown in the figure come directly from the data used for the Johnson and Krueger (2005) study I described above. In that study, standardized variables were used, but this may not always be the optimal metric. Under this model, latent genetic influences (denoted by "A" for genetic influences that are considered additive: Each gene involved presumably contributes something to the manifestation of the trait independently of the contributions of the other genes involved) on HP are constant for all individuals in the population and independent of both shared and nonshared environmental influences (denoted by "C" for common environmental influences that act to make members of twin pairs similar to each other, regardless of their zygosity, and denoted by "E" for environmental influences and measurement error that act to make members of twin pairs different from each other, respectively). C and E are, like A, constant across the population, and all three are independent of each other. No specific genes or specific environmental effects are measured. The model includes no provision for gene–environment interplay and in fact is based on the assumption that no such interplay is present (Jinks & Fulker, 1970). It is like a standard photograph: a still-life snapshot of a constrained version of the genetic and environmental situation.

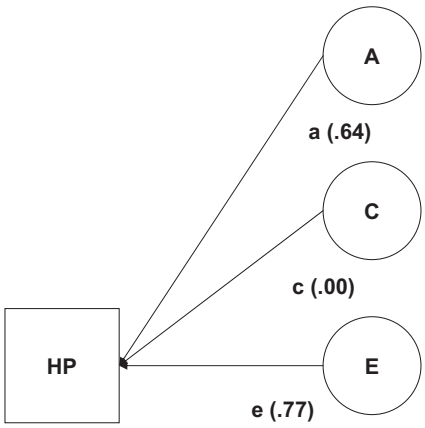

Figure 1. Standard model of genetic and environmental influences on a trait, such as health problems (HP). "A" refers to additive genetic influences, "C" to shared environmental influences, and "E" to nonshared environmental influences. The open square represents the measured variable of primary interest, and the open circles represent the latent variables. Parameter estimates are in parentheses.

Use of this model to study HP still provides important information, even if gene–environment interplay is involved. The resulting estimates are, however, applicable only on an overall, average population-level basis, and they contain systematic distortions that are due to any gene–environment interplay that does exist. These distortions have different effects, depending on the nature of the gene–environment interplay. Specifically, quantitative G × E between genetic and shared environmental influences acts to increase estimates of genetic influence; quantitative G × E between genetic and nonshared environmental influences acts to increase estimates of nonshared environmental influence (Jinks & Fulker, 1970; Purcell, 2002). The r_{GE} between genetic and shared environmental influences acts to increase estimates of shared environmental influence; the r_{GE} between genetic and nonshared environmental influences acts to increase estimates of genetic influence (Jinks & Fulker, 1970; Purcell, 2002). In the constant model in Figure 1, the parameter estimates indicate that 41% ($.64^2/[.64^2 + .77^2]$) of the variance in HP is under genetic influence, and the remainder of the variance is under nonshared environmental influence.

A single specific measured environment, household income (HI), which shows the association with the measured phenotype of HP in the income–health gradient, is introduced in Figure 2. The figure shows that HI has a linear relation with HP, such that greater HI is associated with fewer HP. There is no gene–environment interplay involved in this model either, so the estimated genetic and environmental influences remain subject to the limitations and to the distortions described for the model in Figure 1. Consistent with this, the parameter estimates of genetic and environmental influences are the same as in Figure 1, but there is an additional main effect of HI of −.13, indicating that less HI is associated with more HP.

The model shown in Figure 3 adds provision for the possibility that HI moderates the genetic and environmental influences on HP that are independent of the main effect of HI (Purcell, 2002). That is, these genetic and environmental influences on HP are no longer limited to being constant. Instead, they vary with level of HI and thus can move as in a wizard's photo. The figure shows linear relations: Each source of influence can be quantified as a constant

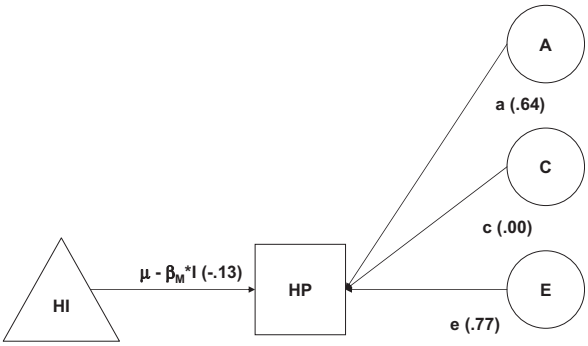

Figure 2. Model of genetic and environmental influences on health problems (HP), including the negative main effect of household income (HI) on HP. "A" refers to additive genetic influences, "C" to shared environmental influences, and "E" to nonshared environmental influences. The open triangle represents the measured variable acting as moderator, the open square reflects the measured variable of primary interest, and the open circles represent the latent variables. Parameter estimates are in parentheses.

plus some coefficient multiplied by HI (e.g., $a + \beta \times HI$), but there is no intrinsic reason that the relation must be linear. In particular, quadratic terms can easily be added and tested for statistical significance.

Here, the possibility of one kind of quantitative G × E, along with analogous possibilities of interactions between environmental influences, is recognized, and the model thus seems very sophisticated. In particular, we see that genetic influences on HP vary with level of HI. When HI is two standard deviations below the mean, genetic variance in HP is .52 $(.46 + .13 \times 2)^2$. Nonshared environmental variance here is .55 $(.74 + 0 \times -2)^2$, so genetic variance is 49% (.52/[.52 + .55]) of the total. In contrast, when HI is two standard deviations above the mean, genetic variance in HP is .04 $(.46 - .13 \times 2)^2$. Nonshared environmental variance is again .55, so genetic variance is 7% (.04/[.04 + .55]) of the total. At mean HI, genetic variance is .21 $(.46 - .13 \times 0)$, or 28% (.21/[.21 + .55]) of the total. The way in which the interactive effects are recognized, however, is so limited that we really learn little about the nature of the association between HI and HP, regardless of whether the model indicates the presence of any of these interactive effects.

This is because the model still includes provision for a main effect of HI on HP, yet it does not explain the genetic and environmental influences on that main effect. We can see this because the variance components, both genetic and environmental but especially genetic, are much smaller in this model than in the models in Figures 1 and 2. This is not so apparent from examination of the proportions of variances involved, but it is very apparent from examination of the raw variance components. The model in Figure 3 does not explicitly quantify the variance common to HP and HI. From this model alone, we therefore do not know how much of the variance in HP is unique to HP and how much is common to HP and HI—or how the common and unique portions of the variance can be attributed to genetic and environmental influences—because only the variance unique to HP is measured. For this reason, I have put a rectangle around the main effect parameter in Figure 3. We do learn something about the original main effect: The parameter estimates for this case indicate that the G × E that the model picks up reduces the undecomposed main effect from −.13 to −.03 (Figure 3 vs. Figure 2). Estimation of the main effect of HI is necessary in this model in order to guarantee that we do not estimate interactive effects that are not actually present (Purcell, 2002), and it provides comparative information about the extent to which the estimated G × E accounts for the observed main effect. Some portion of the income–health gradient remains to be explained, however, and this portion must be bound up in the influences common to HI and HP.

Figure 4 shows the full quantitative gene–environment interplay

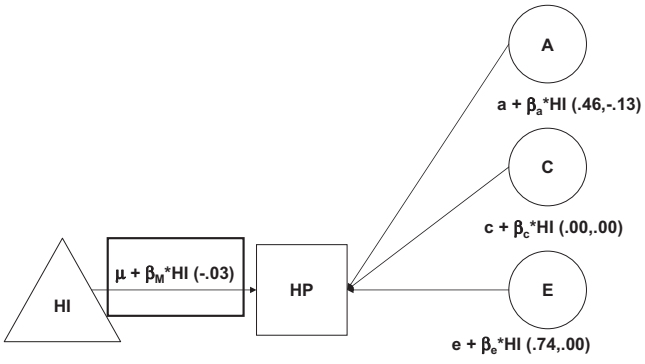

Figure 3. Model of genetic and environmental influences on health problems (HP), allowing for the possibility that household income (HI) moderates the influences unique to HP. "A" refers to additive genetic influences, "C" to shared environmental influences, and "E" to nonshared environmental influences. Parameter estimates are in parentheses. The first number in the pairs is the estimate for A, C, or E, and the second is the estimate for the associated beta. The open triangle represents the measured variable acting as moderator, the open square reflects the measured variable of primary interest, and the open circles represent the latent variables. The rectangle indicates that this pathway is not fully articulated in the model.

