# Moving on from old dichotomies: beyond nature–nurture towards a lifeline perspective

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**Background** Genetics is increasingly being used to explain human behaviours, with growing enthusiasm for what could be termed 'genetic determinism', which an ultra-Darwinist approach seeks to apply to all aspects of the human condition.

**Aims** To consider the validity of the claims concerning the genetics of human behaviour and psychological distress.

**Method** A critical review of the current assumptions about the relative contributions of genetics and the environment.

**Results and conclusions** Organisms are in constant interaction with their environment: that is, organisms select environments just as environments select organisms. Like organisms, environments evolve and are homeodynamic rather than homeostatic; both 'genome' and 'envirome' are abstractions from this continuous dialectic.

**Declaration of interest** None.

It is an attractive proposition, for those uneasy at the extent to which genetic arguments are increasingly being used as explanations for human behaviours, to contrast 'genomes' with 'enviromes'. However, both these seductively attractive terms require some deconstruction, for they hide as much as they reveal. In this context, I here look sceptically at some of the claims concerning the genetics of psychic distress, and the current enthusiasm for what I have called 'neurogenetic determinism' (Rose, 1995) – a tendency that is driven at least in part by a fundamentalist ultra-Darwinism, which seeks explanations for every aspect of the human condition in terms of some so-called evolutionary imperative. I will argue that the combination of behaviour genetics and ultra-Darwinism that has become known as evolutionary psychiatry (Stevens & Price, 1996; Rose & Rose, 2000) is at best misguided.

## THE EPIDEMIOLOGY OF PSYCHIATRIC DIAGNOSES

As a non-epidemiologist, I have always considered that the starting point for any analysis of a condition – once one has called it into existence by naming it – is to try to assess its distribution: geographically, historically and at the least across the broad categories of class and occupation, gender and ethnicity. Rationally, this should provide a basis for any attempts to identify causality. This approach for broad categories of psychic distress reveals a number of striking features (Dohrenwend, 1980); they include the excess diagnoses of schizophrenia in working or lower classes, and the more than two-fold excess of depression diagnoses in women compared with men. More recently, attention has been drawn to the excess schizophrenia diagnoses in the UK among children of Caribbean and Caribbean/ethnic English relationships (Harrison, 1990; King *et al*, 1994).

Now there are a number of obvious ways of accounting for this excess (Sharpley *et al*, 2001, this supplement). Labelling is one; the racist nature of the host society, and the cultural strains that this imposes especially on children of mixed relationships, is another. The one thing that seemed clear to me was that you could not account for the distribution using a genetic model. Nevertheless, when I discussed this problem with a distinguished behaviour geneticist a few years ago it took him only a few moments to come up with such a model. Simple, he said: sample bias reflecting the character of those most likely to emigrate in the first instance, followed by assortative mating. That is, a propensity to madness predisposes you also to migrate and choose a partner of a different colour. This demonstrates two points. The first is that there is no distribution of phenotypes in a population that cannot be made to conform to a genetic model if you are determined enough; you only need to make the right assumptions about assortative mating, partial genetic dominance and incomplete penetrance, and anything goes. The second is the current enthusiasm on the part of behaviour geneticists to, so to speak, suck the environment into the genome. Thus, Bouchard, among others, has argued that many apparently environmental effects are actually the consequence of a genome predisposing an individual to choose particular environments – that is, to make a bad marriage, to seek risk, or whatever. The seductive power of genetic determinism here speaks for itself (e.g. Bouchard, 1997; see also Plomin & Craig, 2001, this supplement).

There are yet other factors that affect diagnosis, though they are less frequently spoken about: economic, social and historical criteria – or even fashion. Thus Warner has explained the rather broader criteria for the diagnosis of schizophrenia as opposed to manic depression previously employed in the USA in terms of the interests of the pharmaceutical industry in prescribing proprietary drugs rather than the common – and cheaper – lithium (Warner, 1985).

