

EDITORIAL

## Genotype–environment interaction in antisocial behaviour<sup>1</sup>

The question of nature *versus* nurture in most forms of human behaviour has been raised many times but has never been solved to the mutual satisfaction of the parties concerned. The current controversy over the importance of genes and the environment in determining IQ is a case in point. In the area of psychopathology, research using adoptees over the past fifteen years has mainly focused upon demonstrating a genetic factor in a variety of psychiatric conditions: schizophrenia (Heston, 1966; Kety *et al.* 1968; Rosenthal *et al.* 1968; Wender *et al.* 1968; Karlsson, 1966), unipolar and bipolar affective disorders (Mendlewicz & Rainer, 1977; Cadoret, 1978), alcoholism (Bohman, 1978; Goodwin *et al.* 1973, 1974; Cadoret *et al.* 1980), antisocial personality (Crowe, 1974; Schulsinger, 1972), and antisocial forms of behaviour such as criminality (Hutchings & Mednick, 1977). Most of these studies have succeeded in showing the importance of a genetic factor in these varied conditions.

It is noteworthy that this recent injection of genetic factors into aetiologies of conditions that previously had been felt to be largely the product of environment has not generated the heat of the IQ nature–nurture controversy. In part, this might reflect such factors as the lack of implication of major racial differences in the ‘genetic factors’ (the adoption studies cited above deal almost entirely with Caucasian samples and race is not mentioned as a confounding variable), or it could reflect the relatively small number of inheritance studies in psychopathology compared with IQ. Or again, no recent adoption studies have suggested specific social action (or even implied it) to alter the genetic factor. However, the potential for great nature *versus* nurture controversy exists, especially for those psychopathological conditions which are strongly associated with social or environmental factors. One such category of conditions is antisocial personality, which in numerous studies has been associated with (lower) social class, disturbed family background (Robins, 1966; West & Farrington, 1977; Glueck & Glueck, 1968) and, more important, potentially controllable environmental factors, such as type of schools attended (Rutter *et al.* 1979). Social manipulation is already practised by society (as in removing children from certain abusive or neglectful parents). In considering possible social action aimed at reducing the incidence of antisocial personality or antisocial behaviour, genetic and environmental effects would have to be carefully distinguished. More important would be evidence of genotype–environment interaction – the potentiation of genetic effects in the presence of *certain* environments, or other interactions such as environments which ‘protect’ against the effects of a given genotype. Obviously, genotype–environment interactions would be of practical importance in suggesting more *specific* and *individualized* changes. The remainder of this paper will review some recent evidence for the importance of genetic and environmental factors and their interaction in antisocial behaviour.

In some of the adoption studies cited above, environmental factors have been investigated because certain adoptee experimental designs lend themselves to an assessment of the effect of environment. Negative results have been reported in alcoholism (Goodwin *et al.* 1973, 1974; Cadoret *et al.* 1980) and schizophrenia (Wender *et al.* 1968). However, more positive evidence of the importance of environmental factors has come out of adoption studies of antisocial personality or antisocial behaviour such as criminality. An early report of environmental influences on adoptee criminal behaviour came from Hutchings’ analysis of data correlating registered criminality in adoptees with registered criminality in biological *and* adoptive parents (Hutchings, 1972). A multiple regression

<sup>1</sup> Address for correspondence: Dr R. J. Cadoret, Department of Psychiatry, University of Iowa School of Medicine, 500 Newton Road, Iowa City, Iowa 52242, USA.