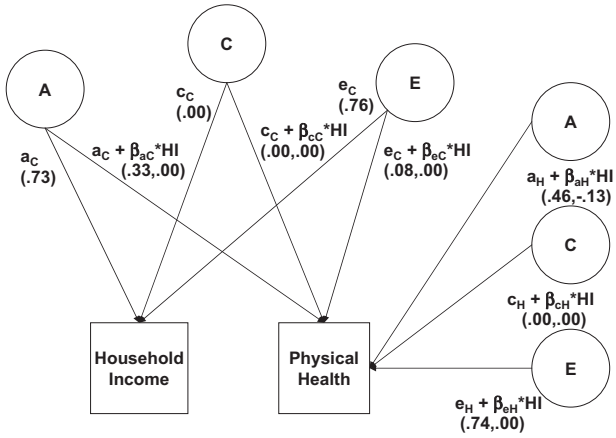

Figure 4. Full model of genetic and environmental influences on health problems (HP), allowing for the possibility that household income (HI) moderates both the influences common to HP and HI and the influences unique to HP. "A" refers to additive genetic influences, "C" to shared environmental influences, and "E" to nonshared environmental influences. Parameter estimates are in parentheses. The open squares reflect the measured variables of primary interest, and the open circles represent the latent variables.

model (FQGEIM). This is the full model of the possible ways in which HI may be associated with HP (Purcell, 2002). "Full model of the possible ways" may seem like a strong claim, but it is appropriate. This is because the model articulates all reasonable possibilities, at least with respect to these two admittedly highly complex variables and the overall distinction between unspecified genetic and environmental influences at the quantitative level at a single point in time. The model I am terming *full* can be enhanced still further by considering the possibilities of nonadditive as well as the additive genetic influences and assortative mating, but provisions for these introduce model identification problems in most samples and at best refine the overall picture provided by the model, so I have omitted them here to simplify presentation. Under this model, the main effect of HI on HP that was shown in the rectangle in Figure 3 is decomposed into its genetic and environmental components. This allows for the estimation of genetic and environmental influences common to both HI and HP so that we can see their size relative to those that are unique to HP. This also allows for the possibility that HI moderates these common genetic and environmental influences as well as those unique to HP. Of course, not all of these interactive effects need to be present, and in this example they are not: The only interactive effect is quantitative G × E on the variance that is unique to HP, so the betas associated with all but the genetic variance unique to HP are 0. The model simply allows for their measurement to the extent that they are present. Because of this, this model is like a wizard's photo: The subjects in it can move about at will.

There is another major point that this model makes clear: HI is not just a measure of an external environmental effect on the individual. It is a trait of the individual, like HP, and is subject to genetic and environmental influences in the same ways. Like the influences on HP, some of these influences on HI may be shared with HP (and with those on other traits), but some may be unique to HI. I have specified the model so that HP is the trait of interest and HI is the moderator, but there is no reason that the situation could not be reversed. In fact, this is another major feature of the FQGEIM. As I have specified it, with HP as the trait of interest and HI as the moderator, I am using it to examine the effects of HI on HP. Research involving the income–health gradient has indicated that most of the effects appear to flow in this direction (Adler & Snibbe, 2003), but there is evidence for smaller effects of HP on HI as well (Adler & Snibbe, 2003). The nature of the genetic and environmental influences involved in these effects could be explored with the FQGEIM in the same way, simply by reversing the order of entry of the variables in the model.

This full model also provides estimates of r_{GE} as well as estimates of correlations among environmental influences. The model makes clear the intrinsic relationship between quantitative G × E and r_{GE} at the quantitative genetic level. From the terms in the model, r_{GE} is calculated as follows:

$$r_{GE} = \frac{a_C + \beta_{aC} \times HI}{\sqrt{(a_C + \beta_{aC} \times HI)^2 + (a_{HP} + \beta_{HP} \times HI)^2}}. \quad (1)$$

Analogous formulas can be written for the correlations between the environmental influences, which are termed shared or nonshared environmental correlations. The formula looks messy, but it is analogous to the conceptualization of the ordinary correlation as the square root of the proportion of the variance common to the two variables being correlated. The notation is the same as in the figures, so the "a"s refer to the parameters for genetic influences. The subscript "C"s on the "a"s indicate that these genetic influences are common to both HI and HP. The subscript HPs indicate that these genetic influences are unique to HP. The numerator in the formula is the square root of the portion of variance in HP common to HI and HP. The denominator in the formula is the square root of the full variance in HP; its first squared term represents the portion of variance in HP common to HI and HP, and its second represents the portion of variance unique to HP. The formula generates amounts that range from –1 to 1 in the manner usual to correlations. The formula also points out that the term r_{GE} is something of a misnomer: It is shorthand for what is usually referred to as gene–environment correlation, but the mathematical expression really refers to the extent to which there are genetic influences common to a trait and some other variable that could be considered the environment in which the trait occurs. Another shorthand term sometimes used is r_a, and I use this term in referring to specific calculated values.

Examination of Equation 1 makes clear that r_{GE} and G × E are inextricably linked. It also shows that the linkages between them function lawfully. If there are no genetic influences common to HP and HI, there is no r_{GE}. But whenever there are genetic influences common to HP and to HI, r_{GE} will be more substantial at some parts of the range of HI than at others, most often at one end of the range. The parts of the range of HI in which r_{GE} is most substantial will not always be the same. Rather, it will depend on several factors. The most important is the relative magnitudes of genetic influences common to HP and HI and unique to HP across the range of HI, that is, the maximum possible magnitude of r_{GE}. But factors related to the G × E effect are also important. These factors include its magnitude, whether it expands or contracts variance with increases in HI, and whether it affects the genetic variance common to HP and HI or the genetic variance unique to HP.

When there is no moderation by HI on genetic influences common to HI and HP, the numerator and the first term of the denominator are constant, so the formula reduces to the following:

$$r_{GE} = \frac{a_C}{\sqrt{a_C^2 + (a_{HP} + \beta_{HP} \times HI)^2}}. \quad (2)$$

In this case, the direction of the moderation by HI on the genetic variance unique to HP determines what happens to r_{GE}. If the beta parameter is positive, so that genetic influences on HP expand when HI is high, then the genetic correlation is lower in high-HI environments than in low-HI environments. This has to be true: It is a direct result of the relations among the parts of the model and is dictated by the terms of the correlation formula. In contrast, if the beta parameter is negative (as is the case here) so that genetic influences on HP expand when HI is low, then the genetic correlation is higher in high-HI environments than in low-HI environments. Again, this has to be true: The genetic correlation is linked directly to the nature of the quantitative G × E effect of the moderator HI. Figure 5 summarizes the parameter estimates that actually resulted from the model for HP and HI in the MIDUS data (Johnson & Krueger, 2005). These results indicate that the simplified models that did not include provision for gene–environment interplay actually did not produce overall estimates of genetic and environmental influences that were substantively distorted. That is, at two standard deviations above mean HI, genetic

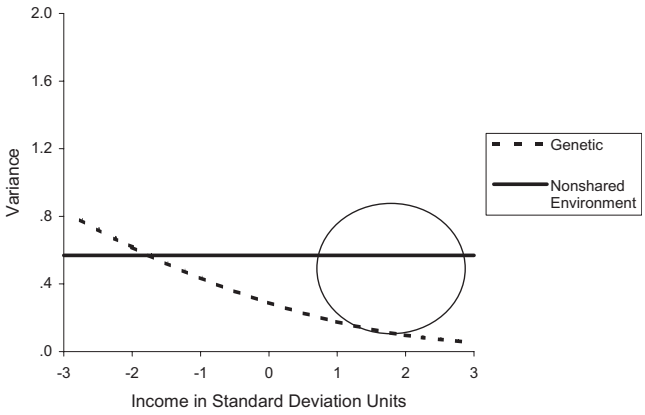

Figure 5. Variance in chronic health problems over range of income, by source of variance, from actual MacArthur Survey of Midlife Development in the United States data. The circle shows the location of higher gene–environment correlation.

variance in HP was .10; and at two standard deviations below mean HI it was .62. Somewhere in the middle of the distribution, not far from the mean of HI, it was .41, just as in the model shown in Figure 1. This is because the overstatement of average nonshared environmental influences caused by the G × E between genetic and nonshared environmental influences was offset by the overstatement of average genetic influences caused by the r_{GE} between the same genetic and environmental influences. This kind of situation is likely common, but it should be measured rather than assumed.

When there is no moderation of the genetic influences that are unique to HP, the second term in the denominator of Equation 1 is constant, so the formula reduces to the following:

$$r_{GE} = \frac{a_C + \beta_{aC} \times HI}{\sqrt{(a_C + \beta_{aC} \times HI)^2 + a_{HP}{}^2}}. \quad (3)$$

Again, the direction of the moderation by HI on the genetic variance common to HI and HP determines what happens to r_{GE}. If the beta parameter is positive, so that the common genetic variance expands when HI is high, then the genetic and environmental correlation is higher when HI is high than in low-HI environments. If the beta parameter is negative, so that the common genetic variance expands when HI is low, then the genetic and environmental correlation is higher when HI is low than in high-HI environments. Of course, if there is quantitative G × E on both the genetic variance common to HI and HP and unique to HP, all bets are off as to how the r_{GE} will move. It depends on the relative sizes of the common and unique genetic variances and the relative strengths and directions of the quantitative G × E effects. Additional complications also arise if HI moderates the environmental variance in HP. The important points are, however, that these factors do determine the links between quantitative G × E and r_{GE} at the quantitative genetic level and that the single model shown in Figure 4 will illuminate these associations.

