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Integrating nature and nurture: Implications of person–environment correlations and interactions for developmental psychopathology

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Abstract

The developmental interplay between nature and nurture is discussed, with particular reference to implications for research in developmental psychopathology. The general principles include individual differences in reactivity to the environment, two-way interplay between intraindividual biology and environmental influences, and the need to consider broader social contextual features. Individuals actively process their experiences; they also act on their environment to shape and select their experiences, and individual characteristics change over time. Key findings on genetic effects include their ubiquitous influence, the multifactorial origin of most psychopathology, the involvement of several genes in most mental disorders, some genetic effects operate through dimensional risk features rather than directly on disorder, some genetic effects are dependent on gene–environment correlations and interactions, and genetic effects increase with age. Key findings on environmental effects include their ubiquitous influence, the genetic mediation of some supposed environmental effects, the importance of passive gene–environment correlations, the paucity of evidence regarding environmental effects on lifetime liability to psychopathology, the lack of understanding of environmental effects on the organism, and the importance of nonshared environmental effects. Research strategies to investigate environmental risk mediation include the range of genetically sensitive designs, migration studies, secular trend investigations, studies of nonfamilial environments, and examination of intraindividual change in relation to measured environmental alterations. Proximal processes involved in person–environment interplay are discussed in relation to person–environment interactions and evocative and active person–environment correlations.

Some two decades ago, Eisenberg (1977) argued that a developmental perspective constituted the essential underlying concept in the psychiatry of both adults and children, because the process of development provided the crucial link between genetic determinants and environmental variables, between sociology and individual psychology, and between physiogenic and psychogenic causes. The same theme has been taken up and developed by other writers (see e.g., Cicchetti, 1984, 1990; Rutter & Rutter, 1993) and it is not surprising that the bringing together of social, genetic, and developmental perspectives constitutes one of the cornerstones of the research approach that has come to be called "developmental psychopathology" (Cicchetti & Cohen, 1995; Rutter, 1996).

The terms "nature" and "nurture" seem to

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imply a polarity but, of course, neither operates in a vacuum. Genetic effects have to be manifest with respect to organisms developing in a particular environmental milieu, and environmental effects have to operate on organisms that differ with respect to genetically influenced individual characteristics. Accordingly, quantitative genetics came to focus on the "how much of each" question, partitioning the variance in populations according to the extent to which individual differences were attributable to genetic or nongenetic factors. The findings have been consistent and striking. Substantial, but rarely overwhelming, genetic effects have been found with virtually all forms of human behavior (Plomin, 1986; Plomin, DeFries, McClearn, & Rutter, 1996; Plomin & McClearn, 1993; Rutter et al., 1990). This has been so not only with major mental disorders such as schizophrenia (Kendler, 1990), or autism (Rutter, Bailey, Simonoff, & Pickles, in press), and major behavioral traits such as personality dimensions (Loehlin, 1992), but also attitudes and beliefs (Eaves et al., 1989) and individual differences in exposure to life events and experiences (Plomin, 1994a, 1994b, 1995a; Plomin & Bergeman, 1991). It is clear that any researchers who ignore genetic effects do so at their peril.

Equally, however, the genetic evidence has been clear-cut in demonstrating the substantial, but rarely overwhelming, effect of nongenetic influences (Plomin, 1994a, 1994b; Rutter, 1985a, 1985b, 1995a). Pairs of monozygotic (MZ) twins tend to be much more alike in their behavior than are dizygotic (DZ) twins, but MZ pairs are far from identical in their behavior in spite of the fact that they have the same set of genes. Typically, pairs of MZ twins show correlations of about 0.4–0.6 for measures of personality or psychopathology (Plomin, 1986), and even the concordance for strongly genetic disorders such as schizophrenia and bipolar affective disorder is only some 50–80% (McGuffin & Murray, 1991). Researchers who ignore environmental influences also do so at their peril.

Despite this weight of evidence, controversies remain. First, there are researchers who tend to dismiss the importance of environmental effects either because there is so little evidence of a major impact from specific environments, as measured (Rowe, 1994), or on the grounds that environments have little effect unless they represent extreme departures from normality (Scarr, 1992). It is indeed the case that good evidence of major influences of specific environments is sparse; however, that constitutes a challenge for the future and not a reason to dismiss environmental effects. A parallel criticism can be applied to genetic effects (Rose, 1995) on the grounds that, although the evidence suggests that there are important genetic effects, there is remarkably little evidence on how such effects operate. Again, that constitutes an issue to be tackled and not a reason for despair.

The second controversy derives from the claim that, because quantitative genetics is concerned with partitioning genetic and environmental effects on individual variations within that population, the findings are uninformative about the determination of any trait with respect to individuals (Baumrind, 1993; Gottlieb, 1995; Johnston, 1987; Lerner & von Eye, 1992). Nearly 40 years ago, Anastasi (1958) might be thought to have made the same point in arguing that the focus should be on "how" heredity and environment contribute to development and not "how much" variation they account for. The goal must be to use research findings to gain an understanding of how behaviors or disorders arise. The quantification of heritability, in of itself, is rather uninformative about causal processes and it is not helpful in taking decisions about the potential value of interventions (Morton, 1974). What is mistaken, however, is the notion that studies of populations cannot be used to investigate causal mechanisms (Rutter, 1994a). Most developmental research, as well as the whole of epidemiology, uses group analyses for this very purpose. The "how much?" focus of quantitative genetics constitutes an essential step in tackling the "how?" question (Dolan & Molenaar, 1995; Plomin, 1994b, 1995a; Turkheimer, Goldsmith, & Gottesman, 1995).

A further concern that is often expressed is that much quantitative genetic research is based on linear models that ignore gene–environment correlations and interactions, the

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effects of assortative mating, and cultural variations (Baumrind, 1993; Jackson, 1993). That is fair criticism with respect to much quantitative research in the past but it fails to recognize the extent to which quantitative researchers have accepted the importance of these concepts and have developed techniques for taking them into account (see Eaves, Last, Martin, & Jinks, 1977; Mather & Jinks, 1982; Neale & Cardon, 1992; Plomin, 1995a, 1995b). As Bronfenbrenner and Ceci (1994) have emphasized, there is a need to examine the proximal processes involved in the interplay between organisms and their environments if the development of phenotypes is to be understood, but, as they also underline, the means are available to do just that.

Our main purpose in this paper is to consider the evidence on the various types of interplay between nature and nurture in order to consider the implications for research in the field of developmental psychopathology. We focus first on some general principles of nature–nurture interplay as they apply to development and to behavioral variations; we then consider some "lessons" and challenges deriving from some key findings on genetic and on environmental risk mechanisms. These are used to lead on to a discussion of some of the specifics with respect to passive, evocative, and active person (and gene)–environment correlations and person (and gene)–environment interactions; in each case we focus especially on the implication for research strategies and tactics.

As the concepts of gene–environment correlations (rG–E) and interactions (G × E) pervade the paper, it is appropriate to make their meaning explicit at the outset.[1] Gene–environment correlations (rG–E) refer to situations in which variations in genetic liability are systematically associated with variations in specific environmental circumstances; and gene–environment interactions (G × E) to a type of genetic liability that involves a differential susceptibility to specific environmental features. An understanding of the manifold ways in which these two forms of nature–nurture interplay may be manifest is crucial to an appreciation of the risk and protective mechanisms operating over the course of development in the liability of psychopathology.

Some General Principles Regarding Nature–Nurture Interplay

Before proceeding to consider the details of the possible proximal processes involved in

1. From an evolutionary perspective, both rG–E and G × E express genetic differences in the ways in which organisms adapt to environmental demands. Both have their origins in genetic diversity, and the frequency of alleles underlying rG–E and G × E may be altered by natural and artificial selections (Chadwick & Cardew, 1996). In any organism where there is a capacity to respond adaptively to environmental change (either by responding to it or ignoring it), genetic differences in sensitivity to particular environmental changes (G × E) are to be expected. In species that have evolved patterns of parenting and social interaction, and in which individuals are more or less free to select and explore their environments, rG–E is to be expected because exposure to particular environments may depend either on the genotypes of parents or siblings making up the social environment, or on the adaptive responses of each genetically unique individual.

   The basic principles deriving from an extensive history of G × E in experimental organisms (see Mather & Jinks, 1982) are genes control responses to the environment in a rich variety of ways; the adaptive significance of different types of G × E alters as a function of the environment in question; and often, different genes control sensitivity to different environmental changes and these may differ, too, from those that underlie overall individual differences in traits. Such considerations both rule out any assumption that G × E can be equated with the statistical concept of interaction (see Mather & Jinks, 1982) and require adequate measurement of specific environments (see Kendler & Eaves, 1986). However, there are several animal models for G × E that are potentially instructive for developmental behavioral genetics (see e.g., Broadhurst & Jinks, 1966; Fulker, 1970).

   Two intellectual traditions bear on an understanding of rG–E. First, there are the biometrical genetic models pioneered by Jinks and Fulker (1970), but deriving from Cattell's (1963) ideas about societal reactions to genetically influenced differences in behavior, and leading on to more contemporary path models for mixed genetic and cultural inheritance (see e.g., Rice, Cloninger, & Reich, 1978; Truett et al., 1994). Second, there are the approaches based on a recognition that the maternal genotype is part of the environment in which progeny develop and that the genetic component of maternal effects can be analyzed in the same way as any other trait (see Mather & Jinks, 1982). This led to models of both cultural inheritance and sibling effects (see Cavalli–Sforza & Feldman, 1973, 1981; Eaves, 1976).

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nature–nurture interplay, it is necessary to note a few general principles regarding such interplay, as they apply to development, and to individual differences in behavior. These general issues are summarized in Engel's (1960, 1978) biopsychosocial model, Bronfenbrenner and Ceci's (1994) bioecological model, Hinde's (1987) integration of biology and culture, Plomin's (1995a) bringing together of nature and nurture, and Rutter and Rutter's (1993) concepts of person–environment interplay in developmental processes. These writers differ somewhat in their terminology and in the details of some of their propositions but six main principles are implicit or explicit. They are expressed here in developmental terms but they closely mirror those that derive from evolutionary and genetic concepts (see Footnote 1).

First, individuals differ in their reactivity to the environment. Indeed, many behavioral features are defined in these terms. Thus, behavioral inhibition is defined in terms of autonomic and behavioral responsivity to challenging or stressful situations (Reznick, Hegeman, Kaufman, Woods, & Jacobs, 1992; Suomi, 1991). Similarly, extraversion is defined in terms of people's interest in, and response to, social situations. Two very different examples illustrate both the importance of these differences and some of the associated research issues. Cohen, Tyrrell, and Smith (1991), using a rigorous experimental design, showed that psychological stress was systematically associated with an increased risk of acute infectious respiratory illness following experimental administration of nasal drops containing a low infectious dose of one of five respiratory viruses. The finding is important in its demonstration that, even with infectious agents, individuals vary greatly in their susceptibility and that "stress" plays a role in modifying immune responses. However, as the authors point out, their design cannot differentiate between stress as a response to environmental events and stress as a reflection of personality features. A genetic design could make that crucial differentiation. Sapolsky (1990), in his study of free ranging baboons in an African reserve, showed striking differences between dominant and subordinate animals in their reaction to the stress of dart-induced disorientation and anaesthesia. Further research went on to show, however, that the differences were not primarily due to social rank as such, but rather reflected the personality characteristics of a subgroup of dominant males. These characteristics primarily concerned the use of effective coping strategies that provided a means for a sense of control and an outlet for distress. Clearly, some very important things were going on in the interplay between the animals and their stress experiences but what was driving what? In so far as genetic factors are involved in the individual differences, through which aspects of behavior or physiology did they operate?

Second, there is a two-way interplay between individuals and their environments, as demonstrated by both experimental and naturalistic studies. For example, studies of sex hormones, dominance, and aggression in male rhesus monkeys have shown that just as sex hormones influence behavior, so also behavior modifies sex hormone levels (Rose, Holaday, & Bernstein, 1971). Similarly, Raleigh and McGuire (1991) showed that 5-hydroxyindoleacetic acid (5-HIAA) levels in vervet monkeys altered with changes in social status; not only are individual differences in levels of 5-HIAA heritable, but they are also responsive to forces in the environment. Mazur, Booth, and Dabbs (1992) showed that in humans the winner of a closely matched chess game also had a rise in testosterone levels whereas losers showed a fall.

It is sometimes assumed that biological measures must reflect nature; however, that is not so. They are open to the influence of both genetic and environmental factors and genetic designs are necessary to sort out their origins. The experimental data also indicate that there cannot be a single answer to the relative importance of genetic and environmental influences. Much is likely to depend on the environmental conditions.

These data all refer to the immediate situation but the same is likely to apply over the longer term. Thus, Pianta and Egeland (1994), using a longitudinal design over a 1-year pe-

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riod, showed that stress experiences were associated with the onset of depression but also that the occurrence of depression was associated with a later increase in stressful happenings (see also Rohde, Lewinsohn, & Seeley, 1994, for a similar finding).

A further example of two-way effects concerns the role of inattention in inhibiting learning. For example, both intensive and extensive studies have suggested that, not only is task failure associated with lapses in attention, but also that inattention inhibits learning (Imai & Anderson, 1992; Rowe & Rowe, 1992). Probably, much the same applies to exposure to reading material and the growth of reading skills (Cipielewski & Stanovich, 1992; Scarborough, 1991; Stanovich & Cunningham, 1993). That is, children with individual characteristics that make it more difficult for them to learn to read, not surprisingly, read less. But, in turn, their lack of exposure to reading materials further interferes with their acquisition of reading skills. The data are provocative and important but, although the findings point strongly to a two-way interplay, none are based on designs that enable the effects of nature and nurture to be differentiated.

Third, the interplay between persons and their environments needs to be considered within an ecological framework, both because the individual processes associated with features such as family disruption may vary by broader social or cultural context (see e.g., Manning & Landale, 1996; Nettles & Pleck, 1994; Rutter, 1990b) and because the proximal processes associated with features such as poverty and social disadvantage may lie in their effects on family interactions (see e.g., Brody et al., 1994; Cicchetti & Lynch, 1993; Conger et al., 1992; Dodge, Pettit, & Bates, 1994; Sloggett & Joshi, 1994).