approach was used, with criminality in the adoptee as the dependent variable and a variety of independent variables (mostly dealing with criminal behaviour or the presence of other psychiatric problems in adoptive and biological backgrounds). The results of the analysis were that biological background (registered criminality) accounted for a significant amount of the variance in adoptee criminality (5.4%) and that the addition of an environmental factor of criminality in at least one adoptive parent increased the 'explained' variance significantly from 5.4% to 8%. In an adoption study where adoptees separated at birth were followed up at adolescence and later ages, Cadoret and co-workers found evidence for both environmental and genetic factors in adolescent antisocial forms of behaviour. Using a count of the number of adolescent antisocial forms of behaviour as a dependent variable in a multiple regression analysis, these authors found that different independent variables predicted antisocial count in males and females (Cadoret & Cain, 1980, 1981). In males, antisocial behaviour was increased by: (1) having an alcoholic biological relative, (2) living as an adoptee in an adverse adoptive home environment (where either a parent or a sib had a behaviour or psychiatric problem), or (3) being exposed as an infant to a 'discontinuous mothering' environment (for example, placement of the adoptee during the first six months of life in a college home economics department 'home management house' where students learned to care for infants; each adoptee was cared for by approximately 20–40 different students). For females, the only significant predictor of adolescent antisocial behaviour was having a biological parent who exhibited antisocial behaviour. However, the coefficients for the females for an adverse adoptive home environment and for 'discontinuous mothering' were in a similar direction to those of the males but failed to achieve significance. In both male and female samples, the genetic effect 'accounted for' about 5% of the variance. In the males, the environmental effects independently added another 3% to the explained variance. The females had no significant increase in controlled variance by the addition of the same environmental variables, a finding which is compatible with the generally expressed belief that boys may be more sensitive than girls to environmental causal factors important in antisocial behaviour (Wolkind & Rutter, 1973). That genetic factors in both the Cadoret *et al.* data and the Hutchings data explained more variance than the environmental cannot be taken as evidence that genetic factors are more important as causes of antisocial behaviour. There are a number of reasons for this, one of the most obvious being the limitation of environments in adoptive homes. Because of the selection of families who wish to adopt, certain environments will be eliminated or will be rare (for example, very low socioeconomic homes with a high amount of social turmoil due to alcohol, drug abuse, etc.), while other family environments will be more plentiful than normally found in the general population (for example, stable marriages with a very low divorce rate). This type of environmental restriction in adoptee samples could well disguise the presence in the real world of much more significant environmental effects, where studies of antisocial individuals are almost always correlated positively with large numbers of unfavourable psychosocial problems in the environment (Robins, 1966; West & Farrington, 1977). A second obvious limitation of studies such as this is the selection of the environmental variables themselves – a very significant predictor could have been overlooked completely in the original data collection.

There is an important statistical reason why such estimates of the relative importance of genetic or environmental factors could be very mistaken. In the type of multiple regression analyses performed by Cadoret *et al.* or Hutchings, the environmental and genetic effects are analogous to main effects in an analysis of variance; that is, the genetic effect in the multiple regression equation is 'averaged' over all sampled environments and the environmental effect is 'averaged' over all sampled genotypes. However, with two factors – genetic and environmental – one factor might behave differently in the presence of different degrees (or in some cases, presence or absence) of the second factor. When this occurs in an analysis of variance its presence is detected by an interaction term, and main or average effects are no longer valid to estimate the effect of different factors. In the Cadoret & Cain (1981) data given above an environmental effect, such as adverse adoptive home environment, might act to produce a high rate of antisocial behaviour only in the presence of a genotype from an antisocial or alcoholic parent. The same environmental factor in the presence of a genotype from a 'normal' parent might result in no increase or a slight increase in antisocial

behaviour. In this situation, the assessment of the relative importance of a genetic or environmental factor is not easily answered because both are important, and the magnitude of one effect depends on how much of the other factor is present.

