book reviews

Genes and behaviour: nature and nurture interplay explained

By Michael Rutter. Blackwell Publishing Ltd, Oxford 2006. 272 pp. £16.99.

This book, by one of the most experienced child psychiatrists in the UK, with a special interest in autism, uses the clinical presentation of phenotypes to bridge the gap separating them from the genotypes defined by DNA and related techniques. A welcome inversion of the usual approach of attempts by experts on the interpretation of genotypes to master the phenotype. But there are problems on both sides. What was once known as 'mental deficiency' now shelters the many causes of disturbed behaviour, including autism, now included under 'pervasive developmental disorders', under various euphemisms. Autism implies, to those who live in hope, a condition that can be cured by therapy: it can hardly fail to be rare because of the many forms of backwardness interrupting normal development. There are problems in both Rutter's approach and the commoner inverse approach when experts on genetic analysis, usually indifferent to assumptions on which there is general agreement by clinicians and anthropologists, pursue their advanced expertise regardless of reality and its restraints.

The book is difficult to read due to poor copy-editing into a mid-Atlantic dialect, with erratic suppression of the genitive, and an unusual syntax often extending to over 30 comma-free words and occasionally over 50. The simple copying of the title of papers after each chapter has not been done, the reader having to do this by reference to a number. A glossary is included, an excellent addition, and mainly accurate, but with some unacceptable ambiguities with inadequate help from an unusually selective and parochial bibliography.

Affected sib-pair is defined without reference to the parental typing implied. The key sib-pair paper of Penrose (1935), which has controls but no parents, with the advantage of very simple arithmetic, is omitted. Animal models include only the effect of induced mutations on behaviour – usually in mice. Their major value in defining relevant landmarks and loci by comparative mapping in other species, ancient and modern, is omitted. Epistasis does not require two genes; one suffices and is probably more common in this variously used term.

Haplotype is defined in its 'HapMap' sense, when it allows for a sort of 'average effect', permitting very odd structures, incapable of surviving meiosis, to qualify: recent usage that should be termed 'inferred haplotype' or 'HapMap' as opposed to its classical definition in which, as expected on grounds of mechanism, any recombinant event would lead to two shorter haplotypes. LOD is capitalised, leading to unnecessary confusion with the more recent MLOD that lacks the essential feature of additivity. Barnard introduced the term 'lod', to be followed by Morton and Ott, who related it to common logarithms. Morton introduced his 'rule of three' in 1955 as approximately equivalent to a significance test at a level 0.05 for 'a single locus and a single test locus'. It is now widely misused and misquoted. 'Polygenic' is defined adequately, but the Latin 'multifactorial' introduced by Penrose has a wider and clearer remit and is usually preferred.

The bibliography gives little help to the glossary: it has over 500 references including over 50 with Rutter as first or only author and, in general, a very parochial selection with multiple representation of papers with common or overlapping authorship. Omissions include all most all contributions before Galton's elaboration of his ancestral model, mentioned in the text but lacking a reference. After the turn of the last century, when the framework of well-defined terms was developed with elegance and clarity, Bateson, Wheldon, Pearson, Punnett, Morgan, Haldane, Hogben, and later Waddington, CAB Smith, Newton Morton, Renwick and McKusick escape mention. References to McKeown and Weatherall exclude their major contributions. Fisher, initialled 'RE' has a reference to the Royal Society of London: it rejected his paper, later published by the Royal Society of Edinburgh.

The first three chapters, covering 62 pages, include assertions of a serious lack of integrity in various authors of distinction. Page 4 states 'except in rare circumstances genes were not determinative of either psychological or mental disorders'. But there are numerous recessive disorders disrupting intellect early in life and rather fewer dominant disorders of later life. Cyril Burt is accused of 'outright fraud' but the circumstances of eviction of his department to the Welsh coast by the Luftwaffe, without his records, imposed problems on memory: his exaggeration of the correlations of his earlier work is formally irrelevant to the implications asserted. His extensive prewar work seems faultless.

Eysenck and Jensen are criticised for accepting various grants that might have influenced their research, but without evidence. Jensen, who claimed that African-Americans were less bright than 'white' Americans, is hardly making an unexpected statement – the African chiefs are unlikely to have chosen their brightest subjects to sell to the Arab slave traders. Nor does the obvious acquired pallor of the American black reflect well on that minority of whites responsible. It is stated, 'Although he [Jensen] has been unwilling publicly to admit it, his arguments are known to be flawed' – the reasons given for this assertion are certainly flawed.