Fourth, a further principle is that people *process* their experiences rather than just serve as passive recipients of environmental forces. Children's questions and comments vividly illustrate the ways in which they are constantly constructing schemes of what they know, trying out their ideas on how to fit new knowledge into those schemes, or deciding that the schemes need modification (Dunn, 1988). It is likely that children's ability to understand other people's thought processes and other people's reactions to them plays an important role in their social relationships (Dunn, 1993). The importance of people's cognitive processing of their experiences was neatly shown in the British longitudinal study of civil servants. The *anticipation* of job loss affected health even before people's employment status had changed (Ferrie, Shipley, Marmot, Stansfeld, & Davey–Smith, 1995). Much research has shown that the impact of negative life events on people's physical and mental health is influenced by the social context of the experiences (Brown & Harris, 1978, 1989). This is usually considered as if the whole was an environmental effect. However, the reasons why people vary in the way they view their experiences is in part a consequence of their genetically influenced personality, as well as their prior experiences.

Fifth, people *act on their environment* so as to shape and select their experiences (Plomin, DeFries, & Fulker, 1988; Scarr, 1992; Scarr & McCartney, 1983). Recognition that this is so means that it is not possible to consider the effects of experiences as if they were randomly distributed and were independent of how people behaved. The importance of taking this into account was recognized early on by Brown and Harris (1978) in their study of life events. It was an important methodological advance to examine the effects of life events only in terms of those that were considered independent of the person's psychopathological disorder. That was a step forward but, of course, people shape and select their experiences for reasons that go well beyond psychopathology (Sandberg et al., 1993). Finally, individual characteristics change over time and, in a very real sense, that is what development is all about. Genetic research has been important in demonstrating that the changes that take place as people grow older are a consequence not only of biological maturation, but also of genetic and environmental factors that shape individual differences.

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Some Key Findings on Genetic Effects

There is a mass of detailed genetic findings that have implication for future research directions, some of which are discussed below. Six main general findings, however, may be singled out as those that need to guide research strategies and tactics.

First, as already noted, a substantial genetic influence has been evident with respect to almost all human behavior, accounting for some 20–60% of population variance, and sometimes more than that. The implication is that the role of genetic factors must be taken seriously with respect to the whole of developmental psychopathology. Although disorders vary somewhat in the strength of their genetic component, the main message lies in the finding that genetic influences are ubiquitous. On the whole, the minor variations in heritability within the middle of the range are of less importance. There are some exceptions, however, such as autism in which the heritability for the underlying liability exceeds 90% (Rutter et al., in press), suggesting that the identification of the genetic mechanisms could well provide keys to the causal process. There are also a few single gene conditions associated with psychopathology—such as Huntington's disease, the Prader Willi syndrome, and early-onset familial Alzheimer's disease. But these account for a tiny proportion of psychopathological disorders.

Second, as implicit in the first point, most mental disorders are multifactorial in the sense that they involve a mixture of genetic and environmental influences. This has two main implications (Rutter, 1994b). First, quantitative genetic studies need to include direct measurement of postulated environmental factors and the statistical analyses need to address the possibility that genetic effects may be partially dependent on particular environmental circumstances. Second, molecular genetic studies need to shift focus from analysis of extended pedigrees (in the expectation that single gene conditions will be identified) to those that are better suited to the detection of genes that play a contributory role, albeit a major one, in multifactorial disorders. These include methods based on affected sib pairs (preferably extended to include parents) or, where quantitative phenotypic measurement is possible, highly discordant sib pairs.[2]

Third, most mental disorders are likely to involve several different genes, and not just one (Rutter, 1994b). That conclusion is based on two findings. First, with the few multifactorial medical disorders in which genes have been localized or identified, it seems that in most cases more than one route to disorder is involved (Sing, Haviland, & Reilly, 1996). Second, it appears that particular gene combinations are operative in the case of some mental disorders. For example, with autism, the very marked fall-off in rate between MZ co-twins and DZ co-twins, and the sharp fall-off in rate going from first degree to second degree relatives, points strongly to the likely involvement of several interacting genes (Pickles et al., 1995). That is because, although DZ pairs share half their segregating genes on average, they share only a quarter of two-gene combinations, and an eighth of three-gene combinations. By contrast, because MZ pairs share all their genes, they also share all gene combinations. Thus, several genes may be implicated because there are different major genes contributions to genetically heterogeneous forms of the disorder, because different genes are involved in different routes to the same disorder, or because the liability requires a combination of susceptibility genes.

Fourth, genetic influences may apply to dimensional risk factors, rather than to diseases or disorders as such. Until recently, much molecular genetic research in the field of psychiatry has focused on a search for the gene or genes for schizophrenia, depression, or Tourette's syndrome. It is possible that genes will

2. The design implications here are complicated and go beyond the aims of this paper. Thus, extended family designs can be used with multifactorial disorders despite the serious problems involved in both phenotypic designation and specification of mode of inheritance (see Peltonen, 1995), and the difficulties in deciding when a lod score is statistically significant (Lander & Kruglyak, 1995). The crucial points concern the need to recognize that the genetic effect may not apply to the disorder per se and that the dangers of false positives (deriving from misspecification of the phenotype and/or mode of inheritance) are considerable.

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be found for these disorders. For example, several studies have now shown linkage between a liability to schizophrenia and an area on the short arm of chromosome 6 (Peltonen, 1995). Equally, however, it is likely that, for many conditions, genes will operate on dimensional or categorical risk factors that are separate from disorder, although they create a liability to it or protection from it. Thus, two molecular genetic studies have identified a specific genetic locus on the short arm of chromosome 11 that constitutes to variation in the temperamental trait of novelty seeking (Cloninger, Adolfsson, & Svrakic, 1996). Twin study data also suggest that the dimension of neuroticism in women accounts for much of the liability to episodes of major depression of mild to moderate severity (Kendler, Neale, Kessler, Heath, & Eaves, 1993b). An example of a protective effect is provided by the flushing reaction to alcohol seen in many people of Asiatic origin, which plays a major role in their much reduced liability to alcoholism (McGue, 1995).

Both human and animal studies have shown the potential of a focus on risk factors, rather than disease or disorder as such. Thus, in the medical arena, the identification of a locus for airway hyperresponsiveness (i.e., a sensitivity that leads the airways to constrict) is potentially relevant on the etiology of asthma (De Sanctis et al., 1995). An example in the psychopathological arena is provided by Flint et al.'s (1995) QTL study of emotional reactivity (an equivalent of a tendency to respond with anxiety). In other cases, the dimension may be somewhat closer to the categorical disorder. The clear implication is that genetic research (both quantitative and molecular) needs to consider the possibility that disorder categories are based on continuously distributed dimensions of liability and that these dimensions may involve either subclinical manifestations of the phenomenon or risk factors that are more distant from the phenotype.

The extension of disease categories into broader dimensions is a distinct possibility, too, even with qualitatively distinct forms of psychopathology. Thus, it appears that the liability for schizophrenia includes schizotypal and paranoid personality disorders, as well as schizophrenic psychoses (Kendler, Neale, & Walsh, 1995). Also, the phenotype of autism seems to extend into a broader range of social and communicative abnormalities that are not associated with either the mental retardation or gross social impairment that usually accompanies autism as traditionally diagnosed (Rutter et al., in press).

There are many examples in developmental psychopathology of disorders for which there are multiple risk factors, each of which may be subject to genetic influences. For example, with respect to persistent antisocial behavior, empirical findings from epidemiological, clinical, and longitudinal studies have shown that hyperactivity/impulsivity, low autonomic reactivity, sensation-seeking/risk taking, aggressivity, and cognitive impairment/poor executive planning all constitute indices of risk (Stoff, Breiling, & Maser, in press). It is not as yet known whether these reflect different facets of the same risk dimension or, rather, different routes to antisocial behavior. Multivariate quantitative genetic studies can help resolve this issue by their identification of the behaviors for which genes code, and which mediate the psychopathological risk. For example, the traditional across-twin, within-trait correlations have shown that both the condition of dyslexia and the trait of phonological processing involves a substantial genetic component. By extending the analyses to across-twin, across-trait correlations it is possible to examine the overlap between the two. That is, by comparing MZ and DZ pairs regarding the extent to which phonological processing in one twin is associated with dyslexia in the other, it is possible to infer the extent to which the genetic liability to dyslexia is mediated through the dimension of phonological processing.[3] In this case, the findings suggested that, to a considerable extent, it was

3. Longitudinal data are needed to differentiate between a causal process in which the same genetic liability underlies phonological processing and dyslexia (i.e., that both are reflections of the same liability but there is no causal route from one to the other), and one in which the genetic overlap stems from a causal route in which a deficit in phonological processing leads to reading difficulties. The same issue applies to the later examples in the same paragraph.

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(Olson, Wise, & Rack, 1989). The design can be strengthened by including an over-time element. That is, it is possible to provide a better leverage on the testing of the causal hypothesis by examining whether the risk dimension in one twin at Time 1 is associated with the onset of the categorical disorder in both the twin and the co-twin at Time 2. This could be applied, for instance, to the postulated association between behavioral inhibition and a liability to anxiety disorders (Hirshfeld et al., 1992). It has been used by Kendler et al. (1993b) in relation to the role of neuroticism in vulnerability to major depression. Silberg et al. (1996a, 1996b) have similarly shown, with cross-sectional data, that most of the genetic effect on antisocial behavior in young people comes through the route of hyperactivity.

A further key facet of this same point about dimensional risk and protective factors is that exactly the same trait may be a risk factor for one form of psychopathology but a protective factor for another. For example, the phenomenon of behavioral inhibition with high autonomic reactivity has been shown to be a risk factor for anxiety disorders (Hirshfeld et al., 1992) but a protective factor for delinquency (Lahey, McBurnett, Loeber, & Hart, 1995). As yet, these risk and protective features have not been examined within a genetic design and it remains to be determined whether these represent the route of genetic mediation.

Fifth, genetic effects may be indirect, as well as direct. That is, they may operate through gene–environment correlations and gene–environment interactions. The consideration of how these may operate, together with their research implications, constitutes the main focus of the body of this article.

Sixth, genetic effects on psychopathology and cognitive skills tend to increase with age (Eaves, Long, & Heath, 1986; Plomin, 1986). At first sight, that sounds counterintuitive in that the genes are already all in place at the time the child is born and environmental influences are only just beginning to operate. How, then, can the increase in genetic effect come about? The evidence that they do increase is apparent, for example, in the tendency for MZ pairs to become somewhat more alike (for many traits) in the preschool years and then remain similar, whereas DZ pairs tend to diverge increasingly in their behavior (McCartney, Bernieri, & Harris, 1990). There are several rather different ways in which the increasing genetic effect could come about (Eaves et al., 1986). It might reflect, for example, the diminishing effect of prenatal influences. These are likely to be more important with twins than singletons because of the higher rate of obstetric and perinatal complications in twins and because there are greater intrauterine differences within MZ pairs than within DZ pairs. Another possibility is that measures alter their meaning as children grow older. This would be true with respect to the changing content of cognitive tests, as well as the meaning of many behavioral traits. A third consideration is that whereas there tend to be quite high over-time correlations for genetic effects (that is, the *same* genetic influences operate over the course of development), to an important degree, some environmental effects tend to be relatively time specific. (See, e.g., Kendler et al.'s 1993a findings with respect to major depression in women and Fulker, Cherny, & Cardon's 1993 findings with respect to specific environmental effects on cognitive development.) This difference in temporal continuity between genetic and environmental effects means that the effects of the former are more likely to be cumulative than are the latter. A fourth possible reason for any increase in genetic effects is that they operate on the individual's susceptibility to environmental influences. Alternatively, they may affect individual differences in exposure to environmental influences. We consider both these last possibilities in greater detail below; however, the point here is that they provide a mechanism by which genetic effects can amplify. Of course, although the genes are in place from the outset, that does not necessarily mean that their effect has become overt at that point (Gottesman & Goldsmith, 1994). For example, it is well established that there are strong genetic influences on the timing of puberty (see e.g., Pickles et al., 1994). Some mutant genes, such as that for Huntington's disease, may not "switch on"

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until well into adult life. Also, brain development continues into early adult life (Weinberger & Lipska, 1995) and the process of development is strongly influenced by genetic forces.

Some Key Findings on Environmental Effects

The first point is the parallel to the same one with respect to genetic factors; namely, there is extensive evidence that there is a substantial environmental influence on almost all human behavior. This is shown by several rather different sorts of evidence. As we have noted, twin and adoptee studies are consistent in showing that nongenetic factors account for about half the population variance for most traits and disorders (Plomin, 1994a, 1994b). The probable role of environmental factors is also shown by anomalies in the genetic evidence. For example, the Danish twin data suggest a stronger genetic component for antisocial behavior than do the Danish adoption data. Also, despite the fact that DZ twins showed the same degree of genetic similarities for siblings, there is a stronger correlation for antisocial behavior between DZ twins than between full sibs (see Bock & Goode, 1996). These disparities in findings contrast with the stronger consistency evident with some other forms of psychopathology, such as schizophrenia (McGuffin, Owen, O'Donovan, Thapar, & Gottesman, 1994). The importance of environmental factors in psychopathology has also been shown by a variety of other designs. Thus, the marked rise over the last half century in the rates of crime and of suicidal behavior must be due to some environmental mechanism because the gene pool could not change that quickly (Rutter & Smith, 1995). Environmental effects are also indicated by the evidence of within-individual change following specific experiences, especially where a longitudinal design includes examination of the effects of environmental reversal (Rutter, 1994a, 1996). Also, environmental influences have been shown through the study of nonfamilial environments, again using longitudinal data, for example, with the study of school effects (Maughan, 1994; Mortimore, 1995; Rutter & Rutter, 1993).

We noted with genetic effects that, although there was excellent evidence that they were operative, very little was known about *which* genes were influential or *how* they operated. Exactly the same applies with respect to environmental factors. Very little is known on which aspects of the environment carry the risk for different types of psychopathology or what they do to the organism. It is not that there is any shortage of statistical correlations with all manner of putative environmental variables. Rather, the ignorance stems from three other features of much of the research. First, scarcely any of the evidence stems from genetically sensitive designs; the consequence is that there is a continuing uncertainty on whether the apparent effect is actually environmentally mediated. Second, many of the data stem from retrospective or cross-sectional studies in which there is uncertainty over the time relationships. Where longitudinal data have been available, they have often forced a reinterpretation of the findings. Thus, although divorce is associated with psychopathology in the children, longitudinal data have shown that much (but not all) of the rise in psychopathology was evident in the children before divorce took place (Block, Block, & Gjerde, 1986; Cherlin et al., 1991; Elliott & Richards, 1991). Third, few of the studies have contrasted competing hypotheses on possible modes of environmental mediation. When they have done so, the findings have often been informative. For example, Fergusson, Horwood, and Lynskey (1992) found that whereas discord was associated with antisocial behavior even in the absence of family change, exposure to family change in the absence of parental discord did not lead to an increased risk of offending.