Thus it is important to detect interaction in the case of genetic and environmental variables, and in some respects it is almost meaningless to talk about the relative importance of one factor over the other (except in the situation where no interaction occurs). Plomin *et al.* (1977) present a method of detecting genotype–environment interaction using adoption data. The method involves fitting an analysis of variance model to adoption data of the type where adoptees are separated at birth from their biological parents and placed with genetically unrelated adoptive parents. This design enables one to specify a genetic effect (the biological parent background) and an environmental effect (for example, adoptive parent or family conditions), and to generate an interaction term by multiplying together the separate genetic and environmental separate terms in the model. For their examples Plomin *et al.* use adoption data, with IQ as the dependent variable and biological and adoptive IQs as independent variables in a factorial design with an interaction term. In their analysis of IQ data no interaction was significant. However, when the Cadoret *et al.* data (Cadoret & Cain, 1981) were cast in a similar model, a significant interaction was found with a multiple regression equation. Defining the genetic effect (G) as a biological parent background of either alcoholism or antisocial behaviour, the environmental factor (E) as an adverse adoptive home, and the dependent variable as the number of adolescent antisocial symptoms, a multiplicative interaction term (G × E) demonstrated a highly significant interaction ( $P < 0.0001$ ). Substituting discontinuous mothering in the equation for (E) also gave evidence for interaction ( $P < 0.058$ ). Without an interaction term, these variables had predicted about 8–10% of the variance in the dependent variable, adolescent antisocial behaviour (Cadoret & Cain, 1982); however, with the interaction term, the predicted variance rose to 16–18%. Another way of demonstrating the importance of the interaction is to compute estimated means from the regression equation. When this is calculated for the model in which the E factor is an adverse adoptive home, the absence of genetic and environmental factors would predict an average of 1.1 antisocial forms of behaviour per individual. In the presence of an adverse adoptive environment *alone*, an average of 1.3 antisocial forms of behaviour are predicted. With a positive genetic factor alone (either alcoholic or antisocial biological background present), an average of 1.9 antisocial forms of behaviour is predicted. However, when *both* genetic and environmental factors are present, the average antisocial behaviour count is 4.5.

How are findings of this type connected with the nature–nurture controversy? There are a number of considerations and questions, some of which can be answered by recourse to data, while other criticisms are of a more epistemological nature. Questions such as selective placement (genotype–environment correlation) accounting for apparent interaction can be answered to some extent by showing from these data that selective placement, as measured by correlating genetic background (alcohol and/or antisocial behaviour) with adoptive home environment (the presence of disturbed behaviour or socioeconomic level of the adoptive home), was not a factor, since there were no significant correlations. In the case of the interaction involving disturbed behaviour in adoptive parents and sibs, it is not clear from these data what the causal direction of the effect is. We do know that these environmental factors occurred some time *after* the adoptee had been placed, but their temporal relationship to the adoptee's adolescent behaviour problems is not clear. Thus, child-to-parent effects could be important – for example, a disturbed adoptee causing behaviour problems in parents or sibs. In the interaction between the discontinuous mothering factor and biological background we have borderline significance of the interaction term, but an interesting one in which two temporally remote events together 'produce' a higher rate of adolescent antisocial behaviour. Here it is harder to see child-to-environment effects as a confounding factor.

On the more theoretical side, there are significant questions as to the validity of the use of such analyses of variance models to estimate genetic, environmental and interaction components. These questions have been raised primarily in reaction to the IQ nature–nurture controversy. One critic (Lewontin, 1974) has pointed out that the analysis of variance does not isolate distinct causes of variation 'because the amount of environmental variance that appears depends upon the genotypic

distribution while the amount of genetic variance depends upon the environmental distribution'. In part, this problem arises from our inability to sample in a representative fashion the range of environments, as well as our difficulty in inferring genotype from phenotype (Motulsky, 1978). If one takes Lewontin's criticism literally, then conclusions about the importance of interaction would be hard to support from analyses of this type. This is unfortunate because interaction, if present, offers an unparalleled opportunity for potential intervention in the psychopathological process: for example, if some environments are more 'deleterious' than others for a given genotype they can be avoided. One way to confirm the importance of interaction is to seek it in other experimental paradigms, using other types of analyses. For example, Cattell has proposed an elaborate scheme for partitioning variance (MAVA; Cattell *et al.* 1957), using data from twins, etc. Other authors have proposed different models to partition observed behavioural variability into genetic and various environmental factors (Morton, 1974; Rao *et al.* 1974). All these procedures use linear models to partition the variance and thus are still open to the basic criticisms voiced by Lewontin (1974). However, if a number of different models, using different samples – for example, twin data *versus* adoption data – reached similar conclusions concerning important factors and their interaction, then an additional basis of validity of factors would be met. Even so, the ultimate judge of validity of factors or interactions is the actual experimental manipulation, including random assignment of conditions, as pointed out by Kempthorne (1978) in a different critique of the use of analysis of variance in defining answers to nature *versus* nurture questions.