Table 1 shows how the relations between quantitative G × E and r_{GE} vary with different combinations of common and unique genetic and environmental variance components and different strengths and directions of quantitative G × E effects. Column 1 of the table shows all the parameters from the full model of log of chronic physical illnesses (HP) moderated by log of household income (HI) from the MIDUS data, modified slightly from Johnson and Krueger (2005) to simplify presentation because that model included a provision for nonadditive genetic variance. In addition to the model parameters, column 1 shows the correlations between genetic and environmental influences on HP and HI derived from the model parameters. Because these correlations differ across the range of HI when quantitative G × E is present, the derived correlations are shown at two standard deviations below mean HI, at the mean of HI, and two standard deviations above the mean of HI. Column 1 also shows the raw components of variance in HP attributable to genetic and environmental influences derived from the model parameters. Because quantitative G × E alters the components of variance in HP with level of HI, the variance components are also shown at three levels of HI. To find the proportions of variance commonly used, one would divide one component by the sum of the two. So, for example, at two standard deviations below mean HI, genetic influences account for 52% (.62/[.62+.57]) of total variance in HP, whereas at two standard deviations above mean HI, genetic influences account for only 15% (.10/[.10+.57]) of HP. Finally, column 1 shows the overall main effect (the correlation between HP and HI) and the parts of this overall main effect attributable to G × E, involving common and unique genetic influences.

In the actual data, the G × E effect involved only genetic influences unique to HP, and the effect acted to increase genetic influences on HP in the presence of lower HI. At the same time, there were some genetic influences common to HP and HI, and these influences were constant across the range of HI. This meant that r_{GE} was higher in the presence of higher HI. It also implied that the genes likely primarily influencing HP in low-HI situations were not the same as the genes likely primarily influencing HP in high-HI situations. Because there was no income moderation of environmental influences, the full main effect was mediated genetically. About one quarter of the variance was due to common genetic influences and the other three quarters was due to environmental effects of HI on unique genetic variance in HP. Figure 5 provides a graph of the actual data situation.

To provide a sense of how the parts of the model fit together, the remaining columns of Table 1 show what happens to the model parameters and derived statistics when the nature of the quantitative G × E is arbitrarily manipulated. All of the model parameters and derived statistics are shown, regardless of whether they vary in any of the manipulations, because it helps to make clear exactly what varies and what does not with each manipulation. I have limited the manipulations to trading moderation of genetic influences for moderation of nonshared environmental influences in order to keep the examples reasonably straightforward, but in real life there is no reason that there could not be moderation of both genetic and nonshared environmental influences, nor is there any reason that the direction of moderation of the two kinds of influence would necessarily be in the same direction. Furthermore, I have not addressed the possibility of moderation of shared environmental influences, again only in order to keep the examples reasonably straightforward, as moderation of this kind can also take place. The FQGEIM can estimate all of these forms of moderation as well. As with any quantitative genetic model, the power to do so in a given sample will vary with the kinds of genetic relatedness present in the sample, the relative magnitudes of the

Table 1
Actual and Hypothetical Results From Quantitative Genetic Model of Income–Health Gradient

Parameter or derived result	Actual data (1)	Place G × E effect on common instead of unique (2)	Reverse direction of G × E effect (3)	Place G × E effect on E instead of A (4)	(2) & (3)	(2) & (4)	(3) & (4)	(2), (3), & (4)
Influences on HI								
a_{HI}	.73	.73	.73	.73	.73	.73	.73	.73
c_{HI}	.00	.00	.00	.00	.00	.00	.00	.00
e_{HI}	.76	.76	.76	.76	.76	.76	.76	.76
Influences on HP that are common to HI								
a_C	.20	.20	.20	.20	.20	.20	.20	.20
c_C	.00	.00	.00	.00	.00	.00	.00	.00
e_C	−.08	−.08	−.08	−.08	−.08	−.08	.08	.08
Influences on HP that are unique to HP								
a_{HP}	.50	.50	.50	.50	.50	.50	.50	.50
c_{HP}	.00	.00	.00	.00	.00	.00	.00	.00
e_{HP}	.75	.75	.75	.75	.75	.75	.75	.75
Moderating parameters on influences on HP that are common to HI								
β_{aC}	.00	**−.13**	.00	.00	**.13**	.00	.00	.00
β_{cC}	.00	.00	.00	.00	.00	.00	.00	.00
β_{eC}	.00	.00	.00	.00	.00	**−.13**	.00	**.13**
Moderating parameters on influences on HP that are unique to HP								
β_{aHP}	.13	**.00**	**.13**	**.00**	**.00**	**.00**	**.00**	**.00**
β_{cHP}	.00	.00	.00	.00	.00	.00	.00	.00
β_{eHP}	.00	.00	.00	**−.13**	.00	.00	**.13**	.00
Correlations between genetic influences on HI and HP								
r_a at $-2SD_{HI}$	−.25	−.68	−.64	−.37	.12	−.37	−.37	−.37
r_a at mean HI	−.37	−.37	−.37	−.37	−.37	−.37	−.37	−.37
r_a at $2SD_{HI}$	−.64	.12	−.25	−.37	−.68	−.37	−.37	−.37
Correlations between nonshared environmental influences on HI and HP								
r_e at $-2SD_{HI}$	−.11	−.11	−.11	−.16	−.11	−.41	−.08	.23
r_e at mean HI	−.11	−.11	−.11	−.11	−.11	−.11	−.11	−.11
r_e at $2\ SD_{HI}$	−.11	−.11	−.11	−.08	−.11	.23	−.16	−.41
Genetic variance in HP								
A_{HP}^2 at $-2SD_{HI}$	.62	.46	.10	.29	.25	.29	.29	.29
A_{HP}^2 at mean HI	.29	.29	.29	.29	.29	.29	.29	.29
A_{HP}^2 at $2SD_{HI}$	.10	.25	.62	.29	.46	.29	.29	.29
Nonshared environmental variance in HP								
E_{HP}^2 at $-2SD_{HI}$	.57	.57	.57	.25	.57	.68	1.03	.59
E_{HP}^2 at mean HI	.57	.57	.57	.57	.57	.57	.57	.57
E_{HP}^2 at $2SD_{HI}$	.57	.57	.57	1.03	.57	.59	.25	.68
Main effects								
Overall	−.13	−.13	−.13	−.13	−.13	−.13	−.13	−.13
Common	−.03	−.10	−.03	−.02	−.10	−.09	−.03	−.02
Unique	−.10	−.03	−.10	−.11	−.03	−.04	−.10	−.11

Note. The genetic (G) and environmental (E) influences are variance components, not proportions of variance. The parameters altered, in each scenario are indicated in bold. As in the text "a" and "A" refer to genetic influences; "c" and "C" refer to shared environmental influences; "e" and "E" refer to environmental influences. In subscript, C refers to influences common to household income (HI) and chronic health problems (HP); β refers to the moderating parameters in the model. Thus, for example, β_{cC} refers to the moderating parameter on shared environmental influences common to HI and HP; r_a at $2\ SD_{HI}$ refers to the extent to which genetic influences on HP are common to those on HI at two standard deviations below mean HI; E_{HP}^2 at $-2SD_{HI}$ refers to nonshared environmental variance unique to HP at two standard deviations below mean HI. The genetic correlations differ from those shown in Johnson and Krueger (2005) because I made a simplifying assumption that there was only additive genetic variance in HP for this presentation.

relevant components of variance, and the degrees of moderation present.

In the first manipulation, in column 2 of Table 1, the only manipulation is that the quantitative G × E is moved from the genetic variance unique to HP to the genetic variance common to HI and HP. The magnitude of the moderation by HI remains the same. As the table shows, this has two effects on r_{GE}: It increases the change in r_{GE}s across the range of HI because the effect is greater in relation to the smaller genetic variance common to HP and HI than that unique to HP. Much more important, it reverses the direction of the moderating effect so that r_{GE} is lower in higher HI than in lower HI situations. This takes place because moderation of the genetic influences common to HP and HI affects the numerator of the formula for r_{GE} as well as the denominator. Note that genetic influences on HP at mean HI remain constant, and the overall change in genetic influences with change in HI is smaller than when HI moderates the genetic influences unique to HP. As with the change in r_{GE}, this takes place because fewer of the genetic influences on HP are common to both HP and HI than are unique to HP. In this situation, the main effect is still completely genetically mediated, but about three quarters is due to genetic influences common to HI and HP, whereas only one quarter is due to environmental effects on genetic influences unique to HP. Figure 6 provides a graph of this situation.