Genetic mediation of supposed environmental effects

The third crucial finding on environmental effects stems from studies using genetic designs. They have indicated that many supposed environmental variables and postulated environmental effects actually reflect, in part,

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genetic influences (Plomin, 1994b, 1995b; Plomin & Bergeman, 1991). Both of these findings argue strongly for the necessity of systematic study of measured psychosocial risk factors within genetically sensitive designs. It should be noted, however, that the genetic involvement in environmental effects actually reflects two rather different questions (which are likely to involve different mechanisms). First, there is the evidence from twin studies that genetic factors play a role in individual variations in exposure to environmental factors. For example, several twin studies have shown this with respect to life events (Kendler et al., 1993a; McGuffin, Katz, & Rutherford, 1991; Plomin, Lichtenstein, Pedersen, McClearn, & Nesselroade, 1990). Second, genetic designs have shown that some effects that appear environmentally mediated are actually a function, in part, of genetic mediation. Thus, it has been found that about half the effect of the HOME measure of family environment on the Bayley measure of mental development at the age of 2 years is attributable to genetic factors (Plomin, 1995b). Similarly, genetic factors have been found to account for well over half of the effect of mothers' negativity on adolescents' antisocial behavior and depression (Plomin, 1995b). It is necessary to keep these two sorts of effects separate because the origins of a risk variable and its mode of mediation have no necessary connection with one another (Rutter, Silberg, & Simonoff, 1993). Thus, the reasons why people smoke cigarettes are to be found in personality variables and sociocultural influences (as well as the availability of tobacco products), but the effects of smoking on disease are mediated via carcinogens, carbon monoxide, effects on blood vessels, and irritation of the passages of the lung. It is important that genetic research use designs that can separate identification of the origins of risk factors from the mode of action of those factors.

Longitudinal studies involving within-individual change provide the way forward. Ideally, they should include reversal. The causal hypothesis regarding carcinogenic tars in tobacco smoke and lung cancer received powerful support from the evidence that the risk of lung cancer went down when people stopped smoking. Similar studies of within-individual change are also informative in the psychopathological arena. Thus, both Sampson and Laub (1993) and Quinton, Pickles, Maughan, and Rutter (1993) showed the protective effect of a harmonious marriage by finding within-individual change over time in antisocial behavior that was linked with the positive marriage experience. Of course, it is important to check that the apparent change is not a function of unmeasured aspects of the phenotype and various statistical approaches are relevant for the purpose (see e.g., Gottman, 1995; Pickles & Rutter, 1991; Quinton et al., 1993; Sampson & Laub, 1993).

Passive gene–environment correlations

The genetic mediation of what are thought to be environmental effects comes about because of various sorts of correlations between genes and experiences (Eaves et al., 1977; Plomin, DeFries, & Loehlin, 1977). We focus, here, on what have been termed "passive" correlations. That is, parents' genes, insofar as they influence parental behavior, are also influences on the child's experiences. The fact that some parents are hostile and rejecting of their children whereas other are loving and supporting may derive in part from genetically influenced personality features of the parents. A probable effect of this kind was evident in Rutter and Quinton's (1984) study of the effects of parental mental disorder on family discord and children's exposure to hostile behavior. Compared with a general population comparison group living in the same geographical area, discord and hostile behavior was much more frequent in the families in which one or other parent had some psychiatric disorder. The evidence was strong that the adverse family environment was a consequence of factors associated with the parental psychopathology, but, because it was not a genetic design, it could not determine the extent to which this was genetically or environmentally mediated.

The effects of passive gene–environment correlations have received surprisingly little attention in the research literature and their

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study constitutes a major research priority. Their potential importance is shown by the combination of three well-established findings. First, the presence of psychopathology in the parent is often the single best indicator of risk to the child for the same psychopathology. Indeed, that has constituted the basis of most of the high risk longitudinal studies. Thus, parental criminality is the best risk indicator for antisocial behavior in the offspring (Farrington, 1995a, 1995b); mild mental retardation shows a strong tendency to aggregate in families (Simonoff, Bolton, & Rutter, 1996); and parental depression constitutes a potential risk factor for depression in the offspring (Harrington, 1994). Second, these forms of psychopathology involve a substantial genetic component that is likely to be relevant for the same form of disorder in the children. Third, numerous studies have shown that these same forms of parental psychopathology are associated with serious distortions of parenting and of family relationships that carry a major psychiatric risk even when they occur in the absence of parental mental disorder (Downey & Coyne, 1990; Rutter, 1989b, 1996). The importance of this trio of findings is that they point to two important possibilities. First, part of the psychopathological risks to the children stemming from parental disorder may be *environmentally* mediated despite the genetic component in the parental disorder. In other words, the mediational route is indirectly operating via the creation of environmental risks (see Kendler et al., 1996, for an example of this effect in the case of parental alcoholism, parental loss, and the risk of alcoholism in the offspring). Second, what *appears* to be an environmental risk may actually reflect genetic mediation (i.e., the environments thought to be risky are simply epiphenomena of the genetic liability and do not have a direct risk impact on the children). Obviously, it is crucial to differentiate between the two alternatives. One further piece of evidence pointing to the possibility of genetically stimulated environmental risk mediation is that, in many instances, the psychopathological risks to the offspring of parents with mental disorder cover a wide range of psychopathology and not just the one type shown by the ill parent (Shillady et al., 1997). This suggests (but does not prove) environmental mediation because many (but not all) of the genetic effects for major mental disorders are relatively diagnosis specific (Rutter, 1989b). Care must be taken, however, in how this apparent lack of diagnostic specificity is interpreted. Much depends on the extent to which psychopathology in childhood and psychopathology in adulthood, in the same individuals, exhibit the same features (see Rutter, 1995b).

This set of findings make a strong case for studying the effects of passive gene–environment correlation but they do not demonstrate either how the correlations arise or their effects on risk to the offspring. Three main research needs are particularly obvious. First, there are key aspects of psychopathology for which we know almost nothing about their effects on family life and parenting; that would apply, for example, to mild retardation in parents; far less is known about the effects of anxiety disorders in parents than depression in parents; and, until recently, little was known about the parenting provided by women with eating disorders (but see Stein, Woolley, Cooper, & Fairburn, 1994). Second, even where there is much evidence, we lack knowledge on the causal processes involved in the connections between parental psychopathology and parenting. For example, there are many studies on the family interactions of parents with depression (see Downey & Coyne, 1990; Rutter, 1990a), but do the effects derive from personality disorders or personality features associated with the depression or do they derive from the depressive disorder per se (DeMulder & Radke–Yarrow, 1991)? Relatively little use has been made of the research strategy of following parents to assess parenting qualities both during and between episodes, or that of using treatment designs to determine whether relief of depression is systematically associated with changes in patterns of family life. Given the strong association between personality disorders and depression (Klein, Kupfer, & Shea, 1993), it is particularly important to separate the effects of these two features. Follow-up studies from childhood to adult life would also be informative on the possible routes by which parenting

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difficulties come about. For example, insofar as mental retardation in parents constitutes a risk factor for parenting, does this derive from the low IQ of the parents, from their socially disadvantaged background, or from the emotional and behavioral disturbance that is associated with lower cognitive levels? The third and greatest need is for research that connects up the parental psychopathology, the associated abnormalities in family relationships and parenting, and the risks for psychopathology in the children.

That is crucial because the fact that parental mental disorder is associated with abnormalities in family life and relationships does not necessarily mean that those abnormalities mediate the environmental risk for psychopathology in the children. It may be relevant that if such abnormalities are caused by parental psychopathology they are likely to constitute a family-wide influence. At first sight, that would seem to mean that they may not mediate much risk in view of the evidence that nonshared environmental effects (i.e., those specific to individuals) predominate; however, that does not follow (see below). What is crucial for the study of the consequences of passive gene–environment correlations is appropriate identification, and accurate measurement, of the postulated environmental risk factors, shared or nonshared. These might include fetal damage (from alcohol or drugs), involvement in parental symptoms, family discord, parental neglect, lack of provision of learning experiences (e.g., by listening to the children read), or breakdowns in parenting (e.g., resulting in the children going into group foster care—see Rutter, 1989a). Measurements of these need to be both family-wide and child specific.

Environmental effects on lifetime liability to psychopathology

A specific facet of the relative ignorance on the mode of operation of environmental risk effects is the lack of good data, especially in the field of adult psychopathology, on environmental effects with respect to lifetime liability to particular forms of psychopathology. The main emphasis has been on examination of the role of acute life events carrying long-term negative threat in the precipitation or onset of depressive, and other, disorders. The temporal association between the life events and the onset of disorder provides quite persuasive evidence that a contribution to a causal process is involved. However, depressive disorders, like many other psychiatric conditions, are essentially recurrent. Accordingly, the more important question concerns the role of environmental factors in the liability to depressive disorders over time, rather than the timing of one particular episode. Both case-control and longitudinal studies can be informative with respect to liability over time but identification of specific environmental mediation requires some form of genetically sensitive design.

All studies have shown marked individual differences in people's susceptibility to risk environments. Life events researchers have approached this question in terms of vulnerability factors that are thought to operate environmentally—such as adverse patterns of rearing during early childhood (see Harris, Brown, & Bifulco, 1990). Longitudinal data from the first British national cohort study provided striking evidence that vulnerability from childhood (as indexed by a combination of adverse experiences and deviant behavior) was associated with a much increased likelihood of developing psychiatric symptoms following adult stress experiences (Rodgers, 1990). We may safely conclude that people's prior experiences and behavior make a difference to how they respond to environmental stress. The question again, however, concerns the extent to which this vulnerability is genetically or environmentally mediated.

Environmental effects on the organism

Remarkably little is known on what environmental effects *do* to the organism (Rutter, 1986, 1989a). Insofar as environmental effects are at all persistent over time, it is essential to ask how the continuity over time is mediated. Or, put another way, what is involved in the translation from undergoing a risk experience into acquiring a risk for psychopath-

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ology? Has the biological substrate been altered? That could be the case, as shown by the animal findings of the effects of early stress experiences on the later structure and function of the neuroendocrine system (Hennessey & Levine, 1979). Alternatively, are the effects on cognitive biases and styles of cognitive processing? The results from the prospective longitudinal study undertaken by Dodge, Pettit, Bates, and Valente (1995) of children exposed to early physical abuse suggests that that may play a role in relation to the risk of later aggression. Or is the effect on self-esteem and feelings of helplessness, as suggested by the retrospective data in Harris et al.'s (1990) study of women with depression? There is no doubt that negative thought processes constitute a major part of depression, and there are good reasons for supposing that they may well play a role in the maintenance of depression; however, it is much less certain whether they play a key role in its initial causation (Teasdale & Barnard, 1993). Or, instead, does the answer lie in effects on people's working models of social relationships, as Cicchetti, Toth, and Lynch (1995) suggest may be the case? The research question is not an easy one to tackle, if only because longitudinal data extending from the initial risk experience to the acquisition of later psychopathology is required as a minimum. Only a few such studies have been published. Chase–Lansdale, Cherlin, and Kiernan (1995), using data from the British National Child Development Study (NCDS), showed that the effects of parental divorce during childhood and adolescence on the mental health of the same individuals at age 23 operated indirectly via greater emotional difficulties, lower levels of school achievement, and family economic status at age 16. Kessler and Magee (1994) used data from a two-wave longitudinal study in the United States to examine the effects of childhood family violence on recurrent depression in adult life. The findings showed that the mediation lay in the effects of childhood violence in predisposing to chronic adult interpersonal stress. Both sets of findings are informative but, once more, the designs could not differentiate between genetic and environmental mediation.

Shared and nonshared environmental effects

Finally, genetic data have been crucially important in showing that nonshared environmental effects predominate over shared effects (Plomin & Daniels, 1987). The finding is likely to be valid but it needs to be noted that estimates of nonshared effects include measurement error and, therefore, tend to overestimate that form of environmental influence. What the finding means is that environmental influences tend to operate differentially on each child in the family in a way that serves to make siblings different rather than similar. The most obvious way in which nonshared effects come about is when children have different experiences outside the family—in school, in the peer group, or in the community. Thus, this might come about because one child is mugged on the way to school, or has a stressful admission to hospital, or becomes a member of a delinquent peer group whereas his brothers and sister do not. A second, rather different, way in which nonshared environmental effects may come about is through the differential *impact* of what, on the face of it, are family-wide experiences. For example, when parents are depressed and generally irritable, it is quite common for them to focus their negative feelings on one particular child in the family, a form of focused scapegoating. For example, in our study of families with a mentally ill parent (Rutter, 1990b), we looked at the extent to which parental criticism and hostility were related to the children's temperamental characteristics. High levels of parental criticism were most likely to be focused on children with difficult temperaments.

By contrast, shared environmental effects arise when a family-wide influence impinges in much the same way on all children in the same family. On the face of it, one might suppose that this would occur with respect to events like death of a parent or experiences such a overcrowding in the home. It is important to note, however, that what the data show is that shared *effects* tend to be minor and that is not the same thing at all as saying that shared influences are unimportant. The difference arises because the children do not re-

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spond in the same way to the same experience. Whether or not children are affected adversely by parental death or overcrowding will depend on their age at the time, their temperamental features, the way the parents deal with the matter, and so forth.

The lesson, therefore, is not that we should ignore family-wide influences but, rather, that we should use sib–sib comparisons to understand better why such experiences do operate in a differential fashion (Richters & Weintraub, 1990). This may come about because of differences between the children in their involvement in the risk experience. Radke–Yarrow and her colleagues (Radke–Yarrow, Richters, & Wilson, 1988) showed that some depressed mothers tended to seek comfort with their daughters and Hetherington (1989) noted that children varied in the extent to which they got drawn into family conflict and quarrels. This seems to matter. Thus, Reiss et al. (1995) found that although parental conflict/negativity accounted for over half the variance in children's antisocial behavior, the effects were child specific. That is, the risks arose through negative feelings in the parent that were focused on one particular child. Indeed, the more negativity that was aimed at the sibling, the lower the risk for antisocial behavior in the child not involved in the discord. The findings did not differentiate between genetic and environmental mediation and, because the data were cross-sectional, the direction of effect remains uncertain. Still, the findings do point to the need to study the differential impact of psychosocial adversity and stress in greater detail. The differential impact may also come about because children process their experiences in different ways.