It is hard to believe that the explanations for these temporal shifts in diagnosis lie in the biological realm. Take, for my final example in this context, the diagnosis currently called attention-deficit hyperactivity disorder (ADHD). As is well known, up to 10% of young Americans are now considered to be suffering from this condition, and there is a virtual epidemic of prescription of methylphenidate hydrochloride (Ritalin) to treat it – or at least to mask its



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symptoms. The mainstream US literature is clear; ADHD is not the result of poor parenting or teaching, or inadequate schools and social environment, and it is not just about naughty kids. It is a genuine organic brain dysfunction, characterised by irregularities in dopamine neurotransmission, and there is a strong genetic factor involved (Wender, 1987). To the critical eye this evidence is extremely weak, to put it no more strongly, and there is indeed a powerful oppositional movement to the diagnosis and the use of methylphenidate within the USA itself (Breggin, 1998; Grandpre, 1999). Cross the Atlantic to Europe, and the diagnosis is much rarer. It varies from country to country, but its incidence is between one-hundredth and one-tenth of that in the USA. Indeed, the only country that comes close to the US incidence is Australia. However, this is not a stable situation. In the UK, for example, the incidence of the ADHD diagnosis seems to be steadily rising, aided by a significant parental pressure group and a few convinced psychiatric practitioners. Some 90 000 Ritalin prescriptions per year were being issued by 1997, and a recent United Nations report (UN, 1999) has highlighted the dangers of an epidemic of prescribing.

Why these differences? It is hard to believe that there are such great dissimilarities between either the genomes or even the physical environments of American and European children. Nor does it seem likely that there has been an increase in the spontaneous mutation rate such that the disordered gene presumed to lead to the disordered molecule and hence the dysfunctional brains of ADHD children is suddenly increasing in the UK. One could argue that some hitherto unrecognised environmental factor, dietary or social, is suddenly being brought into play, but this sounds unconvincing. This leaves two possible explanations: either the condition has always been present in UK children at the same rate as in the USA, but it has hitherto not been diagnosed correctly – the view taken by some of ADHD's advocates (see http://www.bmj.com/cgi/content/full/317/7174/1707 for responses to Rose, 1998); or the diagnosis itself is a matter of fashion, and the UK's scientific and cultural cringe to the USA is in evidence.

## UNPACKING ENVIROMES AND GENOMES

The counterposition of envirome and genome is a neat way of emphasising the relevance of both, and of encouraging the consensual belief that in the aetiology of any condition there must be some relationship between the two. However, in many ways it is too easy, because it implies some sort of balance between two interacting objects or forces. If one is not a 'geneticist' then one is an 'environmentalist'. It is high time to ditch the dichotomising approach, the division between nature and nurture, genes and environment, which has bedevilled analysis of these questions in the Western scientific traditions that have dominated thinking in the twentieth century. It would be nice to be able to grow up a bit as we pass the Christian millennium. Nor is the classical social science view that the biological is what happens before birth, the social what happens afterwards, acceptable. We need a non-dichotomising, developmental approach, as a way to understand living organisms in general and humans in particular.

It is obvious to all that the 'environment' is a portmanteau word covering many phenomena and processes. Thus, for any individual gene-sized bit of DNA, all the other genes in the organism's genome are part of its 'environment'; for the DNA as a whole, the nucleus and the metabolic orchestra of intracellular mechanisms; for these, the cell; tissues and organs; for organisms, the external physical environment and the other living forms within it; for social animals, conspecifics; and for humans, our own social, cultural and technological histories. Furthermore, neither environments, nor the ways they interact between levels, are constant during an individual's life time; the intra-uterine environment would spell death to any postnatal mammal, to take the most obvious example.