The second manipulation, shown in column 3 of Table 1, changes only the direction of the moderating effect of HI on the genetic influences unique to HP. This reverses the effects on both the genetic variance and r_{GE}: Genetic variance is now higher in high-HI environments than in low-HI environments, and r_{GE} is higher in low-HI environments than in high-HI environments. There is no overall effect on the magnitudes of genetic or environmental influences, and the main effect is the same as in the actual data. This is shown in Figure 7. Column 4 of Table 1 and Figure 8 show what happens when the moderating effect is moved from the genetic variance unique to HP to the nonshared environmental variance unique to HP. Now both the genetic variance and r_{GE} are constant across the range of HI, but the nonshared environmental variance increases sharply. As proportions of total variance, genetic influences go down as HI goes up. Though of the same strength, the moderating effect on the nonshared environmental variance unique to HP has a greater effect on total nonshared environmental variance than was the case with the moderating effect on the genetic variance in the actual data because the nonshared environmental variance unique to HP is a greater proportion of the total nonshared environmental variance in HP than is the case with the genetic variance. In this situation, the main effect is mediated environmentally.

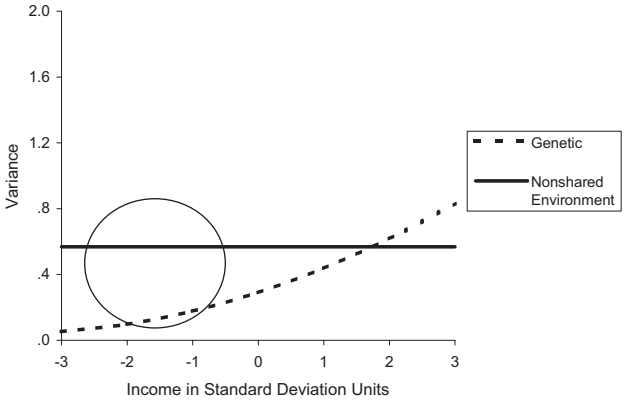

Figure 7. Variance in chronic health problems over range of income, by source of variance, with the direction of quantitative gene–environment interaction reversed. The circle shows the location of higher gene–environment correlation.

The remaining columns of Table 1 show combinations of the first three manipulations. When the moderating effect is moved from the genetic variance unique to HP to the genetic variance common to HP and HI and the direction of effect is reversed (Table 1, column 5), the moderating effect on total genetic variance is dampened, and genetic variance and r_{GE} are both higher in high-HI environments than in low-HI environments. The main effect is again mediated genetically and much more strongly through the genetic variance common to HP and HI. This situation is shown in Figure 9. Moving the moderating effect to the nonshared environmental variance common to HP and HI

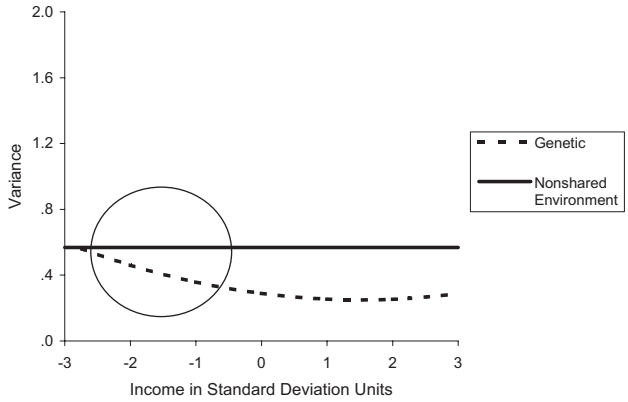

Figure 6. Variance in chronic health problems over range of income, by source of variance, with the quantitative gene–environment interaction moved from genetic variance unique to health problems to genetic variance common to health problems and income. The circle shows the location of higher gene–environment correlation.

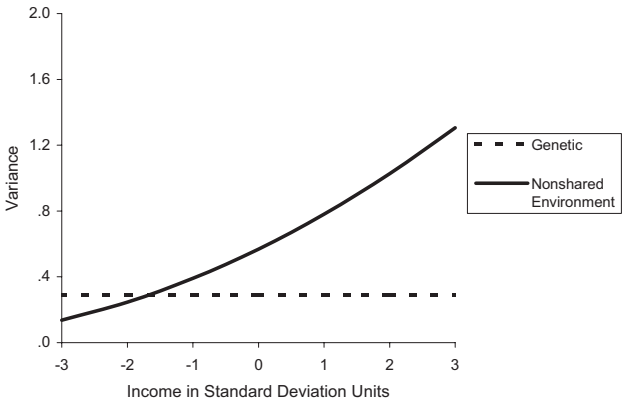

Figure 8. Variance in chronic health problems over range of income, by source of variance, with the moderating effect moved to unique, nonshared environmental variance. The gene–environment correlation is constant over range of income.

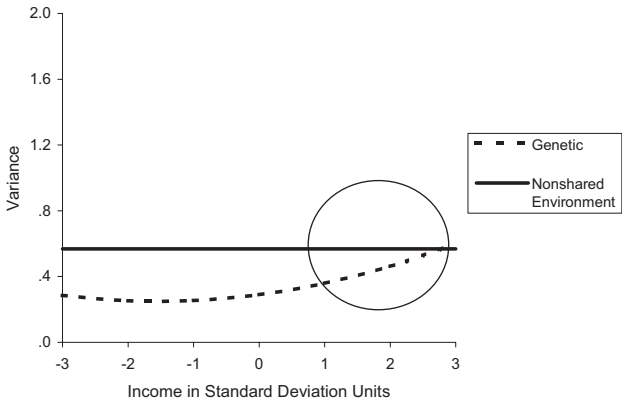

Figure 9. Variance in chronic health problems over range of income, by source of variance, with the quantitative gene–environment interaction effect moved from genetic variance unique to health problems to genetic variance common to health problems and income, direction reversed. The circle shows the location of higher gene–environment correlation.

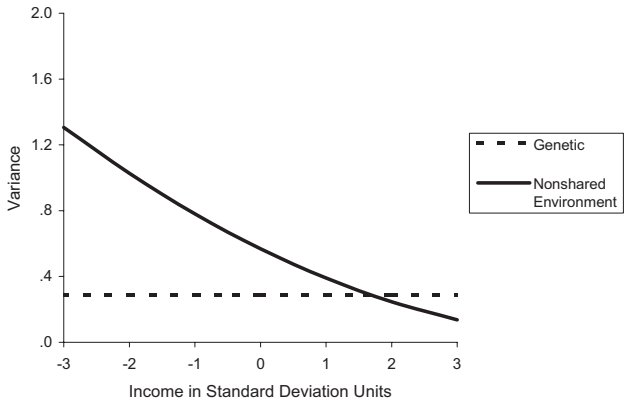

Figure 11. Variance in chronic health problems over range of income, by source of variance, with the moderating effect moved to nonshared environmental variance unique to health problems and income, direction of effect reversed. The gene–environment correlation is constant over range of income.

has a more surprising result, shown in column 6 of Table 1 and in Figure 10. As expected, genetic variance and r_{GE} are now constant, but nonshared environmental variance takes a quadratic form in which it is greater in both low-HI and high-HI environments than in mid-HI environments. The overall effect, however, is rather small. This takes place because nonshared environmental variance common to HP and HI is such a small proportion of total nonshared environmental variance. Once again, the main effect is mediated environmentally and the majority of it acts through the variance common to HP and HI. Reversing the directions of the effects in the situations shown in Figures 8 and 10 has the results one would anticipate: As shown in columns 7 and 8 of Table 1 and Figures 11 and 12, everything is essentially reversed.

These manipulations make clear that the system of relations among genetic and environmental influences on HI and HP is very sensitive to the location of moderating effects of HI on variance in HP. It would, of course, be conceptually possible for HI to affect HP uniformly, with each dollar of additional household income acting to reduce HP by a fixed amount that has no effect on variance in HP. If this were the case, total as well as genetic and nonshared environmental variance in HP would be constant across the range of HI, and r_{GE} would be a constant function of the relative amounts of genetic variance in HP common to HP and HI and unique to HP. But the existence of r_{GE}, which is an inevitable result of any genetic variance common to HP and HI, implies that such a system will not be static over time. This is because individuals who differ genetically in ways that influence both HP and HI will actively seek out as well as passively receive different environmental experiences involving HI, but they will do this with varying degrees of success over time. This introduces the likelihood that genetic differences in HP will be expressed to differing degrees in the different HI environments experienced. This, of course, is G $\times$ E, with consequences for variance in HP of the kinds shown in the manipulations presented here. Thus, as long as there is genetic variance common to two traits, the presence of

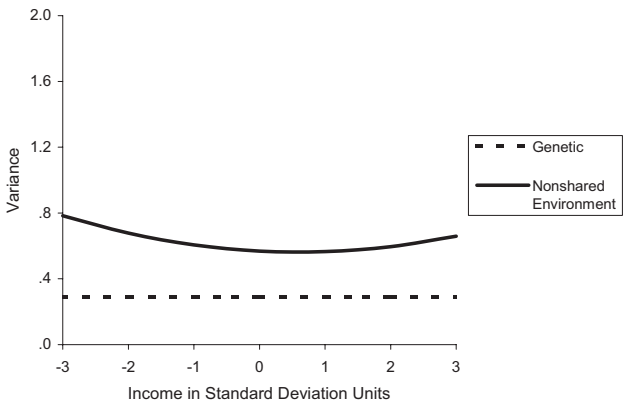

Figure 10. Variance in chronic health problems over range of income, by source of variance, with the moderating effect moved to nonshared environmental variance common to health problems and income. The gene–environment correlation is constant over range of income.