Contrast and assimilation effects

A further sort of environmental effects arises through another form of gene–environment interplay, this time operating in the same generation (Eaves, 1976).[4] That is, one child's genotype shapes the environment of other children in the same family through contrast or assimilation effects. Contrast effects may arise, for example, through one child's dominance causing a sibling to become more submissive (or vice versa). Assimilation represents the opposite process by which sibling interaction brings the pairs' behavior closer together. For example, cooperative behavior between MZ twins represents something of this kind (Segal, 1984), and perhaps so do the joint delinquent activities of brothers (Rowe, Rodgers, & Meseck–Bushey, 1992). That is, the interaction between the siblings may serve to either exaggerate or reduce initial differences between the children. For example, that could be the case with respect to the personality characteristic of extraversion where the within-pair correlation for DZ twins is much below half that for MZ twins. The same has been found with hyperactivity, especially in boys (Silberg et al., 1996b). Equally, however, this could come about because of rating biases (i.e., parents focus too much on the differences between twins rather than making ratings of behavior in relation to children in general).

Differential treatment of children by parents

Contrasts between siblings may also arise as a result of differential treatment by parents. Daniels and Plomin (1985) developed a measure to tap the extent to which there is differential parental interactions with the children, and Dunn and Plomin (1990) suggested that it may be more important for children that they tend to be treated less well than their siblings than that the home as a whole tends to have rather a negative ethos. This has not proved an easy notion to investigate and the importance of this effect remains to be determined. Finally, nonshared environmental effects may derive from individual differences in people's susceptibility to psychosocial hazards (person–environment interactions—see below).

4. Assortative mating provides a further example of *r*G–E in the sense that the genotype of one partner may play a role in the selection of the parenting environment provided by the other (see Rice et al., 1978; Heath et al., 1985). Assortment may also be relevant for both the marital relationship (Houts, Robins, & Huston, 1996) and the persistence of personality characteristics in the individual partners (Caspi & Herbener, 1993).

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"Chance" effects

Traditionally, it has usually been assumed that effects have to be either genetic or environmental. Various researchers (e.g., Goodman, 1991; Molenaar, Boomsma, & Dolan, 1993) have pointed out, however, that because biological processes operate in a probabilistic fashion, chance also plays a role. Thus, in females, one of their two X chromosomes is always inactivated but it seems that which one it is that is inactivated is randomly determined. Similarly, in the Kartagener syndrome, whether the viscera are in the usual place or right to left inverted seems random. Of course, it is never possible to be entirely sure that there is not some unknown environmental factor that is bringing this about, but the finding that the occurrence is roughly 50–50 suggests chance operation. The mechanisms operative in purely chance phenomena are not open to investigation.[5] Nevertheless, there are nongenetic effects that are not attributable to specific environments that warrant attention. For example, the rate of congenital anomalies rises with maternal age (presumably as a consequence of the eggs being older and therefore of "lower" quality). The role of probabilistic imperfections in the development of psychopathology can be examined through the study of congenital anomalies, or of dermatoglyphic patterns—focusing on differences within MZ pairs.

It is clear then that environmental effects may reflect nature–nurture interplay deriving from either gene–environment correlations or gene–environment interactions (Eaves et al., 1977). The research goal has to be that of understanding how these person–environment interplay mechanisms are involved in the proximal processes leading to disorder. In considering these in more detail, most of the evidence that we will cite refers to person–environment interplay and not gene–environment interplay as such. The difference is an important one because persons are not synonymous with genes, because risk and protective mechanisms involve person characteristics, and because person characteristics are influenced by both genes and environment. It is not of much help to know that there is some form of gene–environment interplay unless one also knows how that is manifest in the functioning of the individual. That is where person–environment interplay studies are informative. They provide crucial signposts to the sort of person characteristics that seem to play a role and which might constitute the route by which genetic effects operate. In other words, they provide clues as to the possible attributes for which genes might code (through their gene products). It is clearly essential to move on to the next step of examining person–environment correlations and interactions within a genetically sensitive design in order to determine how the genetic effects are operating. That remains a task for the future but we will make a few suggestions on possible strategies.

Research designs to investigate environmental risk mediation

Before doing that, it is necessary to pause for a moment to consider what is needed to delineate more clearly how environmental factors operate. Just as it was important to move on from the finding that genetic factors play a role in the liability to psychopathology to the more focused question on the genetic routes by which liability comes about, parallel questions have to be asked about the environment. The well documented examples in medicine and biology of gene–environment correlations and interactions nearly all refer to the interplay between quite specific genetic effects and quite specific environmental circumstances. There is not a lot to be gained by "black box" analyses of the interplay between genes and environments; rather, it is necessary to test specific hypotheses about particular effects (Eaves et al., 1977; Kendler & Eaves, 1986; Rutter & Pickles, 1991). But for that to be possible, it will be necessary to have rather better data than we do at the moment on environmental effects.

For obvious reasons, the use of genetically sensitive designs (such as twin, adoptee, and

5. That is not entirely true in that it is possible to determine the genetic mechanism involved in the random allocation process (see Lyon, 1996, on the X chromosome inactivation effect).

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blended family studies) constitutes one essential strategy (see Heath, Kendler, Eaves, & Markell, 1985, for a discussion of the relative power of different genetic designs). The study of the characteristics of the families of adoptees and psychopathology in the adopted children constitutes a powerful strategy. It is desirable to have information on the biological parents because of the need to take into account possible selective placement. The privacy rules in most countries make it difficult, if not impossible, to employ complete adoptee designs. The rapidly diminishing rate of adoption of infants means, also, that adopted children nowadays constitute a much more atypical group than they did in the past. Also, restrictions on the kinds of people who are accepted as adopting parents means that there is likely to be a more limited range of some types of high risk environments that are relevant for the development of psychopathology. Nevertheless, the study of adoptees constitutes a good design for the study of environmental effects (Cadoret, Yates, Troughton, Woodworth, & Stewart, 1995; Plomin et al., 1988).

Extended twin-family designs provide another strategy and a rather different set of strengths and weaknesses (Kendler et al., 1996; Meyer et al., 1997). Specific environmental effects can be assessed through the examination of within-pair differences in MZ pairs. Shared environmental effects can be examined by introducing measures of the postulated environmental factor into a multivariate model that takes into account the correlation between the phenotypes of parent and child, when assessed for a comparable age period. Using this approach, Meyer et al. (1997) were able to show that, at least in their relatively low-risk sample, the low correlation between overall family discord and conduct disorder in the child was entirely a function of genetic factors. By contrast, there was some environmental mediation associated with a child-focused lack of family adaptability and cohesiveness. Kendler et al. (1996) showed an environmental effect of childhood parental loss on alcoholism in women. The strength of this approach is that it takes adequate account of the role of genetic factors operating on the phenotypes of parent and child when examining the role of environmental factors. It has three main limitations, however. First, it will underestimate environmental effects that are brought about by a genetically influenced environmental factor because the causal path is still environmental even though it is genetically "driven." Second, it assesses only shared environmental effects (parental loss and family discord are shared as measured but may produce nonshared effects because they impinge differently on different children). Third, no account is taken of genetic variations in susceptibility to the environmental risk factor. To deal with these issues, it will be necessary to combine the strategy with other research designs.

Although the extended twin-family design constitutes a potentially powerful research strategy for the study of environmental risks, its strength is crucially dependent on good measurement of the postulated environment risk factors, and on the use of high risk samples where the effects are likely to be seen. As noted below, nested designs may be advantageous for this purpose to obtain more discriminating measures on crucial subgroups.

Developmentalists sometimes express concern that genetic findings are based on the highly atypical populations of adoptees and twins (Baumrind, 1993; Jackson, 1993). Although these groups are not as unusual as sometimes argued, there certainly is a need to use designs that involve more ordinary populations. Given the unfortunately very high rate of divorce and separation in modern day societies, blended families provide just such an opportunity. Reiss et al. (1995) have pioneered this approach. The genetic control is provided by the difference in level of genetic similarity (within the same families) between genetically unrelated siblings deriving from the step-parents' previous marriages, half-siblings, and full siblings. Multivariate analyses allow the partitioning of the variance into genetic and environmental effects, as with twin and adoptee designs, and it is readily possible to incorporate measures of the hypothesized environmental risk variables (see Pike, McGuire, Hetherington, Reiss, & Plomin, in press). Nevertheless, there is the inevitable complication that the environments will not

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be randomly distributed in relation to the genes.

One of the possible disadvantages of most twin and adoptee studies is that they are based on samples that are not particularly high risk and require large samples for the multivariate analyses needed. One consequence of the large sample size is that the measures of environmental risk factors are necessarily somewhat crude and undiscriminating. The reliance on general population samples also means that the proportion of subjects showing overt psychopathology will usually be quite small. Most analyses, therefore, rely on the study of variations within the normal range. The findings may not necessarily be the same as those that apply to overt disorder or to high risk environments. One good solution lies in the use of nested designs in which much more intensive, detailed, and discriminating measures are applied to the key representative subgroups in the population concerned, focusing on those with and without the psychopathology under study. For this strategy to be effective, it is, of course, crucial that the intensive measures map on to the cruder measures available in the total population and that the sampling allow analyses to go from the subgroups to the total population and back again.

In addition, there are several nongenetic designs that provide a means of isolating the effects of environmental influences. Five general strategies warrant mention.

First, there is the natural experiment of adoption of children into ordinary well-functioning families, who had spent their first few years in extremely adverse conditions. The degree of recovery following removal to a normal environment provides an index of the extent to which the initial deficit was a function of the environmental conditions prior to adoption. The degree to which the deficit persists also provides an index of the continuing effects of the early adversities, provided that a dose–response relationship with environmental conditions can be demonstrated. Studies of the children adopted into well-functioning families in the United Kingdom and North America after appalling psychosocial and nutritional privation in Romania constitute an example of this strategy (Rutter & ERA Study Team, 1997).

A somewhat comparable strategy, but one that focuses on group differences, rather than intraindividual change, is provided by migration studies. For example, Marmot and Syme (1976) showed that, among men of Japanese ancestry, there was an unusually low rate of coronary artery disease in those living in Japan but a higher rate in those living in California. This seemed to be a function of acculturation to Western styles of living. If disease rates change when populations move from one environment to another, a major cause of the disease must reside in the environment or life-style of the population concerned. Conversely, the finding that diabetes mellitus with insulin resistance is very common in South Asians regardless of where they are living suggests that the explanation lies in some constitutional variable (in their case, associated with a tendency to deposit fat around the waist) rather than environmental circumstances (although excessive calorie intake and lack of exercise may constitute contributing factors). The psychopathological example of the use of this strategy is provided by investigations of the reasons why schizophrenia is increased among Afro-Caribbeans living in the United Kingdom whereas the rate of schizophrenia is not increased in the Caribbean itself (Castle, Wessely, Der, & Murray, 1991; Van Os, Castle, Takei, Der, & Murray, 1996). The implication here is that there is something about patterns of life in this country that carries a particular risk for Afro-Caribbeans—either because they are constitutionally more vulnerable or because the environmental stressors impinge on them to a much greater extent than they do on the indigenous white population.

A further set of designs is provided by the study of group differences that cannot plausibly be attributed to genetic factors. For example, that applies to major changes in levels of psychopathology over relatively short periods of time (Rutter & Smith, 1995). Thus, this situation is provided by the rise in suicide rates and crime over the last half century in most industrialized countries. The leverage in the study of causal questions has to be provided by group differences over the same time period in possible causal factors. For example,

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attention may be focused on the fact that the rise in suicide rates applies to younger age groups but not older ones, and applies to young males but not young females (Rutter & Smith, 1995). Similarly, a contrast may be made between France, where the suicide rate in young males has gone up, and Germany, where it has not. For obvious reasons, the study of causal influences is much assisted if the secular trends can be examined over time periods in which rates of psychopathology have gone down as well as up. The research strategy undoubtedly has a potential but it has yet to be explored. Inevitably, however, there are difficulties in moving from group associations to individual risk processes.

A second example of capitalizing on a difference that could not be genetic is the contrast between twins and singletons, in which impaired language development is more common in the former (Rutter & Redshaw, 1991). The cause for the effect on language is likely to lie either in obstetric factors (which are much commoner in twins) or in postnatal differences in patterns of family interaction (which also differ between twins and singletons). The test of the causal hypothesis lies in determining whether the hypothesized environmental risks that differentiate the two groups also differentiate within groups, according to the dependent variable of language.

Another variant of the same strategy is provided by a focus on the effects of schools, as an example of a nonfamilial environment. The test of the environmental effects is provided by determining whether there are systematic associations between characteristics of the school as a social and educational environment and the behavior and attainments of the pupils at the time of leaving the school, after taking into account variations between schools in the characteristics of the children at the time of intake (Maughan, 1994; Mortimore, 1995). A somewhat similar tactic to that used with schools may be employed with the study of peer group influences by examining changes in the similarity of friends over time (Rowe, Woulbroun, & Gulley, 1994). Convergence in behavioral or attitudinal characteristics over time suggests a peer influence. Of course, people are likely to choose peer groups that fit in with their own interests and it is crucial that analyses separate the effects of peer selection and peer influence; pooling data across studies, the findings suggest that both effects are operative.

Finally, environmental effects may be examined by the study of within-individual change in relation to defined and measured environmental characteristics (Rutter, 1994a). The causal test lies in the combination of evidence that the changes in behavior over time are *not* a function of the individual's prior behavioral characteristics and the evidence that the changes *are* systematically associated (preferably in a dose–response fashion) with changes in the environment. In each case it is necessary to check that the effect is not mediated by some third variable (see Baron & Kenny, 1986) and that the causal arrow runs from the environment to the child and not the other way around (see Bell & Chapman, 1986; Russell & Russell, 1992). Provided that the statistical analyses take proper account of measurement error (especially biases in such error) the design provides a good test. It has been used with effect to examine the effects of unemployment on delinquency (Farrington, 1995b) and on emotional disturbance (Kessler, Turner, & House, 1987), the effects of moving away from inner London on delinquency (Farrington, 1995b), and the effects of a harmonious marriage in reducing the likelihood of a continuation of antisocial behavior and improving social functioning in individuals who had shown previous conduct disturbance (Quinton et al., 1993; Sampson & Laub, 1993).

As the examples given indicate, although there are effective studies demonstrating environmental effects on psychopathology, they are limited in number and cover only a small range of environmental risk factors and a small range of psychopathology.

Proximal Processes in Person–Environment Interplay

Person–environment interactions

As already discussed, there are many examples in medicine and biology of differential

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responses to experiences.[6] The example of hay fever well illustrates the phenomenon. Pollens in the atmosphere, representing allergens, become pervasive during the springtime and early summer and are known to cause hay fever. However, only some people are susceptible to this allergic effect. The individual differences in susceptibility to pollens are genetically influenced to a considerable extent but they are also affected by other variables, such as infections. There are many examples in the literature on psychopathology of individual differences in responses to risk environment but much less is known on the individual characteristics, or their origin, that mediate the variations in vulnerability. Moreover, many of the findings deal with variables that are some way from the proximal processes involved in reactivity to environmental risk experiences. Thus, reference has already been made to Rodgers' (1990) finding that vulnerability from childhood, as evidenced in a combination of emotional difficulties and adverse experiences, was associated with an increased likelihood of the development of psychiatric symptoms following experience of a stressor in adult life. Clearly, there is something to be explained but what is it about the individual in adult life that is associated with increased susceptibility and does this derive from genetic or environmental factors?