Genotype–environment interactions are potentially very important – theoretically as, for example, in the area of sociobiology (Eaves *et al.* 1978), as well as practically, especially from the standpoint of preventive psychiatry (Dorus, 1973). Gene–environment interactions might be the most important part of social psychiatry of the future. For the present, however, gene–environment interactions are extremely rare in human behaviour genetics (Schaie *et al.* 1975), but their detection is sufficiently important to encourage the pursuit of samples which are difficult to collect, such as adoptees, separated and non-separated twins, etc., along with the parallel use of the most efficient statistical models to measure effects. The type of controversy and polemics of the IQ nature–nurture question should be avoided, if possible, by insisting on adequately designed studies, cross-checking conclusions from different approaches, and the final validation by experimental manipulation where morally and physically possible.

REMI J. CADORET

## REFERENCES

- Bohman, M. (1978). Some genetic aspects of alcoholism and criminality. *Archives of General Psychiatry* **35**, 259–276.
- Cadoret, R. J. (1978). Evidence for genetic inheritance of primary affective disorder in adoptees. *American Journal of Psychiatry* **135**, 463–466.
- Cadoret, R. J. & Cain, C. A. (1980). Sex differences in predictors of antisocial behavior in adoptees. *Archives of General Psychiatry* **37**, 1171–1175.
- Cadoret, R. J. & Cain, C. A. (1981). Environmental and genetic factors in predicting adolescent antisocial behaviors in adoptees. *Psychiatric Journal of the University of Ottawa* **6**(4), 220–225.
- Cadoret, R. J. & Cain, C. A. (1982). Genetic–environmental interaction in adoption studies of antisocial behavior. Presented at the IIIrd World Congress on Biological Psychiatry. Stockholm, 1981. *Proceedings of the IIIrd World Congress on Biological Psychiatry*. Elsevier/North-Holland: Amsterdam (in the press).
- Cadoret, R. J., Cain, C. A. & Grove, W. M. (1980). Development of alcoholism in adoptees raised apart from alcoholic biologic relatives. *Archives of General Psychiatry* **37**, 561–563.
- Cattell, R. B., Stice, G. F. & Kristy, N. F. (1957). A first approximation to nature–nurture ratios for eleven primary personality factors in objective tests. *Journal of Abnormal Social Psychology* **54**, 143–159.
- Crowe, R. R. (1974). An adoption study of antisocial personality. *Archives of General Psychiatry* **31**, 785–791.
- Dorus, E. (1973). Importance of studying gene–environment interactions in psychiatric disorders. *Archives of General Psychiatry* **36**, 720.
- Eaves, L. J., Last, K. A., Young, P. A. & Martin, N. G. (1978). Model-fitting approaches to the analysis of human behaviour. *Hereditary (London)* **41**, 249–320.
- Glueck, S. & Glueck, E. (1968). *Delinquents and Nondelinquents in Perspective*. Harvard University Press: Cambridge, Mass.
- Goodwin, D. W., Schulsinger, F., Hermansen, L., Guze, S. & Winokur, G. (1973). Alcohol problems in adoptees raised apart from alcoholic biologic parents. *Archives of General Psychiatry* **28**, 238–343.
- Goodwin, D. W., Schulsinger, F., Moller, N., Hermansen, L., Winokur, G. & Guze, S. (1974). Drinking problems in adopted and nonadopted sons of alcoholics. *Archives of General Psychiatry* **31**, 164–169.
- Heston, L. (1966). Psychiatric disorders in foster home reared children of schizophrenic mothers. *British Journal of Psychiatry* **112**, 819–825.
- Hutchings, B. (1972). Environmental and genetic factors in psychopathology and criminality. Thesis submitted for degree of M.Phil. University of London.