What is much less well understood, except by molecular biologists, is that the concept of the 'genome' as a unitary construction is equally misleading. To listen to many behaviour geneticists you would believe that genes were virtually fixed objects, arranged like beads on a chromosome string, each virtually immutably responsible for a single phenotypic feature. But genes are not such prime movers. The shorthand phrase 'a gene for' even as simple a character as eye colour is thoroughly misleading. The colour of the human iris depends on the presence in the cells of particular pigments: in the absence of pigment, the eye is blue; increasing quantities of the pigments provide colours, which range from green to brown. Let us take for granted those developmental processes that lead to the formation of the eye, and within the eye the iris, and consider only the pigments themselves. The biochemical steps that lead to the synthesis of the eye pigments involve many different enzymes. Hence many structural – let alone regulatory – genes must also be required in the generation of an iris of a particular colour.

So to biochemists, if not geneticists, there is no longer any gene 'for' eye colour. A gene 'for' blue eyes has now to be reinterpreted as meaning 'one or more genes in whose absence the metabolic pathway, which leads to pigmented eyes, terminates at the blue eye stage'. The modern concept of the relationship between DNA sequences and the proteins they code for is of a fluid genome, with DNA strands being transcribed, excised, edited, shuffled, multiply translated, under the control of a myriad transcription factors and control sequences in which the entire cellular orchestra is called into play (see Rose, 1997 for a fuller discussion of these points).

The contrast between the way that modern molecular biology conceives of the role of genes and the way that behaviour genetics does is perhaps best summarised in Table 1. Behaviour geneticists, in order to get their equations partitioning our genomic and environmental effects, have to go through the following sequence of assumptions. The first is that the phenotype they are concerned with exists, and can be unequivocally described and its distribution in a population determined. Eye colour may reasonably be regarded as such a phenotype. However, especially in the light of the comments I have already made, any suggestion that depression, schizophrenia – or for that matter intelligence, aggression, conservatism or whatever – is such a unitary phenotype seems to me a priori to be doubtful. Such diagnoses and descriptions are inevitably the result of a series of contracts, between diagnoser and diagnosee, shaped by history, culture, technology and current power relationships. Thus they lie inevitably in the realm of the social.

The second assumption is that statistical methods, based on analysis of pedigrees, concordances and so on, can be used to partition out genetic and environmental 'contributions' to that phenotype. For some conditions with unequivocal phenotypes and clear-cut pedigrees, it is possible to identify relevant genes. The genetics of Huntington's or Tay–Sachs disease are



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**Table 1** Differing views of the gene

| Behaviour geneticists | Molecular biologists |
|---|---|
| Gene as a theoretical entity | Gene as a term applied to varying sequences of DNA |
| Genes seen as unitary and indivisible, rather as atoms were before the days of nuclear physics | Genome fluid; DNA strands subject to alternative reading frames, splicing and editing processes |
| Beanbag models of gene expression | Gene expression contingent on cellular regulation at levels from the genomic to the organismic |
| Assumption of linear one-to-one relationship between genotype and phenotype | Sometimes a linear, one-to-one relationship between genotype and phenotype, but this is not typical |
| 'Preformationist' assumption of 'empty organism' that ignores developmental trajectories | The ontogeny of information |
| Genetic primacy – deviations are 'phenocopies' or modelled by incomplete penetrance or partial dominance | Some phenotypic conditions mimicked by genetic conditions – e.g. schizophrenia, breast cancer, Alzheimer's disease ('genocopies') |

clearly understood, and the disorders are seemingly independent of any feasible range of environmental manipulations. For other conditions, the possession of certain genes – for example, particular alleles of the gene that codes for apolipoprotein $\epsilon$ – is a probabilistic risk factor (along with many others, such as a history of head injury) for Alzheimer's disease; but such clear-cut identification, even of genetic risk factors, has not proved possible for most of the conditions with which psychiatrists are generally concerned. Claims that there are gene markers, or even genes, that are predictive of schizophrenia or depression have been made and withdrawn so many times now as to encourage only healthy scepticism. Hence the huge statistical apparatus with which behaviour genetics concerns itself, leading to claims about that much misunderstood concept, heritability.