Similarly, Vorria et al. (1997a, 1997b) found that institution-reared children in Greece showed a marked elevation of emotional/behavioral disturbance (as assessed by parent and teacher ratings, and also observational measures) as compared with a general population comparison group. However, within the institutional group, this high rate of disturbance was *not* evident in the children admitted into residential care as a result of family poverty or parental sickness or death. The design was not such as to be able to differentiate between genetic and environmental origins of this resilience in the face of what for other children proved to be a risk experience. Ormel, Stewart, and Sanderman (1989) came nearer to proximal processes in their demonstration that adults showing high neuroticism measured six years prior to the first measurement of life situation change were much more likely than those low on neuroticism to exhibit an increase in psychological distress following a life situation change. Because the data referred to a change over time, it can be safely inferred that the differences did indeed reflect individual variations in reactivity. The same was found for low self-esteem, but it fell just short of statistical significance, although the effect was quite a large one by any reckoning—serving as a reminder of the relative statistical insensitivity of most analyses for interaction effects—especially when dealing with changes over time.

Ormel et al.'s (1989) design was not appropriate to separate genetic and environmental effects but other studies have shown both the relatively high heritability of neuroticism and its role in liability to depression (Kendler et al., 1993b). In the absence of a direct measure of genetic liability (as would be provided by molecular genetic findings), genetic liability has to be inferred indirectly. Kendler, Kessler et al. (1995) did this in a twin study by assuming that genetic liability was greatest when there was an affected MZ co-twin and lowest when there was an unaffected MZ co-twin. Intermediate values of genetic liability were provided by an affected DZ co-twin and an unaffected DZ co-twin. Their data showed that the likelihood of an onset of a major depressive disorder following a stressful life event was greater for individuals with an inferred high genetic liability than those with a low one.

Adoptee studies probably provide a better research leverage on the question. Attention, however, has to be paid, not to proportion of variance explained (which is bound to be low because the adoptee strategy is specifically *designed* to remove the overlap between genetic risk and environmental risk) but, rather, to the relative risk in relation to the situation for individuals who lack both genetic and en-

6. In this section, we focus on psychopathology-specific interactions. It is important to note, however, that there are very important genetically influenced, or determined, general person characteristics such as sex or maturational level that are known to influence reactivity to the environment. These are outside the scope of this paper but constitute important topics in their own right.

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vironmental risk factors. Bohman (1996) used this design with a study of petty criminality. Only just less than 3% of individuals without a criminal biological parent and without major risk experiences in the adoptive family showed petty criminality. The risk doubled with the occurrence of environmental risk in the absence of genetic risk, went up to 12% with genetic risk in the absence of environmental risk, but rose to 40% when both genetic and environmental risk were present. The findings show, therefore, that it is individuals at genetic risk who showed the greatest vulnerability to environmental adversities. The same type of gene–environment interaction has also been evident in other adoptee studies (Cadoret, Cain, & Crowe, 1983; Cadoret et al., 1995; Hutchings & Mednick, 1975).

One of the few gene–environment interactions detected in large scale epidemiological studies is that with marital status found by Heath, Jardine, and Martin (1989). Genetic effects accounted for only 31% of the variance in alcohol consumption of married respondents but 60% of the variance of unmarried respondents. The mechanism that this reflects is uncertain but it may be a consequence of different patterns of drinking when married and, hence, the possibly different meaning of high and low levels of consumption.

Although the extensive evidence on individual differences in susceptibility to risk environments strongly suggests the likely existence of important person–environment interactions, there is a paucity of evidence on their operation. Three challenges need to be met. First, there is a need for better delineation of the genetic risk. The existence of, say, criminality in a biological parent is not in itself very informative because it says nothing about the route by which the genetic risk operates. What are needed are twin and adoptee designs in which genetic factors can be explicitly connected with individual traits that are much closer to the proximal processes likely to be involved in person–environment interactions. Obviously, molecular genetics identification of the specific genes involved would be even more helpful (and, in the long run, essential).

A parallel need is for a much better conceptualization and delineation of the environmental risk factors that might be important in such interactions. Such measures need to be child focused in view of the evidence of the importance of nonshared environmental effects. Also, such measures need to deal with microenvironment features that are likely to play a major role in the key proximal processes. Broad variables such as social class, or overcrowding, may be useful as risk indicators but they are of extremely limited value for the study of risk processes. The third need is for designs that focus explicitly on hypotheses concerned with the specific ways in which the interaction processes are thought to work, and focus also on the subgroups in which they are thought to be operative. Both Kendler and Eaves (1986) and Rutter and Pickles (1991) have made explicit suggestions in that connection. It is crucial to appreciate that the way forward does not lie simply in the detection of statistical person–environment or gene–environment effects. That is because the biological processes underlying statistical interactions are multiple and require different approaches for their detection (Kendler & Eaves, 1986; Mather & Jinks, 1982; Rutter, 1983; Rutter & Pickles, 1991), because most known interaction processes apply to specific subgroups and not to the population as a whole (Rutter & Pickles, 1991), because statistical interaction effects require variation in *both* the genetic and environmental variables and this will not apply to population wide risks to which only those with a genetic risk are vulnerable (as with pollens and hay fever), and because the usual total population multivariate statistics to detect interactions have weak power (Wahlsten, 1990). It should be added, too, that care needs to be taken to differentiate between the strength of effects at the individual level in people where the processes operate and the population-wide effects as measured by proportion of variance explained. The latter will always give a most misleading impression of the former if the individuals involved in the process in question constitute a small proportion of the total population (Rutter, 1987).

Evocative person–environment correlations

Evocative correlations refer to the situation in which one person's characteristics serve to

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elicit particular responses in other people. There is widespread evidence of the operation of this phenomenon (Engfer, Walper, & Rutter, 1994). Thus, the popularity of children is affected, not just by their behavior, but also by their physical attractiveness, name, and reputation. Such correlations operate throughout the span of development and a variety of different research methods have been used to investigate them. The phenomenon is first evident in the womb. Thus, it is well known that twins tend to have a shorter period of gestation than singletons, and, indeed, it is more adaptive for them to do so (Rutter & Redshaw, 1991). Also, as shown, for example, by the findings on Down syndrome, genetically abnormal fetuses may be associated with an increased level of obstetric complications (Rutter et al., in press).

Several forms of experimental design have been used to test for evocative person–environment correlations. For example, Brunk and Henggeler (1984) trained children to behave in anxious–dependent, or oppositional ways. The children were then placed in situations in which adults were expected to engage them in particular tasks. The results showed that the adults' behavior, as shown for example in disciplinary acts, was much influenced by the behavior of the child. For example, even when the children were being compliant, those behaving oppositionally were much more likely to be subject to discipline—indicating that even over very short periods of time "reputations" (meaning adults' views about the children) begin to be operative.

The effects of child characteristics on parental behavior has also been examined using the strategy of comparing mother–child interactions between groups in which the child did have psychopathology and groups where the child did not. In each case, mothers interact with their own child, somebody else's child of similar characteristics, and somebody else's child of dissimilar characteristics. In this way, it is straightforward to separate the effects of the mother from the effects of the child, together with the consequences of the child being their own or someone else's. This strategy was first used with autistic children (Gardner, 1977) and was later used by Anderson, Lytton, and Romney (1986) to examine the effects of conduct disorder in the child on maternal negative behavior. The findings showed a combination of both child effects and maternal effects.

Naturalistic longitudinal designs have also shown the effects of child behavior on parenting and patterns of family interaction (see e.g., Dodge, Pettit, McClaskey, & Brown, 1986; Lee & Bates, 1985; Patterson, 1982).

Although there is good evidence that evocative correlations occur, less is known about their consequences. Martin, Maccoby, and Jacklin (1981), using a longitudinal design during the preschool years, were able to show the operation of a vicious cycle in boys (although curiously not in girls) in which oppositional behavior tended to lead parents to back away from confrontations and, when they did this, this carried with it an increased likelihood that the oppositional behavior would persist over time. It is possible that gender differences in patterns of evocative correlation may play a role in the development of gender differences in psychopathology.

There are three main research needs in relation to the phenomenon of evocative correlations. First, better data are needed on the extent to which they operate over time. Almost all the well controlled studies (for understandable reasons) have focused on immediate responses rather than more persisting patterns of interaction. Longitudinal studies are needed to examine the importance of effects over time. Second, next to nothing is known about the role of genetic and environmental factors in such evocative correlations. In that the effects are apparent in interactions involving biologically unrelated individuals (such as the peer group), it is clear that at least some of the effects stem from behavior as shown, regardless of its origins. On the other hand, if one is to gain an understanding of the role of such correlations in the intergenerational transmission of psychopathology, it is crucial to examine the relative role of genetic and environmental influences. The study of evocative correlations within a longitudinal twin design would enable that to be done. The third need is to examine the consequences. It is one thing to know that children influence the reactions of other people to them but it is another

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thing to determine whether that matters much with respect to the effects of those reactions on the persistence, or otherwise, of their own behavior. The Martin et al. (1981) study suggests that this may be an important process, as part of a circular reaction, but the data on this are sparse indeed.

Active person–environment correlations

The third type of person–environment correlation is that called "active"—meaning the process by which individuals select and shape their experiences. It differs from evocative correlations in the one crucial respect that evocative correlations concern dyadic (or polyadic) interactions in which the subject is an active participant and in which the experiences concern reactions of other people to the subject's characteristics. By contrast, active correlations concern the selection, shaping and creation of environments that may involve things or people but in which the environment concerns noninteractive properties. The example given earlier of children with reading difficulties opting out of reading opportunities provides an example of that kind. In practice, of course, many person–environment correlations involve a complex mixture of the two. Their separation requires a detailed study of the proximal processes involved. For example, to what extent do some children get more exposure to reading because it is rewarding for other people to listen to them read (an evocative correlation) and to what extent is it due to their seeking out books at the library or asking other people to listen to them read (an active correlation)? The extent to which this difference matters will depend on the specifics. The important issue with respect to evocative correlations is that breaking the chain of effects will depend on what other people do, whereas the main focus, if the correlations are active, needs to be on the child. Plomin (1994b) has described the rather different forms of multivariate analyses needed for the detection of passive and active/reactive correlations.

The importance of people's effects on their environment is most clearly brought out by the findings from long-term longitudinal studies. Thus, Robins (1966), in her follow-up into middle life of children who had attended a child guidance clinic, found that antisocial boys experienced far more adult psychosocial stressors and adversity than did control boys. They were more likely to be divorced, and especially to have multiple divorces, to be unemployed, to have at least 10 job changes in 10 years, to be in an unskilled or semiskilled job, and to be practically without friends. Similarly, Champion, Goodall, and Rutter (1995), in their follow-up of 10-year-olds in inner London, found that those who had shown behavioral difficulties in middle childhood were twice as likely as other children to experience severe negative life events and long-term difficulties some two decades later. Ormel and Wohlfarth (1991) found that long-term difficulties and negative life events could be predicted to some extent from neuroticism levels measured 6 years earlier. Quinton et al. (1993) showed that individuals who showed conduct disturbance in childhood were much more likely than other people to have a marital partner who also showed antisocial behavior. Apart from the effects of antisocial behavior, the tendency for like to marry like is most striking with respect to intelligence and educational attainment (Mare, 1991; Phillips, Fulker, Carey, & Nagoshi, 1988). Low educational attainment is also associated with a substantial increase in the likelihood of a teenage pregnancy (Kiernan, 1995).

There are two ways of viewing these findings, both of which have validity. On the one hand, the increase in psychosocial adversities in adult life that are associated with conduct disorder in childhood can be seen as a reflection of a continuing personality disorder (Robins, 1966). In other words, the effect of the childhood behavior lies in its continuity with adult behavior and it is the adult behavior that brings about the stress and adversity. This is evident, for example, in the effects of conduct disorder on divorce, unemployment, lack of friends, and a discordant marriage with a deviant spouse. On the other hand, even though these experiences are a consequence of the person's disordered behavior, they nevertheless constitute negative experiences that are

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likely to have adverse effects on their own behavior and on its persistence over time. Indeed, as already noted, investigations of intraindividual change in relation to these life experiences (such as unemployment or marital disorder) attest to the importance of the impact of these experiences.

Where we have a severe lack of knowledge, however, is on the proximal processes involved in these person–environment correlations. For example, the tendency for antisocial people to marry other antisocial people could come about in several quite different ways (Eaves, 1979). Whom someone marries is likely to be a function of the person's peer group. For obvious reasons, partners are likely to come from the people seen socially. Pickles and Rutter (1991) showed that, at least for children from a disadvantaged background, this is influenced, too, by the age of cohabitation or marriage. A partnership with a deviant spouse was most likely with those formed in the teens when the young people's social group was largely made up of similar people. Elder (1986) similarly showed that, for disadvantaged youths, postponement of marriage tended to increase the heterogeneity of the pool of potential partners and, in some circumstances, this may be advantageous. Quinton et al. (1993) also showed that the tendency to land up with a deviant spouse was greater when the young people showed a lack of planning in relation to key life transitions, decisions, and challenges. The assortment, therefore, arose from a failure to choose and not from deliberate selection. A third mechanism that needs consideration is that whom a person marries is likely to be affected by their "value" in the marriage market, as it were. Again, the assortment according to antisocial behavior may thereby come about because of a shortage of willing partners rather than because people actually sought out people of similar characteristics. Although there is a substantial literature on the occurrence of assortative mating, there has been very little study of the proximal processes by which this comes about. Delineation of the mechanisms is important in its own right but also it is crucial for an understanding of the interplay between genes and environment with respect to different forms of psychopathology. For example, are the effects on marital assortment greater in the case of antisocial behavior associated with hyperactivity (where the genetic component is strong) than they are for adolescent onset unaccompanied by hyperactivity and inattention (where the genetic component is probably much weaker)?

Two rather different sorts of design are needed to investigate the mechanisms. The respective importance of genetic and environmental factors may be investigated through the study of late adolescent and early adult friendship patterns and partner choice in longitudinal studies of MZ and DZ twin pairs. The possible behavioral mediators of the effects may be examined in the same design. Thus, multivariate analyses focusing on across-twin, across-trait correlations can be used to determine whether the assortment derives from the antisocial behavior as such, or from some genetically associated other characteristic. Put in simplistic fashion, is partnership with a deviant spouse more likely to be concordant in MZ pairs discordant for antisocial behavior or DZ pairs concordant for the same behavior? The other sort of study required is one that looks in some detail at the social relationships (both same sex and opposite sex) in the late adolescent years of high risk and low risk populations in order to determine how pairing comes about and what factors in the individual and in the person's social situation influence the social patterns.