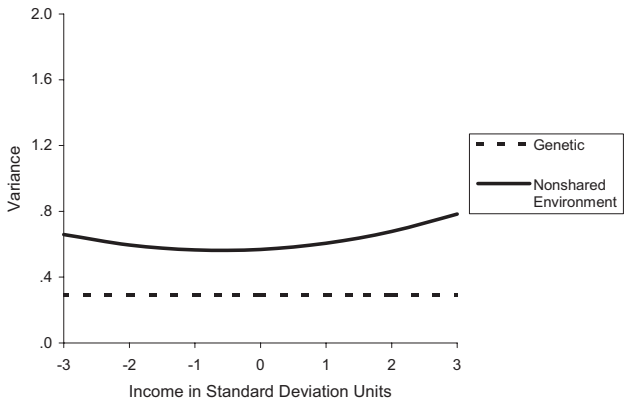

Figure 12. Variance in chronic health problems over range of income, by source of variance, with the moderating effect moved to nonshared environmental variance common to health problems and income, direction of effect reversed. The gene–environment correlation is constant over range of income.

both G × E and r_{GE} is likely, and they will be related in lawfully constrained ways.

At the same time, it should be clear that the balance among these relations may be rather fragile. That is, the balance among the relations in which any two variables are involved may shift depending on associations with other personal or environmental variables that vary from place to place or over time. This may affect the replicability of results from the model without implying in any way that the results of any particular application of the model were not accurate and relevant to the data from which they were derived. This simply implies the need to identify and understand the operative associations with whatever other variables are relevant. I next discuss the theoretical and practical implications of the system of relations among genetic and environmental influences on HI and HP.

Theoretical and Practical Implications of Results From the FQGEIM

Parameter estimates from the FQGEIM provide important evidence relevant to major theories of the incidence and consequences of phenomena of interest. For example, one major and longstanding theoretical debate concerns whether mental illness and behavioral problems, such as antisocial behavior, arise from poor social conditions such as poverty and maltreatment in childhood (social causation) or whether they are caused by preexisting, biologically based vulnerabilities that also result in drift into or creation of unpleasant environmental conditions (social selection). Social selection can occur through shared or nonshared environmental as well as genetic influences, but I focus this discussion on genetically influenced social selection because it is probably the one most commonly considered. The concepts involved in environmentally influenced social selection are the same, and the FQGEIM can estimate their involvement as well. To simplify discussion of genetically influenced social selection, I continue to use the shorthand HP to refer to the manifested trait of concern, be it health problems, mental illness, or behavioral problems. I also continue to use the shorthand HI to refer to unfavorable environmental conditions, be they poverty or maltreatment of any form.

In order for genetically influenced social selection to operate at all, there must be genetic influences common to HP and HI, and the FQGEIM provides an estimate of the degree to which this is true. But genetic influences common to HP and HI are not sufficient to render genetically influenced social selection the primary explanation. This is because genetically influenced social selection can only be taking place where there is some meaningful variation in genetic influences on outcome HP. If genetic variance in HP is constant across the range of HI, r_{GE} must be high across that range, but as discussed above, high r_{GE} implies movement within the range of HI over time, and thus constant genetic variance in HP over HI is unlikely to be a stable situation. If genetic variance in HP is not constant across the range of HI, then of course we have G × E. Genetically influenced selection takes place when r_{GE} is high, and the part of the range in which this is true characterizes the predominant direction of selection. If r_{GE} and genetic variance are both high at the same end of the environmental range, this suggests that social selection predominates. If r_{GE} is low in the part of the range of HI in which there is greatest genetic variance (or vice versa), then the more reasonable interpretation is that environmental conditions are triggering expression of genetic influences unique to HP, which can be summarized as an example of social causation.

Of course this is exactly what the FQGEIM measures. In fact, the model makes possible an important insight about the social process we label *social causation*. To the extent that social forces actually exert effects on the people who experience them, very commonly the most we can say is that they have effects on mean levels or incidence rates of the trait involved, but they do not affect all individuals who experience them in the same way. That is, penetrance is incomplete. For example, poverty may cause greater HP, but not everyone who lives in any given degree of poverty has HP. When penetrance is incomplete in this way, the FQGEIM shows us that, however direct the effects may be on the individuals who experience them, it is not the effect on the mean level that is important in understanding the social causation process involved. Rather, the social causation process will exert differential effects on the variance in the trait that depend on the level and nature of the social processes experienced, and it is the nature of these differential effects on the variance that really provides insight into the specific mechanisms involved. Social causation may involve differential effects on genetic or shared or nonshared environmental variance or any combination of the three, so the process described above, which involves only genetic variance, is but one example of a social causation process. The primary marker of a social causation process is that it involves moderation of genetic and/or environmental variance *unique* to the trait rather than genetic and/or environmental variance *common* to the trait of the social cause.

Table 1 can be used to illustrate how to interpret various kinds of results from the model in terms of social selection versus social causation. The actual HP and HI data (modified slightly as noted above), shown in column 1 of Table 1 and Figure 5, indicate that there are some genetic influences common to HP and HI and that genetic variance unique to HP decreases with increasing HI. Thus genetic variance is greatest in low-HI environments, but these are also the environments in which r_{GE} is lowest. Selection, to the extent it is occurring, restricts genetic expression, and something about the low-HI environment triggers genetic expression. So social selection operates to some degree, but it operates to sort people into higher HI environments, thus restricting the deleterious expression of genetic influences unique to HP. The larger effect, however, is from the action of social causation to enhance deleterious genetic expression. In contrast, if the G × E effect is on genetic variance common to HP and HI, as shown in column 2 in Table 1 and in Figure 6, then the situation is reversed and social selection operates to sort people into lower HI environments. When HI moderates the nonshared environmental rather than the genetic influences, and r_{GE} is therefore constant and of moderate strength throughout the range of HI, as shown in columns 6, 7, and 8 of Table 1 and Figures 10, 11, and 12, then social selection can be said to be operating to the extent of the magnitude of the genetic correlation. Because nonshared environmental variance in HP also changes with HI in these situations, however, we would say that social causation is important as well.

The stress–diathesis model is another example of a well-known theoretical or conceptual framework that can be operationalized and measured with the use of the FQGEIM. According to the stress–diathesis model, the presence of environmental stressors

triggers expression of some trait for which latent predispositions exist. The trait expressed can be positive, for example immune response in reaction to vaccination, but the stress–diathesis model has most commonly been applied to explain maladaptive vulnerabilities to illness, disease states, or lack of well-being. These kinds of traits are generally under genetic influence to some degree; it is clear that genetic vulnerabilities likely are important for some if not most outcomes (Rende & Plomin, 1992). The stress–diathesis model is relevant when genetic and/or environmental variance expands when the environment is poor (i.e., stressful). Expansion of genetic variance with changes in level of an environmental measure is also an example of epigenetic effects, though of course the subject of epigenetics transcends much more than this kind of example. Thus, as noted above, stress–diathesis could be said to generate the actual data from MIDUS for the income–health gradient, shown in column 1 of Table 1 and in Figure 5. It could also be said to generate the situations shown in columns 2 and 7 of Table 1 and in Figures 6 and 11. Note that the implications for the proportion of total variance attributable to genetic influence in HP are completely different, depending on the source of the change in variance in HP with HI. When the source is genetic, the proportion of variance in HP attributable to genetic influence is higher in low-HI environments. When the source is environmental, the reverse is the case. The stress–diathesis model has nothing specific to say about r_{GE} or whether HI moderates the genetic variance common to HP and HI or unique to HP, but of course the FQGEIM measures all this, so it provides additional information to help articulate the social forces resulting in the manifestation of the stress–diathesis relation.