Heritability estimates are concerned with the variance of a trait in a population, assumed to be made up of a component contributed by the genes and a component contributed by the environment, which can simply be added together to give a total of nearly 100%. The remainder, which to make the mathematics work has to be a rather small proportion of the total, is considered to be the product of an interaction between genes and environment. To put it in the form of an equation, if $V$ is the total variance, $G$ the genetic contribution and $E$ the environmental contribution, then:

$$V=G+E+(G\times E)$$

However, the mathematics only works if all the relevant simplifying assumptions are made. If there is a great deal of interaction between genes and environment, if genes interact with each other, and if the relationships are not linear and additive but interactive, the entire mathematical apparatus of heritability estimates falls apart. As Haldane pointed out as long ago as 1946, in general '$m$ genotypes in $n$ environments generate $(mn)!/m!n!$ kinds of interaction'. Consider simply three genotypes and three environments: $(mn)$ is 9, $mn!$ is 362 880, $m!$ and $n!$ are each $3\times2\times1$ or 6, and the number of interactions is no less than 10 080.

Thus the meaningful application of heritability estimates is only possible in very special cases and, I would claim, is quite irrelevant to the study of the causes of psychiatric distress. The estimate only works if the simplifying assumptions are valid; the figure obtained does not apply to an individual but to differences within a randomly interbreeding population, and cannot be applied to differences between populations; it assumes random distribution of genotypes across environments, and the estimate changes if these environments are changed.

Perhaps this is why the application of heritability calculations yields such bizarre results. Consider, for instance, the claim that there is a significant heritable component, at least in the USA, for such features as attitudes to the death penalty, Sabbath observance, working mothers, military drill, White superiority, cousin marriage, royalty, conventional clothes, jazz and divorce, to say nothing of religiosity and political tendency (Rushton, 1995). Faced with this diverse mix (apparently attitudes to 'pajama parties', strait-jackets and coeducation are not heritable), the only conclusion is that daft numerology has overtaken scientific common sense.

## NEUROGENETIC DETERMINISM

Faced with these complexities, one may well be puzzled by the enthusiasm for seeking genetic explanations. And yet the drive to geneticism seems to accelerate. Of course, there is a long (and often dubious) history of claiming genes for behaviour, and while it would be wrong simply to extrapolate the eugenicist past into the present, one cannot entirely dismiss it, because just as individuals have a history that in many ways must be a key to their present, so have scientific disciplines and modes of enquiry. Bridging the gap between biological and social psychiatry must be an aim for us all; but it cannot be done by retreating into entrenched positions, or by insisting that the social is subservient to the biological. I see the current enthusiasms, which offer us genes for everything, from alleged human universals such as male polygamy, female monogamy and the alleged dislike by children of spinach, to human differences in sexual orientation, alcoholism, violent and criminal behaviour, compulsive shopping – even, to quote the former editor of *Science*, homelessness (Koshland, 1989) – as an attempt to short-circuit the complexities of living processes in general and of being human in particular. Life is full of pain and distress. The social utopianism of the great socialist and communist movements that swept the world through much of the twentieth century, and the ameliorative assumptions of the psychotherapeutic movements, have faded or been pushed aside. A new, hard-nosed realism tells us that according to science, life is indeed nasty, brutish and short, full of struggle and shaped neither by divine nor human intentionality, but by the needs of the selfish genes that drive us lumbering robots to do what we must in order to assist them propagate themselves into the next generation. So it is to genetics we must turn for explanations; what cannot be cured must be endured. However,



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although genetics insists that the faults lie not in the outside world but within our very cells, it also holds out promise. It is deterministic but simultaneously claims the Promethean prospect of change. What neither revolution nor psychotherapy can achieve, may be conquered by technology, genetic engineering, or the rational design of pharmaceuticals made possible by advances in molecular genetics. At least, as James Watson has argued, we know how to do genetics, even if we know little about effecting positive social change (Watson, 1986). So let us look for the explanation and treatment of schizophrenia where the clear light of science shines. No matter if it is equivalent to the drunk looking for his doorkey under the lamppost. At least it is something, and can generate research grants.