Closely comparable issues arise with respect to the associations between child behavior and life events and experiences in adult life. The study of proximal processes in relation to this association has scarcely begun; however, Champion and her colleagues (Champion et al., 1995; Rutter, Champion, Quinton, Maughan, & Pickles, 1995) found that, as with marital assortment, the characteristic of planning seemed influential. Individuals who lacked planning showed twice as many long-term difficulties in adult life as those who did exhibit a planning tendency. The finding indicates that the answer is likely to lie, at least in part, in some aspect of the individuals' behavior and style of coping with their life circumstances. So far, however, the evidence is re-

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stricted to a rather distal measure of planning, rather than to findings of how actual life circumstances are dealt with. Clearly, this constitutes an area of rich potential.

Conclusions

Although there is a great deal of evidence indicating that there is a rich and varied interplay between persons and their environments, and every reason to suppose that this involves gene–environment correlations and interactions, surprisingly little is known about the causal mechanisms involved. We have approached the topic first in terms of implications from general principles of development, then from what is known about genetic and environmental effects, and, finally, in terms of person–environment interplay with respect to their implications for the research agenda into the ways in which genes and environments work together in relation to the development of psychopathology and its persistence or desistance over time. Despite the fact that huge areas of ignorance remain, the research tools are available to answer most of the key questions and we have sought to provide some research pointers on possible ways ahead.

With respect to the research needs on genetic effects, both quantitative and molecular genetic studies, using a range of research strategies, are required. Previous research has done much to document the fact that genetic influences are ubiquitous in their effects, and has been informative on the quantification of such effects in relation to different forms of psychopathology; however, we are only just beginning to be able to answer the crucial question of *how* genes work. The need, therefore, now is to pose the basic question of what genes code for, bearing in mind a range of different alternatives including the possibility that they code for a disease category as such (or, rather, the somatic abnormality that underlies the disease—as in Mendelian disorders); for a dimensional liability to a more broadly defined disorder; for a range of different risk dimensions that are not synonymous with disorder, subclinical or otherwise, but which are involved in the various causal routes to disorder; and for types of susceptibility to particular environmental hazards.

The situation on the research needs regarding environmental effects is somewhat comparable. There is good evidence of the importance of environmental influences but there is little specific knowledge on how they operate. A range of different research strategies are required that have the power to differentiate environmental effects on people, from people's effects on their environments, and from genetic influences on psychopathology. The key basic questions include, Which environmental features have which environmentally mediated effects? Do the effects of risk environments on *levels* of psychopathology differ from those on individual differences in psychopathology? What are the effects of environmental risk factors on the organism, and how are the effects carried forward in time? And what are the causes of individual variations in susceptibility to particular environmental hazards?

As we have sought to emphasize throughout this paper, the time is ripe for a bringing together of developmental, genetic, and environmental research strategies in order to focus on the proximal processes involved in the interplay between genes and environment as they apply to the causal mechanisms involved in the initiating, persistence, and desistence of psychopathology. A range of different research strategies using genetic and longitudinal designs are needed, in which the methods are planned to test competing hypotheses on the mechanisms that may be involved with respect to gene–environment interactions, passive gene–environment correlations, reactive person–environment correlations, and active person–environment correlations.

References

Anastasi, A. (1958). Heredity, environment, and the question "How?". *Psychological Review, 75,* 81–95.

Anderson, K. E., Lytton, H., & Romney, D. M. (1986). Mothers' interactions with normal and conduct-disordered boys: Who affects whom? *Developmental Psychology, 22,* 604–609.

Baron, R. M., & Kenny, D. A. (1986). The moderator–mediator variable distinction in social psychological

https://doi.org/10.1017/S0954579497002083 Published online by Cambridge University Press

research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology, 51,* 1173–1182.

Baumrind, D. (1993). The average expectable environment is not good enough: A response to Scarr. *Child Development, 64,* 1299–1317.

Bell, R. Q., & Chapman, M. (1986). Child effects in studies using experimental or brief longitudinal approaches to socialization. *Developmental Psychology, 22,* 595–603.

Block, J. H., Block, J., & Gjerde, P. F. (1986). The personality of children prior to divorce: A prospective study. *Child Development, 57,* 827–840.

Bock, G. R., & Goode, J. A. (Eds.). (1996). *Genetics of criminal and antisocial behaviour. Ciba Foundation Symposium 194.* Chichester, England, & New York: Wiley.

Bohman, M. (1996). Predisposition to criminality: Swedish adoption studies in retrospect. In G. R. Bock & J. A. Goode (Eds.), *Genetics of criminal and antisocial behaviour. Ciba Foundation Symposium 194* (pp. 99–114). Chichester, England, & New York: Wiley.

Broadhurst, P. L., & Jinks, J. L. (1966). Stability and change in the inheritance of behaviour in rats: A further analysis of statistics from a diallel cross. *Proceedings of the Royal Society of London Series B, 165,* 450–472.

Brody, G. H., Stoneman, Z., Flor, D., McCrary, C., Hastings, L., & Conyers, O. (1994). Financial resources, parent psychological functioning, parent co-caregiving, and early adolescent competence in rural two-parent African-American families [Special issue: Children and poverty]. *Child Development, 65,* 590–605.

Bronfenbrenner, U., & Ceci, S. J. (1994). Nature–nurture reconceptualization in developmental perspective: A bioecological model. *Psychological Review, 101,* 568–586.

Brown, G. W., & Harris, T. O. (1978). *Social origins of depression: A study of psychiatric disorder in women.* London: Tavistock.

Brown, G. W., & Harris, T. O. (1989). *Life events and illness.* New York: Guilford Press.

Brunk, M. A., & Henggeler, S. W. (1984). Child influences on adult controls: An experimental investigation. *Developmental Psychology, 20,* 1074–1081.

Cadoret, R. J., Cain, C. A., & Crowe, R. R. (1983). Evidence for gene–environment interaction in the development of adolescent antisocial behavior. *Behavior Genetics, 13,* 301–310.

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

Caspi, A., & Herbener, E. S. (1993). Marital assortment and phenotypic convergence: Longitudinal evidence. *Social Biology, 40,* 48–60.

Castle, D. J., Wessely, S., Der, G., & Murray, R. M. (1991). The incidence of operationally defined schizophrenia in Camberwell. 1965–84. *British Journal of Psychiatry, 159,* 790–794.

Cattell, R. B. (1963). The interaction of hereditary and environmental influences. *British Journal of Statistical Psychology, 16,* 191–210.

Cavalli–Sforza, L. L., & Feldman, M. W. (1973). Cultural versus biological inheritance: Phenotypic transmission from parents to children (A theory of the effect of parental phenotypes on children's phenotypes). *American Journal of Human Genetics, 25,* 618–637.

Cavalli–Sforza, L. L., & Feldman, M. W. (1981). *Cultural transmission and evolution: A quantitative approach.* Princeton, NJ: Princeton University Press.

Chadwick, D., & Cardew, G. (Eds.). (1996). *Variation in the human genome. Ciba Foundation Symposium 197.* Chichester, England, & New York: Wiley.

Champion, L. A., Goodall, G. M., & Rutter, M. (1995). Behavioural problems in children and stressors in early adult life: A 20-year follow-up of London school children. *Psychological Medicine, 25,* 231–246.

Chase–Lansdale, P., Cherlin, A. J., & Kiernan, K. E. (1995). The long-term effects of parental divorce on the mental health of young adults: A developmental perspective. *Child Development, 66,* 1614–1634.

Cherlin, A. J., Furstenberg, J. F. F., Chase–Lansdale, P. L., Kiernan, K. E., Robins, P. K., Morrison, D. R., & Teitler, J. O. (1991). Longitudinal studies of effects of divorce on children in Great Britain and the United States. *Science, 252,* 1386–1389.

Cicchetti, D. (1984). The emergence of developmental psychopathology. *Child Development, 55,* 1–7.

Cicchetti, D. (1990). A historical perspective on the discipline of developmental psychopathology. In J. Rolf, A. Masten, D. Cicchetti, K. Nuechterlein, & S. Weintraub (Eds.), *Risk and protective factors in the development of psychopathology* (pp. 2–28). New York: Cambridge University Press.

Cicchetti, D., & Cohen, D. J. (Eds.). (1995). *Developmental psychopathology: Vol. 1: Theory and method; Vol. 2: Risk, disorder, and adaptation.* New York: Wiley.

Cicchetti, D., & Lynch, M. (1993). Toward an ecological/transactional model of community violence and child maltreatment. *Psychiatry, 56,* 96–118.

Cicchetti, D., Toth, S. L., & Lynch, M. (1995). Bowlby's dream comes full circle: The application of attachment theory to risk and psychopathology. In T. H. Ollendick & R. J. Prinz (Eds.), *Advances in clinical child psychology* (pp. 1–75). New York & London: Plenum Press.

Cipielewski, J., & Stanovich, K. E. (1992). Predicting growth in reading ability from children's exposure to print. *Journal of Experimental Child Psychology, 54,* 74–89.

Cloninger, C. R., Adolfsson, R., & Svrakic, N. M. (1996). Mapping genes for human personality. *Nature Genetics, 12,* 3–4.

Cohen, S., Tyrrell, D. A. J., & Smith, A. P. (1991). Psychological stress and susceptibility to the common cold. *The New England Journal of Medicine, 325,* 606–612.

Conger, R. D., Conger, K. J., Elder, G. H., Lorenz, F. O., Simons, R. L., & Whitbeck, L. B. (1992). A family process model of economic hardship and adjustment of early adolescent boys. *Child Development, 63,* 526–541.

Daniels, D., & Plomin, R. (1985). Differential experience of siblings in the same family. *Developmental Psychology, 21,* 747–760.

DeMulder, E., & Radke–Yarrow, M. (1991). Attachment with affectively ill and well mothers: Concurrent behavioral correlates. *Development and Psychopathology, 3,* 227–242.

De Sanctis, C. T., Merchant, M., Beier, D. R., Dredge, R. D., Grobholz, J. K., Martin, T. R., Lander, E. S., &

https://doi.org/10.1017/S0954579497002083 Published online by Cambridge University Press

Drazen, J. M. (1995). Quantitative locus analysis of airway hyperresponsiveness in A/J and C57BL/6J mice. *Nature Genetics, 11,* 150–154.

Dodge, K. A., Pettit, G. S., & Bates, J. E. (1994). Socialization mediators of the relation between socioeconomic status and child conduct problems. *Child Development, 65,* 649–665.

Dodge, K. A., Pettit, G. S., Bates, J. E., & Valente, E. (1995). Social information-processing patterns partially mediate the effects of early physical abuse on later conduct problems. *Journal of Abnormal Psychology, 104,* 632–643.

Dodge, K. A., Pettit, G. S., McClaskey, C. L., & Brown, M. (1986). Social competence in children. *Monographs of the Society for Research in Child Development, 51,* (2), Serial No. 213.

Dolan, C. V., & Molenaar, P. C. M. (1995). A note on the scope of developmental behaviour genetics. *International Journal of Behavioral Development, 18,* 749–760.

Downey, G., & Coyne, J. C. (1990). Children of depressed parents: An integrative review. *Psychological Bulletin, 108,* 50–76.

Dunn, J. (1988). *The beginnings of social understanding.* Cambridge, MA: Harvard University Press.

Dunn, J. (1993). *Young children's close relationships: Beyond attachment.* Newbury Park, CA: Sage.

Dunn, J., & Plomin, R. (1990). *Separate lives: Why siblings are so different.* New York: Basic Books.

Eaves, L. J. (1976). A model for sibling effects in man. *Heredity, 40,* 205–214.

Eaves, L. J. (1979). The use of twins in the analysis of assortative mating. *Heredity, 43,* 399–409.

Eaves, L. J., Eysenck, H. J., Martin, N. G., Jardine, R., Heath, A. C., Young, P. A., Feingold, L., & Kendler, K. S. (1989). *Genes, culture and personality.* New York: Academic Press.

Eaves, L. J., Last, K. A., Martin, N. G., & Jinks, J. L. (1977). A progressive approach to non-additivity and genotype–environmental covariance in the analysis of human differences. *British Journal of Mathematical and Statistical Psychology, 30,* 1–42.

Eaves, L. J., Long, J., & Heath, A. C. (1986). A theory of developmental change in quantitative phenotypes applied to cognitive development. *Behavior Genetics, 16,* 143–162.

Eisenberg, L. (1977). Development as a unifying concept in psychiatry. *British Journal of Psychiatry, 131,* 225–237.

Elder, J. G. H. (1986). Military times and turning points in men's lives. *Developmental Psychology, 22,* 233–245.

Elliott, B. J., & Richards, M. P. M. (1991). Children and divorce: Educational performance and behavior before and after parental separation. *International Journal of Law and the Family, 5,* 258–276.

Engel, G. L. (1960). A unified concept of health and disease. *Perspectives in Biology and Medicine, 3,* 459–485.

Engel, G. L. (1978). The biopsychosocial model and the education of health professionals. *Annals of the New York Academy of Sciences, 310,* 169–181.

Engfer, A., Walper, S., & Rutter, M. (1994). Individual characteristics as a force in development. In M. Rutter & D. F. Hay (Eds.), *Development through life: A handbook for clinicians* (pp. 79–111). Oxford, England: Blackwell Scientific.

Farrington, D. P. (1995a). The challenge of teenage antisocial behavior. In M. Rutter (Ed.), *Psychosocial disturbances in young people: Challenges for prevention* (pp. 83–130). New York: Cambridge University Press.

Farrington, D. P. (1995b). The development of offending and antisocial behaviour from childhood: Key findings from the Cambridge Study in Delinquent Development. *Journal of Child Psychology and Psychiatry, 36,* 929–964.

Fergusson, D. M., Horwood, L. J., & Lynskey, M. T. (1992). Family change, parental discord and early offending. *Journal of Child Psychology and Psychiatry, 33,* 1059–1075.

Ferrie, J. E., Shipley, M. J., Marmot, M. G., Stansfeld, S., & Davey–Smith, G. (1995). Health effects of anticipation of job change and non-employment: Longitudinal data from the Whitehall II study. *British Medical Journal, 311,* 1264–1269.

Flint, J., Corley, R., DeFries, J. C., Fulker, D. W., Gray, J. A., Miller, S., & Collins, A. C. (1995). A simple genetic basis for a complex psychological trait in laboratory mice. *Science, 269,* 1432–1435.