In their fine article on social context in gene–environment interactions, Shanahan and Hofer (2005) described two variations of the stress–diathesis model. They termed the first of these two variations *social context as compensation*. This variation is relevant when a positive environmental situation acts to suppress the expression of a genetic diathesis. For individuals or categorical measures of environment and trait, the distinction between this variant and the more common version of the stress–diathesis model can be important. For example, we may compare the prevalence of diabetes in populations below the poverty level to that in populations above the poverty level and attribute the difference to the operation of the most common version of the stress–diathesis model. In contrast, we may compare the social adjustment of autistic children placed in an intensive program of early instruction in social functioning to those not placed in such a program and attribute the difference to the operation of the social context as compensation model. When the environmental measure is continuous, however, and the trait in question is highly polygenic and measured at the level of the population so that there are so many individuals involved that the incidence of the trait will vary continuously over the range of the environment, even if the trait is measured categorically, the stress–diathesis and social context as compensation models are equivalent. For example, it is very reasonable to think of the income–health gradient as a manifestation of the stress–diathesis model as described above, but it is just as easy to think of it as a manifestation of social context as compensation in which the benefits of higher income make possible the suppression of genetic diathesis for poor health.

Shanahan and Hofer (2005) called the second of their two variations on the stress–diathesis model *social context as social control*. This variant is relevant when some form of social norm or institutional constraint that restrains people's behavior and limits their choices prevents or minimizes expression of a genetic diathesis. If the relative presence of social control is considered to be the positive environment and the lack of social control is considered to impose stress of some kind, the result with respect to genetic variance is the same as in the stress–diathesis situation: Genetic variance is greatest in the environment in which social control is relatively absent and is smallest in the socially controlled environment. This model highlights the existence of an unstated assumption underlying the FQGEIM: In conceptualizing these models, we assume that the environmental measure (stress, some form of compensation or enrichment, or social control) has the same kind of main effect on all who experience it. But what if this is not the case? For example, the social context as social control model has been used to account for the existence of greater genetic influences on disinhibitory behavior among teenagers in urban than in rural settings (Boomsma, de Geus, van Baal, & Koopmans, 1999; Dick, Rose, Viken, Kaprio, & Koskenvuo, 2001; Legrand, 2004; Rose, Dick, Viken, & Kaprio, 2001). These studies have observed similar prevalences of teen disinhibitory behavior in urban and rural environments but have not investigated whether genetic influences are common to both degree of urbanity of the environment and disinhibitory behavior or are unique to disinhibitory behavior. In addition, the average prevalence of disinhibitory behavior in rural areas may reflect very different mixes of disinhibitory behavior from rural community to rural community. That is, more rural areas may restrict social access, introducing social control of a form that enhances expression of genetic tendencies to behave in a disinhibitory way in some rural areas and suppresses it in others. Such a situation would involve the interaction of two environmental moderators: the restriction of social access due to geographic isolation and the prevailing level of disinhibitory behavior to which social access is available. These kinds of situations may not be unusual.

Shanahan and Hofer (2005) described one additional theoretical or conceptual model involving G × E. They termed this model *social context as enhancement*, but it has also been termed the *bioecological model* (Bronfenbrenner & Ceci, 1994). This model is effectively the opposite of the stress–diathesis model and its two variations. When it is relevant, some positive environmental feature enhances genetic expression of positive or adaptive characteristics. This is another example of the same limited kind of epigenetic programming as the stress–diathesis model. Again, the positive characteristics can be personal qualities under environmental as well as genetic influences, but because personal qualities are under genetic influences to at least some degree, genetic influences will generally be involved. Like the stress–diathesis model, this model says nothing about the relative importance of genetic influences common to the positive environment and to the trait of interest, and thus it says nothing about r_{GE}, but social causation and selection explanations for the links between the positive environment and the trait of interest are determined by measurement of the relative magnitudes of these influences.

Columns 3, 4, and 5 in Table 1 and Figures 7, 8, and 9 illustrate possible examples of the social context as enhancement model. In discussing these examples, I continue to use HP and HI to describe the trait of interest and the environmental moderator for convenience and consistency. It is not quite accurate, however, as HP

cannot be reasonably considered positive or adaptive characteristics. Most examples of this model in the literature have involved education and intelligence (Guo & Stearns, 2002; Heath et al., 1985; Rowe, Jacobson, & van den Oord, 1999; Turkheimer, Haley, Waldron, D'Onofrio, & Gottesman, 2003) as the positive characteristic, so think of HP as "higher performance" for the purpose of these examples. Turkheimer et al.'s (2003) observation that both children's IQ's and the genetic influences on them increased with increasing parental socioeconomic status is typical of the social context as enhancement model.

In column 3 of Table 1 and in Figure 7, genetic variance in HP increases with increasing HI. Because the G × E effect is on the genetic variance unique to HP, r_{GE} is high when both HI and genetic variance are low, and most of the effect would be attributed to social causation rather than social selection. The only difference between this situation and the situation shown in column 5 of Table 1 and in Figure 9 is that the G × E effect falls on genetic variance common to HP and HI. This makes r_{GE} high when HI is high and both genetic variance in HP and proportion of total variance attributable to genetic influences are high. Now most of the effect would be attributed to social selection rather than to social causation. Finally, the situation in which the nonshared environmental variance in HP increases with increasing HI is shown in column 4 of Table 1 and in Figure 8. As noted above, the effect on proportions of variance attributable to genetic and environmental influences is reversed. Because genetic variance in HP is constant across the range of HI, the proportion of total variance due to genetic influences is lower in the high-HI environment than in the low-HI environment.

Fitting G × E Between Specific DNA Sequences and Specific Measured Environments Into the FQGEIM

In the past 5 years or so, there have been many reports of G × E involving specific DNA sequences, psychopathologies or problem behaviors, and measured environments of interest. These reports have been summarized well by Moffitt et al. (2006) and Rutter et al. (2006). All of the reports to date of which I am aware can be thought of as examples of the (generalized) stress–diathesis model. That is, exposure to some environmental pathogen increases the likelihood that a genetic vulnerability to psychopathology will be expressed. This implies that individuals carrying one commonly occurring allele of a gene will develop psychopathology or problem behavior more often in the presence of the environmental pathogen than will individuals carrying another commonly occurring allele of the same gene. In none of these reports, however, does possession of any allele of the gene mean that an individual will automatically develop the deleterious condition, even in the presence of the environmental pathogen; in quantitative genetic terms, penetrance is generally rather low. In fact, in many cases there is no overall association between the possession of any particular allele of the gene and development of the deleterious condition at all. In all of these reports, however, there is a main effect of the environmental pathogen and it is clear that some individuals who do not carry the higher risk allele of the gene still do develop the deleterious condition. Thus, it is clear that these are dynamic situations dealing with exactly the kinds of forces the FQGEIM measures. Because all of these reports follow the same basic pattern, I select one of them to describe in sufficient detail to show how it fits within the FQGEIM.

Caspi et al. (2003) noted that there was substantial evidence that serotonin plays a role in risk of depression and that risk of adult depression also has been reliably associated with childhood maltreatment and the prior experience of stressful life events in early adulthood. At the same time, they noted that there had been several failures to replicate the single report (Lesch et al., 1996) of a main effect that the short allele of a functional polymorphism in the promotor region of the serotonin transporter gene was associated with risk of depression. At the same time, they noted that the experience of stressful life events appeared to confer greater probability of experiencing depression when genetic vulnerability was greater (Kendler et al., 1995). Caspi et al. hypothesized that the inconsistency of the observation of the main effect occurred because the serotonin transporter gene moderates the effect of stressful life events on risk for depression. That is, the short allele increases the risk of depression by restricting gene expression relative to that of the long allele, but only in the presence of stressful life events including childhood maltreatment, which is a classic example of specific DNA sequence G × E. This could explain both the initial reported association and the failures to replicate because the samples may have varied considerably in the degree to which their members had experienced stressful life events, and only those with sufficient exposure would show the genetic association. In the Dunedin Longitudinal Study (Silva, 1990), this proved to be the case (Caspi et al., 2003). The finding appears to be reasonably robust, though the size of the effect is very small and there are possible scaling issues (Eaves, 2006). There have been several replications (Eley et al., 2004; Grabe et al., 2005; Kaufman et al., 2004; Kendler, Kuhn, Vittum, Prescott, & Riley, 2005; Wilhelm et al., 2006; Zalsman et al., 2006), as well as two failures to replicate (Gillepsie, Whitfield, Williams, Heath, & Martin, 2005; Surtees et al., 2006). Since the Caspi et al. (2003) G × E study, there has also been a replication of the original Lesch et al. (1996) study that showed a main effect of the short allele on depression (Hoefgen et al., 2005), but the effect size was so small that it probably does not invalidate Caspi et al.'s (2003) argument.

The results of the Caspi et al. (2003) study indicated that the serotonin transporter genotype had no real effect on risk of depression in the absence of stressful life events. In the presence of prior stressful life events, however, risk of depression increased, and the increase was greater the more copies of the short allele of the serotonin transporter gene an individual possessed. More specifically, the effect of stressful life events on risk of depression in adulthood was over twice as great in individuals with one copy of the short allele of the serotonin transporter gene than in those with none and over three times as great in individuals with two copies of that allele. Thus, in the presence of prior stressful life events, the probability of depression increased with each copy of the short allele of the serotonin transporter gene an individual possessed, and the degree to which the probability of depression increased also increased with the extent of prior exposure to stressful life events. The effect did not apply to stressful events that occurred after the onset of depression. Thus this provides an example of the inference from the results of the FQGEIM for the income–health gradient that the genes contributing to genetic variance in depression at one end of the range of the environmental moderator would not be the same as those contributing to genetic variance at the

other end of that range. The G × E effect apparently results from differential genetic expression of a gene that does not influence the occurrence of stressful events directly.