## SOME PRINCIPLES FOR THE MILLENNIUM

As a contrary view, I have argued that what is needed is a different, more synthetic understanding of the nature of living processes in general, and of the human condition in particular. I have expressed this as a set of principles for the new millennium, drawn from my book *Lifelines* (Rose, 1997) but of some relevance, I trust, to psychiatry.

### One world, many ways of knowing

For any living phenomenon we observe and wish to interpret, there are many possible legitimate descriptions. There are within-level causal explanations; descriptions that locate the organism as part of a more complex ecosystem; molecular, developmental and evolutionary accounts. These accounts cannot be collapsed into the one 'true' explanation in which the living phenomenon becomes 'nothing but' a molecular assemblage, a genetic imperative, or whatever. It all depends on the purposes for which the explanation is required. To put it formally, we live in a material world that is an ontological unity, but which we approach with epistemological diversity. Every aspect of our human existence is simultaneously biological, personal, social and historical.

### It all depends

In living systems, causes are multiple and can be described at many different levels and in many different languages. Phenomena are always complex and richly interconnected. For example, the reasons why any individual becomes depressed or 'hears voices' will certainly relate to that person's unique genotype and developmental history, but also to such 'risk factors' as gender relations, work and living environment. What is required is to seek the determining cause – that is, the one with the major effect on the system. For Huntington's disease the determining cause is clearly genetic, and understanding the genetics and molecular biology may be the best strategy to alleviate or eliminate the condition; but for such social concerns as urban violence, poverty and homelessness, to seek determining causes in genetics and biochemistry, as neurogenetic determinism attempts, is poor science and is likely to lead to poor social prescriptions. Other conditions, such as the psychic anguish of schizophrenia or depression, remain contested zones, where crucial determinants may occur at several levels.

### Being and becoming

Living organisms exist in four dimensions, three of space and one of time, and cannot be read off from the single dimension that constitutes the strand of DNA. Organisms are not empty phenotypes, related one-for-one to particular patterns of genes. Our lives form a developmental trajectory or lifeline, stabilised by the operation of homeodynamic principles. This trajectory is not determined by our genes, nor yet partitioned into neatly dichotomous categories called 'nature' and 'nurture'. Rather, it is an autopoietic process, shaped by the interplay of specificity and plasticity. Insofar as any aspect of life can be said to be 'in the genes', our genes provide the capacity for both specificity (a lifeline relatively impervious to developmental and environmental buffeting) and plasticity (the ability to respond appropriately to unpredictable environmental contingency – that is, to experience). This autopoietic interplay is in some senses captured by that old paradox of Xeno – the arrow shot at a target, which at any instant of time must both be somewhere and in transit to somewhere else. Reductionism ignores the paradox and freezes life at a moment of time. In attempting to capture its 'being', it loses its 'becoming', turning processes into reified objects.

### Organism and environment interpenetrate

Organisms are in constant interaction with their environment: put another way, organism and environment interpenetrate. That is, organisms actively select environments just as environments select organisms (this is my alternative to the Bouchard/Plomin argument about genotypes selecting environments). People move from unfavourable to favourable conditions; we absorb aspects of our environment and in doing so we constantly change our environment. Like organisms, environments evolve and are homeodynamic rather than homeostatic. Both 'genomes' and 'enviromes' are abstractions from this continuous dialectic.

### The past is the key to the present

It follows from this that we cannot predict the pattern of future change. We can only respond to present contingencies. Because humans, like all living organisms, are simultaneously and continually responding to such contingencies and in doing so changing the environment both for themselves and others, we can do no other than track a continually moving and inherently unpredictable target. The odds are always changing, at all levels from the molecular through the individual to the population and species.

### Life constructs its own future

For humans (as for all other living organisms) the future is radically unpredictable. This means that individually and collectively we have the ability to construct our own futures, albeit in circumstances not of our own choosing. Thus it is that our biology makes us free.

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