Fulker, D. W. (1970). Maternal buffering of rodent genotypic responses to stress: A complex genotype–environment interaction. *Behavior Genetics, 1,* 119–124.

Fulker, D. W., Cherny, S. S., & Cardon, L. R. (1993). Continuity and change in cognitive development. In R. Plomin & G. E. McClearn (Eds.), *Nature, nurture, and psychology* (pp. 77–97). Washington, DC: American Psychological Association.

Gardner, J. (1977). *Three aspects of childhood autism: Mother–child interactions, autonomic responsivity, and cognitive functioning.* Unpublished PhD thesis, University of Leicester, Leicester.

Goodman, R. (1991). Growing together and growing apart: The non-genetic forces on children in the same family. In P. McGuffin & R. Murray (Eds.), *The new genetics of mental illness* (pp. 212–224). Oxford, England: Heinemann Medical.

Gottesman, I. I., & Goldsmith, H. H. (1994). Developmental psychopathology of antisocial behavior: Inserting genes into its ontogenesis and epigenesis. In C. A. Nelson (Ed.), *Threats to optimal development: Integrating biological, psychological, and social risk factors* (pp. 69–104). Hillsdale, NJ: Erlbaum.

Gottlieb, G. (1995). Some conceptual deficiencies in "developmental" behavior genetics. *Human Development, 38,* 131–141.

Gottman, J. M. (Ed.). (1995). *The analysis of change.* Mahwah, NJ: Erlbaum.

Harrington, R. C. (1994). *Depressive disorder in childhood and adolescence.* Chichester, England: Wiley.

Harris, T., Brown, G. W., & Bifulco, A. (1990). Loss of parent in childhood and adult psychiatric disorder: A tentative overall model. *Development and Psychopathology, 2,* 311–327.

Heath, A. C., Jardine, R., & Martin, N. G. (1989). Interactive effects on genotype and social environment on alcohol consumption in female twins. *Journal of Studies on Alcohol, 50,* 38–48.

Heath, A. C., Kendler, K. S., Eaves, L. J., & Markell, D. (1985). The resolution of cultural and biological inheritance: Informativeness of different relationships. *Behavior Genetics, 15,* 439–465.

Hennessey, J. W., & Levine, S. (1979). Stress, arousal, and the pituitary-adrenal system: A psychoendocrine hypothesis. In J. M. Sprague & A. N. Epstein (Eds.),

https://doi.org/10.1017/S0954579497002083 Published online by Cambridge University Press

Progress in psychobiology and physiological psychology (pp. 133–178). New York: Academic Press.

Hetherington, E. M. (1989). Coping with family transitions: Winners, losers, and survivors. *Child Development, 60,* 1–14.

Hinde, R. A. (1987). *Individuals, relationships, and culture.* Cambridge, England: Cambridge University Press.

Hirshfeld, D. R., Rosenbaum, J. F., Biederman, J., Bolduc, E. A., Faraone, S. V., Snidman, N., Reznick, J. S., & Kagan, J. (1992). Stable behavioral inhibition and its association with anxiety disorder. *Journal of the American Academy of Child and Adolescent Psychiatry, 31,* 103–111.

Houts, R. M., Robins, E., & Huston, T. L. (1996). Compatibility and the development of premarital relationships. *Journal of Marriage and the Family, 58,* 7–20.

Hutchings, B., & Mednick, S. A. (1975). Registered criminality in the adoptive and biological parents of registered male criminal adoptees. In R. R. Fieve, D. Rosenthal, & H. Brill (Eds.), *Genetic research in psychiatry* (pp. 105–116). Baltimore, MD: Johns Hopkins University Press.

Imai, M., & Anderson, R. C. (1992). Properties of attention during reading lessons. *Journal of Educational Psychology, 84,* 160–173.

Jackson, J. F. (1993). Human behavioral genetics, Scarr's theory, and her views on interventions: A critical review and commentary on their implications for African American children. *Child Development, 64,* 1318–1332.

Jinks, J. L., & Fulker, D. W. (1970). Comparison of the biometrical genetical, MAVA, and classical approaches to the analysis of human behavior. *Psychological Bulletin, 73,* 311–348.

Johnston, T. D. (1987). The persistence of dichotomies in the study of behavioural development. *Development Review, 7,* 149–182.

Kendler, K. S. (1990). Schizophrenia as a complex phenotype. In K. Berg, N. Retterstol, & S. Refsum (Eds.), *From phenotype to gene in common disorders* (pp. 265–286). Copenhagen, Denmark: Munksgaard.

Kendler, K. S., & Eaves, L. J. (1986). Models for the joint effect of genotype and environment on liability to psychiatric illness. *American Journal of Psychiatry, 143,* 279–289.

Kendler, K. S., Kessler, R. C., Walters, E. E., MacLean, C., Neale, M. C., Heath, A. C., & Eaves, L. J. (1995). Stressful life events, genetic liability, and onset of an episode of major depression in women. *American Journal of Psychiatry, 152,* 833–842.

Kendler, K. S., Neale, M. C., Kessler, R. C., Heath, A. C., & Eaves, L. J. (1993a). A longitudinal twin study of 1-year prevalence of major depression in women. *Archives of General Psychiatry, 50,* 843–852.

Kendler, K. S., Neale, M. C., Kessler, R. C., Heath, A. C., & Eaves, L. J. (1993b). A longitudinal twin study of personality and major depression in women. *Archives of General Psychiatry, 50,* 853–862.

Kendler, K. S., Neale, M. C., Prescott, C. A., Kessler, R. C., Heath, A. C., Corey, L. A., & Eaves, L. J. (1996). Childhood parental loss and alcoholism in women: A causal analysis using a twin-family design. *Psychological Medicine, 26,* 79–95.

Kendler, K. S., Neale, M. C., & Walsh, D. (1995). Evaluating the spectrum concept of schizophrenia in the Roscommon family study. *American Journal of Psychiatry, 152,* 749–754.

Kessler, R. C., & Magee, W. J. (1994). Childhood family violence and adult recurrent depression. *Journal of Health and Social Behavior, 35,* 13–27.

Kessler, R. C., Turner, J. B., & House, J. S. (1987). Intervening processes in the relationship between unemployment and health. *Psychological Medicine, 17,* 949–961.

Kiernan, K. E. (1995). *Transition to parenthood: Young mothers, young fathers—Associated factors and later life experiences.* London: London School of Economics.

Klein, M. H., Kupfer, D. J., & Shea, M. T. (Eds.). (1993). *Personality and depression: A current view.* New York: Guilford Press.

Lahey, B. B., McBurnett, K., Loeber, R., & Hart, E. L. (1995). Psychobiology of conduct disorders. In G. P. Scholevar (Ed.), *Conduct disorders in children and adolescents: Assessments and intervention* (pp. 27–44). Washington, DC: American Psychiatric Press.

Lander, E. S., & Kruglyak, L. (1995). Genetic dissection of complex traits: Guidelines for interpreting and reporting linkage results. *Nature Genetics, 11,* 241–247.

Lee, C. L., & Bates, J. E. (1985). Mother–child interaction at age two years and perceived difficult temperament. *Child Development, 56,* 1314–1325.

Lerner, R. M., & von Eye, A. (1992). Sociobiology and human development: Arguments and evidence. *Human Development, 35,* 12–33.

Loehlin, J. C. (1992). *Genes and environment in personality development.* Newbury Park, CA: Sage.

Lyon, M. F. (1996). X-chromosome inactivation: Pinpointing the centre. *Nature, 379,* 116.

Manning, W. D., & Landale, N. S. (1996). Racial and ethnic differences in the role of cohabitation in premarital childbearing. *Journal of Marriage and the Family, 58,* 63–77.

Mare, R. D. (1991). Five decades of educational assortative mating. *American Sociological Review, 56,* 15–32.

Marmot, M. G., & Syme, S. L. (1976). Acculturation and coronary heart disease in Japanese-Americans. *American Journal of Epidemiology, 104,* 225–247.

Martin, J. A., Maccoby, E. E., & Jacklin, C. N. (1981). Mothers' responsiveness to interactive bidding and nonbidding in boys and girls. *Child Development, 52,* 1064–1067.

Mather, K., & Jinks, J. L. (1982). *Biometrical genetics: The study of continuous variation.* London: Chapman Hall.

Maughan, B. (1994). School influences. In M. Rutter & D. F. Hay (Eds.), *Development through life: A handbook for clinicians* (pp. 134–158). Oxford, England: Blackwell Scientific.

Mazur, A., Booth, A., & Dabbs, J. M. (1992). Testosterone and chess competition. *Social Psychology Quarterly, 55,* 70–77.

McCartney, K., Bernieri, F., & Harris, M. J. (1990). Growing up and growing apart: A developmental meta-analysis of twin studies. *Psychological Bulletin, 107,* 226–237.

McGue, M. (1995). Mediators and moderators of alcoholism inheritance. In J. R. Turner, L. R. Cardon, & J. K. Hewitt (Eds.), *Behavior genetic approaches to behavioral medicine* (pp. 17–44). New York: Plenum Press.

McGuffin, P., Katz, R., & Rutherford, J. (1991). Nature, nurture and depression: A twin study. *Psychological Medicine, 21,* 329–335.

https://doi.org/10.1017/S0954579497002083 Published online by Cambridge University Press

McGuffin, P., & Murray, R. (Eds.). (1991). *The new genetics of mental illness.* Oxford, England: Butterworth–Heinemann.

McGuffin, P., Owen, M. J., O'Donovan, M. C., Thapar, A., & Gottesman, I. I. (1994). *Seminars in psychiatric genetics.* London: Royal College of Psychiatrists.

Meyer, J. M., Rutter, M., Simonoff, E., Shillady, C. L., Silberg, J. L., Pickles, A., Hewitt, J. K., Maes, H. H., & Eaves, L. J. (1997). *Familial aggregation for conduct disorder symptomatology: The role of genes, marital discord, and family adaptability.* Manuscript submitted for publication.

Molenaar, P. C. M., Boomsma, D. I., & Dolan, C. V. (1993). A third source of developmental differences. *Behavior Genetics, 23,* 519–524.

Mortimore, P. (1995). The positive effects of schooling. In M. Rutter (Ed.), *Psychosocial disturbance in young people: Challenges for prevention* (pp. 333–363). New York: Cambridge University Press.

Morton, N. E. (1974). Analysis of family resemblance. I. Introduction. *American Journal of Human Genetics, 26,* 318–330.

Neale, M. C., & Cardon, L. R. (1992). *Methodology for genetic studies of twins and families.* Dordrecht, Holland: Kluwer Academic Publishers.

Nettles, S. M., & Pleck, J. H. (1994). Risk, resilience, and development: The multiple ecologies of black adolescents in the United States. In R. J. Haggerty, L. R. Sherrod, N. Garmezy, & M. Rutter (Eds.), *Stress, risk, and resilience in children and adolescents* (pp. 147–181). New York: Cambridge University Press.

Olson, R. K., Wise, B. W., & Rack, J. P. (1989). Dyslexia: Deficits, genetic aetiology, and computer-based remediation. *Irish Journal of Psychology, 10,* 494–508.

Ormel, J., Stewart, R., & Sanderman, R. (1989). Personality as modifier of the life change–distress relationship: A longitudinal modelling approach. *Social Psychiatry and Psychiatric Epidemiology, 24,* 187–195.

Ormel, J., & Wohlfarth, T. (1991). How neuroticism, long-term difficulties, and life situation change influence psychological distress: A longitudinal model. *Journal of Personality and Social Psychology, 60,* 744–755.

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

Peltonen, L. (1995). Schizophrenia: All out for chromosome six. *Nature, 378,* 665–666.

Phillips, K., Fulker, D. W., Carey, G., & Nagoshi, C. T. (1988). Direct marital assortment for cognitive and personality variables. *Behavior Genetics, 18,* 347–356.

Pianta, R. C., & Egeland, B. (1994). Relation between depressive symptoms and stressful life events in a sample of disadvantaged mothers. *Journal of Consulting and Clinical Psychology, 62,* 1229–1234.

Pickles, A., Bolton, P., Macdonald, H., Bailey, A., Le Couteur, A., Sim, L., & Rutter M. (1995). Latent class analysis of recurrence risk for complex phenotypes with selection and measurement error: A twin and family history study of autism. *American Journal of Human Genetics, 57,* 717–726.

Pickles, A., Crouchley, R., Simonoff, E., Eaves, L., Meyer, J., Rutter, M., Hewitt, J., & Silberg, J. (1994). Survival models for developmental genetic data: Age of onset of puberty and antisocial behavior in twins. *Genetic Epidemiology, 11,* 155–170.

Pickles, A., & Rutter, M. (1991). Statistical and conceptual models of "turning points" in developmental processes. In D. Magnusson, L. R. Bergman, G. Rudinger, & B. Törestad (Eds.), *Problems and methods in longitudinal research: Stability and change* (pp. 133–165). Cambridge, England: Cambridge University Press.

Pike, A., McGuire, S., Hetherington, E. M., Reiss, D., & Plomin, R. (in press). Family environment and adolescent depressive symptoms and antisocial behavior: A multivariate genetic analysis. *Developmental Psychology.*

Plomin, R. (1986). *Development, genetics and psychology.* Hillsdale, NJ: Erlbaum.

Plomin, R. (1994a). Genetic research and identification of environmental influences. *Journal of Child Psychology and Psychiatry, 35,* 817–834.

Plomin, R. (1994b). *Genetics and experience: The interplay between nature and nurture.* Thousand Oaks, CA: Sage.

Plomin, R. (1995a). Genetics, environmental risks, and protective factors. In J. R. Turner, L. R. Cardon, & J. K. Hewitt (Eds.), *Behavior genetic approaches in behavioral medicine* (pp. 217–235). New York & London: Plenum Press.

Plomin, R. (1995b). Genetics and children's experiences in the family. *Journal of Child Psychology and Psychiatry, 36,* 33–68.

Plomin, R., & Bergeman, C. S. (1991). The nature of nurture: Genetic influences on "environmental" measures. *Behavioral & Brain Sciences, 14,* 373–386.

Plomin, R., & Daniels, D. (1987). Why are children in the same family so different from one another? *Behavioral and Brain Sciences, 10,* 1–15.

Plomin, R., DeFries, J. C., & Fulker, D. W. (1988). *Nature and nurture during infancy and early childhood.* New York: Cambridge University Press.

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

Plomin, R., DeFries, J. C., McClearn, G., & Rutter, M. (1997). *Behavioral Genetics* (3rd ed.). New York: W. H. Freeman & Co.