This situation can be described by a binomial probability distribution, in which probability of depression increases both across the rows of a matrix defined by numbers of copies of the short allele of the serotonin transporter gene that restricts the gene expression that buffers against depression, and down the columns of that matrix defined by numbers of prior stressful life events experienced. Thus mean levels of depression markers (be they symptom counts or diagnoses) are greater across the rows of the matrix as well as down the columns. But when data are distributed binomially, the variance of the distribution is a function of the mean of the distribution ($\mu = np$, $\sigma = np[1 - p]$), where n is sample size and p is the probability of depression. In particular, the variance of the distribution increases with the probability of depression (at least until $p = .50$), which increases with numbers of prior stressful life events experienced. This means that, in keeping with the stress–diathesis model, as the mean level of depression incidence increases with prior exposure to stressful life events in each serotonin transporter allele row of the matrix, so too does the variance. And because the rows of the matrix vary only genetically, genetic variance increases as well. Of course the same thing happens with the environmental variance associated with the experience of stressful life events, but the important point is that genetic variance increases in the predicted way, with the predicted effect on r_{GE}.

Though the G × E effect involving the serotonin transporter gene explains only a small portion of either the total or the genetic variance in the occurrence of depression (Caspi et al., 2003), the genetic variance that it does explain acts exactly as predicted by the FQGEIM for a miniaturized version of the stress–diathesis model: Genetic variance and thus depression increase in the presence of greater stress. If allelic variation of the serotonin transporter gene also contributes to the probability of having experienced stressful life events, then the genetic variance is common to both the experience of stressful life events and depression, with the expected consequences for r_{GE} as outlined above. If not, then the genetic variance is unique to depression, and the expected consequences for r_{GE} are different. If many genes affect stressful life events and depression according to such miniaturized versions of the stress–diathesis model, then the effects accumulate to the kind of quantitative results described above for the income–health gradient. It is of course possible, however, that some of the genes involved in depression may operate in other ways, burying the effects of the serotonin transporter gene within the overall accumulation of effects. Nonetheless, if we had knowledge of all the genes involved in depression, it should be possible to state each of their individual effects within the FQGEIM and to accumulate them to arrive at a picture of the overall effects. This means that, in situations in which a specific gene has been shown to be showing G × E in some measured environment, the FQGEIM can be used to test the idea that the process involved in the specific identified G × E more generally explains the association between the environmental variable and the phenotype. If so, the search for additional genes operating in similar ways is warranted. If not, the specific observation may not be important in explaining the phenotype, though it could still be important in developing further understanding of some of the biological pathways involved.

Measurement Issues Involving the FQGEIM

Like any model, the FQGEIM provides the most replicable and interpretable results when measurement of the constructs involved is valid, reliable, and accurate. Because the model is complex, it is sensitive to specific sample particularities that may be very small in magnitude. This makes issues of appropriate measurement especially important in the use of this model. There are several measurement issues that should be discussed. All are rather subtle and do not have straightforward solutions.

Perhaps the most important of these issues involves the fact that the FQGEIM is probably most easily implemented in a sample of twins. At the same time, many of the most interesting associations between environmental variables and behavioral outcomes to which the FQGEIM might be applied involve children, including the environmental effects of socioeconomic status, neighborhood characteristics, and aspects of parenting on child behaviors of all kinds. Many of these environmental variables are most easily measured at the level of the twin pair, so that both members of each pair share the same value for the environmental measure. This provides no opportunity to distinguish shared environmental influences from genetic ones (Purcell & Koenen, 2005; Turkheimer, D'Onofrio, Maes, & Eaves, 2005), which limits the ability of the FQGEIM to provide fully interpretable results.

This problem can be circumvented by collecting environmental information relevant to each twin individually. For example, parents can provide information on how they treat each twin separately, and twins (if old enough) can each provide information on how they perceive they are treated. For some kinds of parenting variables, such as parental support, the child's perception may be the critical variable anyway. Similarly, each member of a twin pair can provide information on how they perceive their neighborhood or their family's financial circumstances and attitude toward education. Of course, this requires that a twin study be designed with this issue in mind, and many existing twin studies with otherwise excellent data resources simply may not have access to this level of information. In addition, the underlying issue with most of these variables is that the parents are providing both genetic heritage and environmental circumstances to the children, and the twin design offers no way to disentangle the genetic and environmental influences affecting this intergenerational transmission process. For example, monozygotic (MZ) twins might perceive their family's financial circumstances more similarly than might dizogotic (DZ) twins, but the fact remains that both kinds of twins are perceiving the financial circumstances of the same homes, introducing an apparent shared environmental influence on the effect of perceived financial circumstances. The offspring-of-twins design may prove useful in measuring the intergenerational transmission process (D'Onofrio et al., 2003; Gottesman & Bertelsen, 1989) because it relies on the relative similarity between the different environments that grown MZ and DZ twins provide to their children, who also differ in degree of genetic relatedness.

The issue of measurement scaling is also important. The treatment of measurement scaling has tricky implications, even when there is a clearly objective connection between scale and trait, as in the case of physical size. Most measures of behavioral characteristics, however, do not have such an objective connection, which introduces further complexities. It is tempting to think that each trait has a natural scale that expresses the biological processes

involved. For example, growth in weight would appear to be a geometric rather than an arithmetic process in that a gain of 1 g in the weight of a 20-g mouse is relatively insignificant in relation to the same gain in a 2-g mouse, but a 5% weight gain has the same consequences for each. This would suggest that, rather than weight in grams, the appropriate scale would be the logarithm of the weight in grams. Even for physical size, however, this may be true with respect to some research questions but not others. Such judgments about natural scale are much more difficult when the trait in question is antisocial behavior, depression, or health problems.

Despite the difficulty, the appropriateness of the measurement scale is critical to interpretation of results on the basis of the FQGEIM. This is because the use of an inappropriate measurement scale can introduce spurious interaction effects involving G × E (Eaves, 2006; Falconer & Mackay, 1996). In fact, removal or reduction of G × E is a common reason for the use of scale transformation. This does not, however, mean that G × E is purely an artifact of the scale. Rather, it means that there should be some objective rationale for the measurement scale chosen. Probably the best guidelines available are that the distribution of the trait should be relatively normal, and the variance of the trait should be independent of its mean (Falconer & Mackay, 1996). In addition, data plots should be examined for spurious associations, and the possibility of outlying or highly leveraged points should be considered. The sensitivity of the results to the specific form of measurement should also be tested. This may mean evaluating other transformation functions or other measurement scales, such as continuous and categorical approaches. Fortunately, these are the same general conceptual guidelines as recommended for most commonly used statistical procedures.

Another relevant measurement issue is the possibility that environmental influences as well as genetic influences may vary across the range of an environmental measure. The relation between stressful home environments and antisocial behavior provides an example of the kinds of complexities that can result. Raine (2002) reviewed the literature in this area and noted that results from adoption studies provide clear evidence that adoptees at genetic risk for antisocial behavior (because they had antisocial biological parents) were more likely to become antisocial themselves if their adoptive parents provided stressful home environments, according to any of a number of standards. This is consistent with the stress–diathesis version of the FQGEIM and suggests that genetic variance in antisocial behavior increases in the more stressful environment. At the same time, Raine noted that the literature suggests that certain biological, presumably genetically influenced markers, such as low skin conductance and low resting heart rate, are related to antisocial behavior only in benign social environments. This might appear to indicate that genetic variance increases in more benign social environments, but a more likely explanation is that there are many genetic influences that contribute biological markers of vulnerability to antisocial behavior. Some of these genetic influences may remain constant across the range of social environments, whereas others may decrease in more benign environments and increase in more stressful environments. If, at the same time, environmental influences at least do not increase in more benign environments, those genetic influences that remain constant across the range of environments will be more apparent in the more benign environments than in the more stressful environments. This of course requires thorough measurement and testing. The FQGEIM potentially has the power to disentangle these complex processes, but only if the measures are distinct and accurate in the relevant ways.

The stress–diathesis and social context as enhancement variations of the FQGEIM suggest a generalized mechanism that may describe how genetic influences change under measured environments. It is reasonable to hypothesize that genetic variance in maladaptive traits increases in poorer, more stressful environmental conditions, whereas genetic variance in adaptive traits increases in better environments. This hypothesis has great potential to offer a powerful and unifying explanation for a broad range of social phenomena, and the FQGEIM can be used directly to test its range of applicability. Although elegant, this statement of the hypothesis glosses over important complications in what is meant by maladaptive and adaptive traits. The process of testing the hypothesis is confounded with the process of understanding these complications.