- Hutchings, B. & Mednick, S. A. (1977). Criminality in adoptees and their adoptive and biological parents: a pilot study. In *Biosocial Bases of Criminal Behavior* (ed. S. A. Mednick and K. O. Christiansen), pp. 127–141. Gardner Press: New York.
- Karlsson, J. L. (1966). *The Biologic Basis of Schizophrenia*. Charles C. Thomas: Springfield, Ill.
- Kemphorne, O. (1978). Logical, epistemological and statistical aspects of nature–nurture data interpretation. *Biometrics* **34**, 1–23.
- Kety, S. S., Rosenthal, D., Wender, P. H. & Schulsinger, F. (1968). The types and prevalence of mental illness in the biological and adoptive families of adopted schizophrenics. In *The Transmission of Schizophrenia* (ed. D. Rosenthal and S. S. Kety), pp. 345–362. Pergamon Press: London.
- Lewontin, R. C. (1974). Annotation: the analysis of variance and the analysis of causes. *American Journal of Human Genetics* **26**, 400–411.
- Mendlewicz, J. & Rainer, J. (1977). Adoption study supporting genetic transmission in manic-depressive illness. *Nature* **268**, 327–329.
- Morton, N. E. (1974). Analysis of family resemblances. I. Introduction. *American Journal of Human Genetics* **26**, 318–330.
- Motulsky, A. G. (1978). Medical and human genetics 1977: trends and directions. *American Journal of Human Genetics* **30**, 123–131.
- Plomin, R., DeFries, J. D. & Loehlin, J. C. (1977). Genotype–environment interaction and correlation in the analysis of human behavior. *Psychology Bulletin* **54**, 309–322.
- Rao, D. C., Morton, N. E. & Yee, S. (1974). Analysis of family resemblances. II. A linear model for family correlation. *American Journal of Human Genetics* **26**, 331–359.
- Robins, L. (1966). *Deviant Children Grown Up*. Williams and Wilkins: Baltimore.
- Rosenthal, D., Wender, P. H., Kety, S. S., Schulsinger, F., Welner, J. & Ostergaard, L. (1968). Schizophrenics' offspring reared in adoptive homes. In *The Transmission of Schizophrenia* (ed. D. Rosenthal and S. S. Kety), pp. 377–391. Pergamon Press: London.
- Rutter, M., Maugham, B., Mortimore, P., Ouston, J. & Smith, A. (1979). *Fifteen Thousand Hours. Secondary Schools and Their Effects on Children*. Harvard University Press: Cambridge, Mass.
- Schaie, K. W., Anderson, V., McClearn, G. E. & Money, J. (eds.) (1975). *Developmental Human Behavior Genetics. Nature–Nurture Redefined*. Lexington Books.
- Schulsinger, F. (1972). Psychopathy: heredity and environment. *International Journal of Mental Health* **1**, 190–206.
- Wender, P. H., Rosenthal, D. & Kety, S. S. (1968). A psychiatric assessment of the adoptive parents of schizophrenics. In *The Transmission of Schizophrenia* (ed. D. Rosenthal and S. S. Kety), pp. 235–250. Pergamon Press: London.
- West, D. J. & Farrington, D. P. (1977). *The Delinquent Way of Life*. Heinemann: London.
- Wolkind, S. N. & Rutter, M. (1973). Children who have been 'in care' – an epidemiological study. *Journal of Child Psychology and Psychiatry* **14**, 97–105.