Plomin, R., Lichtenstein, P., Pedersen, N. L., McClearn, G. E., & Nesselroade, J. R. (1990). Genetic influence on life events during the last half of the life span. *Psychology and Aging, 5,* 25–30.

Plomin, R., & McClearn, G. E. (Eds.). (1993). *Nature, nurture, and psychology.* Washington, DC: American Psychological Association.

Quinton, D., Pickles, A., Maughan, B., & Rutter, M. (1993). Partners, peers, and pathways: Assortative pairing and continuities in conduct disorder. *Development and Psychopathology, 5,* 763–783.

Radke–Yarrow, M., Richters, J., & Wilson, W. E. (1988). Child development in the network of relationships. In R. A. Hinde & J. Stevenson–Hinde (Eds.), *Relationships within families: Mutual influences* (pp. 48–67). Oxford, England: Clarendon Press.

Raleigh, M., & McGuire, M. T. (1991). Bidirectional relationships between tryptophan and social behavior in vervet monkeys. *Advances in Experimental Medicine and Biology, 294,* 289–298.

Reiss, D., Hetherington, M., Plomin, R., Howe, G. W., Simmens, S. J., Henderson, S. H., O'Connor, T. J., Bussell, D. A., Anderson, E. R., & Law, T. (1995). Genetic questions for environmental studies: Differential parenting and psychopathology in adolescence. *Archives of General Psychiatry, 52,* 925–936.

https://doi.org/10.1017/S0954579497002083 Published online by Cambridge University Press

Reznick, J. S., Hegeman, I. M., Kaufman, E. R., Woods, S. W., & Jacobs, M. (1992). Retrospective and concurrent self-report of behavioral inhibition and their relation to adult mental health. *Development and Psychopathology, 4,* 301–321.

Rice, J., Cloninger, C. R., & Reich, T. (1978). Multifactorial inheritance with cultural transmission and assortative mating. I. Description and basic properties of the unitary models. *American Journal of Human Genetics, 30,* 618–643.

Richters, J., & Weintraub, S. (1990). Beyond diathesis: Toward an understanding of high-risk environments. In J. Rolf, A. Masten, D. Cicchetti, K. Nuechterlein, & S. Weintraub (Eds.), *Risk and protective factors in the development of psychopathology* (pp. 67–96). New York: Cambridge University Press.

Robins, L. (1966). *Deviant children grown up.* Baltimore: Williams and Wilkins.

Rodgers, B. (1990). Influences of early-life and recent factors on affective disorder in women: An exploration of vulnerability models. In L. Robins & M. Rutter (Eds.), *Straight and devious pathways from childhood to adulthood* (pp. 314–328). Cambridge, England: Cambridge University Press.

Rohde, P., Lewinsohn, P. M., & Seeley, J. R. (1994). Are adolescents changed by an episode of major depression? *Journal of the American Academy of Child and Adolescent Psychiatry, 33,* 1289–1298.

Rose, R. M., Holaday, J. W., & Bernstein, I. S. (1971). Plasma testosterone, dominance risk and aggressive behaviour in male rhesus monkeys. *Nature, 231,* 366–368.

Rose, S. (1995). The rise of neurogenetic determinism. *Nature, 373,* 380–382.

Rowe, D. C. (1994). *The limits of family influence: Genes, experience, and behavior.* New York: Guilford Press.

Rowe, D. C., Rodgers, J. L., & Meseck–Bushey, S. (1992). Sibling delinquency and the family environment: Shared and unshared influences. *Child Development, 63,* 59–67.

Rowe, D. C., Woulbroun, E. J., & Gulley, B. L. (1994). Peers and friends as nonshared environmental influences. In E. M. Hetherington, D. Reiss, & R. Plomin (Eds.), *Separate social worlds of siblings: Impact of nonshared environment on development* (pp. 159–173). Hillsdale, NJ: Erlbaum.

Rowe, K. J., & Rowe, K. S. (1992). The relationship between inattentiveness in the classroom and reading achievement: An explanatory study. *Journal of the American Academy of Child and Adolescent Psychiatry, 31,* 357–368.

Russell, A., & Russell, G. (1992). Child effects in socialization research: Some conceptual and analytic issues. *Social Development, 1,* 163–184.

Rutter, M. (1983). Statistical and personal interactions: Facets and perspectives. In D. Magnusson & V. Allen (Eds.), *Human development: An interactional perspective* (pp. 295–319). New York: Academic Press.

Rutter, M. (1985a). Family and school influences on behavioural development. *Journal of Child Psychology and Psychiatry, 26,* 349–368.

Rutter, M. (1985b). Family and school influences on cognitive development. *Journal of Child Psychology and Psychiatry, 26,* 683–704.

Rutter, M. (1986). Meyerian psychobiology, personality development, and the role of life experiences. *American Journal of Psychiatry, 143,* 1077–1087.

Rutter, M. (1987). Continuities and discontinuities from infancy. In J. Osofsky (Ed.), *Handbook of infant development* (2nd ed., pp. 1256–1296). New York: Wiley.

Rutter, M. (1989a). Pathways from childhood to adult life. *Journal of Child Psychology and Psychiatry, 30,* 23–51.

Rutter, M. (1989b). Psychiatric disorder in parents as a risk factor for children. In D. Shaffer, I. Philips, & N. B. Enzer (Eds.), *Prevention of mental disorders, alcohol and other drug use in children and adolescents* (pp. 157–189). Rockville, MD: Office for Substance Abuse Prevention, US Department of Health and Human Services.

Rutter, M. (1990a). Commentary: Some focus and process considerations regarding effects of parental depression on children. *Developmental Psychology, 26,* 60–67.

Rutter, M. (1990b). Psychosocial resilience and protective mechanisms. In J. Rolf, A. Masten, D. Cicchetti, K. Nuechterlein, & S. Weintraub (Eds.), *Risk and protective factors in the development of psychopathology* (pp. 181–214). New York: Cambridge University Press.

Rutter, M. (1994a). Beyond longitudinal data: Causes, consequences, changes and continuity. *Journal of Consulting and Clinical Psychology, 62,* 928–940.

Rutter, M. (1994b). Psychiatric genetics: Research challenges and pathways forward. *American Journal of Medical Genetics* (*Neuropsychiatric Genetics*)*, 54,* 185–198.

Rutter, M. (1995a). Maternal deprivation. In M. H. Bornstein (Eds.), *Handbook of parenting: Vol. 4. Applied and practical parenting. Part 1: Applied issues in parenting* (pp. 3–31). Mahwah, NJ: Erlbaum.

Rutter, M. (1995b). Relationship between mental disorders in childhood and adulthood. *Acta Psychiatrica Scandinavica, 91,* 73–85.

Rutter, M. (1996a). Developmental psychopathology: Concepts and prospects. In M. Lenzenweger & J. Haugaard (Eds.), *Frontiers of developmental psychopathology* (pp. 209–237). New York: Oxford University Press.

Rutter, M. (1996b). Transitions and turning points in developmental psychopathology: As applied to the age span between childhood and mid-adulthood. *International Journal of Behavioral Development, 19,* 603–626.

Rutter, M., & the English and Romanian (ERA) Adoptees Study Team. (1997). *Developmental catch-up and deficit following adoption after severe privation.* Manuscript submitted for publication.

Rutter, M., Bailey, A., Simonoff, E., & Pickles, A. (in press). Genetic influences and autism. In F. Volkmar & D. Cohen (Eds.), *Handbook of autism.* New York: Wiley.

Rutter, M., Champion, L., Quinton, D., Maughan, B., & Pickles, A. (1995). Understanding individual differences in environmental risk exposure. In P. Moen, G. H. J. Elder, & K. Lüscher (Eds.), *Examining lives in context: Perspectives on the ecology of human development* (pp. 61–93). Washington, DC: American Psychological Association.

Rutter, M., Macdonald, H., Le Couteur, A., Harrington, R., Bolton, P., & Bailey, A. (1990). Genetic factors in child psychiatric disorders. II. Empirical findings. *Journal of Child Psychology and Psychiatry, 31,* 39–83.

https://doi.org/10.1017/S0954579497002083 Published online by Cambridge University Press

Rutter, M., & Pickles, A. (1991). Person–environment interactions: Concepts, mechanisms, and implications for data analysis. In T. D. Wachs & R. Plomin (Eds.), *Conceptualization and measurement of organism–environment interaction* (pp. 105–141). Washington, DC: American Psychological Association.

Rutter, M., & Quinton, D. (1984). Parental psychiatric disorder: Effects on children. *Psychological Medicine, 14,* 853–880.

Rutter, M., & Redshaw, J. (1991). Annotation: Growing up as a twin: Twin–singleton differences in psychological development. *Journal of Child Psychology and Psychiatry, 32,* 885–895.

Rutter, M., & Rutter, M. (1993). *Developing minds: Challenge and continuity across the lifespan.* Harmondsworth, Middlesex, England & New York: Penguin & Basic Books.

Rutter, M., Silberg, J., & Simonoff, E. (1993). Whither behavior genetics? A developmental psychopathology perspective. In R. Plomin & G. E. McClearn (Eds.), *Nature, nurture, and psychology* (pp. 433–456). Washington, DC: American Psychological Association.

Rutter, M., & Smith, D. J. (Eds.). (1995). *Psychosocial disorders in young people: Time trends and their causes.* Chichester, England: Wiley.

Sampson, R. J., & Laub, J. H. (1993). *Crime in the making: Pathways and turning points through life.* Cambridge, MA: Harvard University Press.

Sandberg, S., Rutter, M., Giles, S., Owen, A., Champion, L., Nicholls, J., Prior, V., McGuinness, D., & Drinnan, D. (1993). Assessment of psychosocial experiences in childhood: Methodological issues and some illustrative findings. *Journal of Child Psychology and Psychiatry, 34,* 879–897.

Sapolsky, R. M. (1990). Stress in the wild. *Scientific American, 262,* 116–123.

Scarborough, H. S. (1991). Antecedents to reading disability: Preschool language development and literacy experiences of children from dyslexic families. *Reading and Writing: An Interdisciplinary Journal, 3,* 219–233.

Scarr, S. (1992). Developmental theories for the 1990s: Development and individual differences. *Child Development, 63,* 1–19.

Scarr, S., & McCartney, K. (1983). How people make their own environment: A theory of genotype → environmental effects. *Child Development, 54,* 424–435.

Segal, N. L. (1984). Cooperation, competition, and altruism within twin sets: A reappraisal. *Ethology and Sociobiology, 5,* 163–177.

Shillady, L. L., Silberg, J. L., Simonoff, E., Pickles, A., Maes, H. M., Rutter, M. L., Hewitt, J. K., Eaves, L. J., & Meyer, J. M. (1997). *Parental psychopathology as a risk factor for childhood disorder: A latent class analysis of 1,408 families.* Manuscript submitted for publication.

Silberg, J., Meyer, J., Pickles, A., Simonoff, E., Eaves, L., Hewitt, J., Maes, H., & Rutter, M. (1996a). Heterogeneity among juvenile antisocial behaviors: Findings from the VTSABD. In G. R. Bock & J. A. Goode (Eds.), *Genetics of criminal and antisocial behaviour. Ciba Foundation Symposium 194* (pp. 76–86). Chichester, England, & New York: Wiley.

Silberg, J. L., Rutter, M. L., Meyer, J., Maes, H., Hewitt, J., Simonoff, E., Pickles, A., Loeber, R., & Eaves, L. (1996b). Genetic and environmental influences on the covariation between hyperactivity and conduct disturbance in juvenile twins. *Journal of Child Psychology and Psychiatry.*

Simonoff, E., Bolton, P., & Rutter, M. (1996). Mental retardation: Genetic findings, clinical implications and research agenda. *Journal of Child Psychology and Psychiatry, 37,* 259–280.

Sing, C. F., Haviland, M. B., & Reilly, S. L. (1996). Genetic architecture of common multifactorial diseases. In D. Chadwick & G. Cardew (Eds.), *Variations in the human genome. Ciba Foundation Symposium 197* (pp. 211–232). Chichester, England, & New York: Wiley.

Sloggett, A., & Joshi, H. (1994). Higher mortality in deprived areas: Community or personal disadvantage? *British Medical Journal, 309,* 1470–1474.

Stanovich, K. E., & Cunningham, A. E. (1993). Where does knowledge come from? Specific associations between print exposure and information acquisition. *Journal of Educational Psychology, 85,* 211–229.

Stein, A., Woolley, H., Cooper, S. D., & Fairburn, C. G. (1994). An observational study of mothers with eating disorders and their infants. *Journal of Child Psychology and Psychiatry, 35,* 733–748.

Stoff, D., Breiling, J., & Maser, J. D. (Eds.). (in press). *Handbook of antisocial behavior.* New York: Wiley.

Suomi, S. J. (1991). Early stress and adult emotional reactivity in rhesus monkeys. In G. R. Bock & J. Whelan (Eds.), *The childhood environment and adult disease. Ciba Foundation Symposium 156* (pp. 171–188). Chichester, England: Wiley.

Teasdale, J. D., & Barnard, P. J. (1993). *Affect, cognition, and change: Re-modelling depressive thought.* Hove, England: Erlbaum.

Truett, K. R., Eaves, L. J., Walters, E. E., Heath, A. C., Hewitt, J. K., Meyer, J. M., Silberg, J., Neale, M. C., Martin, N. G., & Kendler, K. S. (1994). A model system for analysis of family resemblance in extended kinships of twins. *Behavior Genetics, 24,* 35–49.

Turkheimer, E., Goldsmith, H. H., & Gottesman, I. I. (1995). Commentary: Some conceptual deficiencies in "developmental" behavior genetics. *Human Development, 38,* 142–153.

Van Os, J., Castle, D. J., Takei, N., Der, G., & Murray, R. M. (1996). Psychotic illness in ethnic minorities: Clarification from the 1991 census. *Psychological Medicine, 26,* 203–208.

Vorria, P., Rutter, M., Pickles, A., Wolkind, S., & Hobsbaum, A. (1997a). *A comparative study of Greek children in long-term residential group care: I. Social, emotional, and behavioural effects.* Manuscript submitted for publication.

Vorria, P., Rutter, M., Pickles, A., Wolkind, S., & Hobsbaum, A. (1997b). *A comparative study of Greek children in long-term residential group care: II. Possible mediating mechanisms.* Manuscript submitted for publication.

Wahlsten, D. (1990). Insensitivity of the analysis of variance to heredity–environment interaction. *Behavioral and Brain Sciences, 13,* 109–161.

Weinberger, D. R., & Lipska, B. K. (1995). Cortical maldevelopment, anti-psychotic drugs, and schizophrenia: A search for common ground. *Schizophrenia Research, 16,* 87–110.

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