The simplest complication is that it may be possible to reverse the definition of a trait and thereby reverse the nature of its adaptiveness. For example, high IQ could be considered an adaptive trait, but low IQ could be considered a maladaptive trait. More subtly, the assignment of adaptive status to traits raises the question of the role of their genetic variance in natural selection and evolution. For the individual, adaptation is the process of coping with one's environment. Within a population, an adaptation is also a genetically influenced trait resulting from natural selection that gives individuals who possess it a reproductive (and therefore gene-transmitting) advantage over individuals who do not. Over time, if such traits reliably confer reproductive advantage, the genes according the advantage gradually increase in frequency in the population precisely because of the reproductive advantage they bestow. Eventually, they become fixed, and genetic variation disappears. The existence of two eyes across many animal species is an example of such a trait. The problem is, however, that environments are not necessarily static over either time or space, and many traits may confer reproductive advantages in some situations but not in others. When a trait goes to fixation, the individuals in the population lose some ability to adapt to different environmental conditions. Evolution would appear to have two major ways of dealing with this.

First, genetic variation may remain in the population. In this case, within a population in which some mobility is possible, individuals with one kind of genotype better suited to one aspect of the environment will tend to seek that aspect of the environment, whereas individuals with another genotype may seek another aspect of the environment. This means, however, that a trait that is adaptive in some environments may be maladaptive in other environments. For example, the tendency to be bold, hasty, and aggressive may confer reproductive advantage when population density is high and the food supply is plentiful, but caution, withdrawal, and thoroughness may serve better when population density is low and the food supply is uncertain (Korte, Koolhaas, Wingfield, & McEwen, 2005). In fact, within the two environments, behavioral traits may not be dependent on the same physiological and neurological processes. For example, aggressiveness may result from motivation to establish status in a conspecific hierarchy when population density is high and food is plentiful but may result from desperation when the food supply is uncertain. The neurological pathways involved in the differing motivations

and thus the genes involved in the two situations may be very different. That adaptability is conditional on circumstances that may complicate identification and measurement of the environment that is actually relevant to changes in genetic variance.

Second, genetic variation may disappear through the process of natural selection, but phenotypic variation may remain because of the existence of conditional adaptations. Conditional adaptations involve different behavioral tactics that are displayed in response to specific features of the environment. Individuals do not vary genetically in their tendencies to express these different behavioral tactics; naturally selected genes influence all individuals to vary their behavior in response to cues that confer advantages to one behavior over another. In this event, there may be a main effect of the environment on the trait but little or no variation in trait response, given the level of the environment. This will likely introduce dependencies between mean and variance, making scale transformation necessary.

Presuming genetic variation remains in the population, there is some evidence in generalities drawn from selective breeding experiments in nonhuman animals for the hypothesis that genetic variance in maladaptive human traits increases in socially constructed poorer, more stressful environmental conditions, whereas genetic variance in adaptive traits increases in better environments. In these experiments, selective breeding for positive characteristics in a good environment tends to pick animals that are highly sensitive to the environment, as does selective breeding for negative characteristics in a bad environment (Falconer & Mackay, 1996). Of course, we do not conduct selective breeding on humans, but this suggests that even in situations in which selective breeding is not being practiced, including those in humans, there may be more observable genetic variation in positive characteristics in good environments and in negative characteristics in bad environments. The contrasting observation regarding selective breeding in nonhuman animals, that is, selective breeding for positive characteristics in a bad environment and for negative characteristics in a good environment tends to pick animals that are relatively impervious to the environment, would appear to be corroborative. Facilitated variation (Kirschner & Gerhart, 2005), or the evolution of flexibility of genetic expression, may underlie these observations.

Conclusion: The Importance of the FQGEIM to Questions Involving Patterns of Behavior

I began this article noting that an epidemiological approach involving the study of the incidence, distribution, and control of problematic or disordered as well as constructive behavior patterns in the population can be useful in psychology. Research in psychology that has used this approach has tended to focus on the identification of environmental factors conferring risks and benefits and estimates of the magnitudes of average environmental effects across the people exposed to them. As behavioral genetic findings have made it clear that genetic influences play important roles in all patterns of behavior, the field has turned increasingly to articulation of the ways in which these genetic influences are manifested and to the identification of the specific DNA sequences involved. Recent reports of G × E that involve specific DNA sequences suggest that there are large differences among individuals in the effects of environmental exposures and point out the need to identify who is at greatest risk from environmental pathogens as well as who can benefit most from environmental advantages. Even once genotyping becomes truly inexpensive, practical implementation of these results will, however, still require knowledge of the genotypes of individuals, a situation with problematic privacy implications. The FQGEIM can be used to provide pilot data, before any DNA is actually collected, indicating whether genetic variance varies with exposure to specific environments in the manner hypothesized if the candidate gene is functioning as expected.

In addition, each specific DNA sequence identified to date that has shown G × E in a measured environment has explained very little of the overall incidence of the problem behavior, and the probability that individuals carrying the identified DNA sequence will actually manifest the identified problem behavior has been low. This means that research strategies focused on specific DNA sequences may be slow to accumulate results that can address the kinds of broad social issues raised in studying environmental influences on complex patterns of behavior such as the incidence and prevalence of smoking, drinking, drug abuse, criminal behavior, educational failure, parental neglect and abuse, and the associations between socioeconomic status and a host of variables ranging from physical health to IQ. Because there are likely so many ways that individuals can come to manifest these kinds of behaviors, there may be situations in which DNA sequence variation does not explain the genetic variance involved because the mechanism is an environmental influence on expression of genetic alleles that do not vary in the population. It may always be necessary to make use of statistical models such as the FQGEIM to complement identification of the specific DNA sequences involved in these behaviors in order to understand the behaviors with any degree of completeness.

As I noted at the beginning of this article, we need a wizard's camera that can capture all its subject's interplay. That is, we need techniques that can evaluate the dynamic situations involved and disentangle the ways in which genetic influences transact with both specific environmental influences and broader social forces to create differential effects on behavior in different segments of the population. Implemented with careful measurement, the FQGEIM is surely one of the most powerful techniques available. Its focus on the relations among sources of genetic and environmental variation may make it possible to reconcile the paradox that genetic influences on behavior are pervasive, yet main effects of specific genetic polymorphisms are rare and inconsistently observed.

It is perhaps surprising that the FQGEIM's power to clarify dynamic social and environmental processes without specifying the specific genes involved suggests a way in which it can also be used to assist in the identification of specific candidate DNA sequences involved in patterns of behavior that differ with environmental exposure. Because the FQGEIM reveals specific environments in which there is greater expression of the genes involved in certain traits, it indicates sources of sample participants that may be more likely to reveal meaningful results in molecular genetic association and linkage studies. Moreover, though the FQGEIM does not require the identification of DNA sequences and specific environmental characteristics that may influence the trait of interest, the model does not limit the specificity of measurement of the traits involved in any way. For example, as knowledge of the neurological mechanisms linking serotonin production and responsivity in the brain, and thus the experience of

stressful life events and depression improves, it should become possible to use this model to evaluate genetic and environmental variance associated with specific aspects of the serotonin expression in depressive symptomatology across the range of specific biological responses to the experience of life stress. This should help to identify additional specific DNA sequences that may be involved.

The associations among genetic and environmental influences on measured environments and behavioral patterns that the FQGEIM illuminates indicate that in addition to identifying who is at greatest risk from environmental pathogens and who can benefit most from environmental advantages, we need to determine the location of the genetic correlation that underlies all G × E situations that involve genetic influences common to both environment and behavior patterns. We then need to ask how we can use that knowledge to decrease expression of genetic vulnerabilities and support the expression of genetic influences on socially constructive adaptive traits. For example, when the stress–diathesis model is relevant to a dysfunctional trait and the higher genetic correlation is in the better environment, what are the specific traits under common genetic influence, and can we teach them to people even in the at-risk environment? How do we break down genetic correlations when they are higher in the at-risk environment? Where is the genetic correlation when social context enhances genetic expression and what specific traits are involved? Is it more socially desirable to try to break the correlation down or to try to build it up, and how can we go about doing either one? How stable are the patterns of genetic correlation and interaction across population groups, and what accounts for any differences observed? These are questions involving broad social policy, and the FQGEIM can address them in a way that knowledge of the specific DNA sequences involved cannot.

Addressing these questions will also help to refine our understanding of the etiology of both problematic and constructive patterns of behavior and will point out areas in which we need to refine and improve the ways we measure both the environmental factors and the associated patterns of behavior. Our answers to these questions have the potential to generate new treatment possibilities involving specific genes and suggest segments of the population most likely to benefit from these new treatment possibilities. Accumulations of results from investigations of the effects of specific DNA sequences in measured environments and results from increasingly finely specified traits and moderators from the FQGEIM should come together over time, but, for now, the two approaches complement each other directly.

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