The next chapter on multiple interactions and environmental influence is difficult to follow. As is the third on 'How much is nature and how much nurture'. It is largely related to what seem unlikely biases in twin studies, hardly an ideal source of relevant data. The 'shortage' of twins in advanced education was first documented by Sandon over a century ago and later in relation to the '11 plus' on large numbers in Birmingham, each pair dropping in measured IQ by about one point by rank. The simplest explanation is that the first follows the parents, the second the first, and so on. This seemed confirmed by those with a still-born sibling – including RA Fisher – having no such problem in spite of their related obstetric problems. Newton and Hogben performed well after extreme prematurity. The rarity of pairs of identical twins of distinction in history, ancient or modern, is obvious.

In Chapter 4 we at last come to 'autism spectrum disorders' and, hopefully a definition of this disorder, much confounded by

therapeutic hope and euphuisms. In spite of 58 listed papers by Rutter *et al* this is hardly simple to find, if indeed present. Most estimates are based on clinical diagnosis quoting the American reference www.ninds.nih.gov/disorders/ – '3.4 for every 1,000' but this seems high.[1] Both the 2005 single-author papers and Rutter relate to reviews – the scanning techniques now available that should define the presence of irreversible developmental in clinical autism are yet to come.

The remaining chapters cover the deep waters of numerical approaches to decipher the influence of various features, but are confounded by a novel use of established terms and a casual disregard for history. Falconer's great book of 1960 was almost 60 years after Pearson's group had developed and tabulated the tetrachromic functions, illustrated their model, and applied it to Galton's data on measurements, especially the height, of various pairs of relatives. This, and Morton's much misquoted comments on a 'lod of three' bounded the era of those pioneers who were fluent in both biological reality and could apply appropriate methods of analysis.

Chapter 7, 'What genes do', is particularly difficult but at least it refers to a recent textbook.[2] This discusses and illustrates the multifactorial problem with particular clarity.

Chapter 8 enters the deep waters of numerical estimates, but not without error. It is difficult to combine sets of data using MLODS, as demonstrated by the failure to find a clear-cut locus at or near a segment on the eighth chromosome related to schizophrenia clearly present in both Iceland and Scotland. The 'haplotype relative risk' (HRR) of method of Falk and Rubinstein, rightly honoured with a reference, uses the classical definition of haplotypes and is exact. The transmission disequilibrium test test involves alleles and is only exact if Mendelian transmission is consistent with obedience to what Stern called Mendel's first law. The chapter ends with the conclusion that genes 'do not have direct effects on any trait or disorder'.

Chapter 9 is on 'finding and understanding specific susceptibility genes'. It is simpler to use the term allele, and these can be 'influential' in which case one is a susceptibility allele and the other a resistance allele. Multifactorial starts with 'Alzheimer's' disease, as in modern usage. Although Alzheimer was stated to have claimed it as a dominant disorder of early middle age, it has since been modernised and is now polygenic and senile. The original paper seems to have escaped bibliographers and should be found and translated if it still exists.

The major value of Rutter's book is in its last three chapters that, even if not devoid of mathematical problems and misprints, and overlooking the well established habit of familial disorders to include rare Mendelian dominants, as well as conditions due to the cumulative effects of alleles with minor influence, as so clearly defined in cancer of the breast – the traditional nurse of the pathology of cancer. These are very important papers, providing a well argued case for a much neglected but very important field of enquiry, and it is good to end on a triad of chapters of such power.

Readers might start with these last three chapters with well argued problems, the argument not being substantially weakened by the minor obstacles imposed by some claims of reality, or confounded by some errors in the figures. They convey a clear and much neglected problem. The other chapters hardly compete with recent textbooks on genetics. The multifactorial problem is particularly well handled in Strachan and Read.

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Reference

1 Rutter M. Incidence of autism spectrum disorders: changes over time and their meaning. *Acta Paediatr* 2005;94:2–15.
2 Strachan T, Read AP. *Human molecular genetics*, 3rd edn. Oxford: Garland Science, 2004.

Dizziness: a practical approach to diagnosis and management

By Adolfo Bronstein and Thomas Lempert. Cambridge University Press, New York 2007. 238 pp. £35.00.

Dizziness is a headache. This seems to have been true, as far we can tell, in all times and places: the Greeks (taking a broad systemic perspective) linked it to the wanderings of the womb, while Avicenna attributed it to melancholia, and everybody agreed that the prognosis was guarded. Shakespeare is far from silent on the topic: in *King Lear*, he has Edgar threaten Gloucester with the miseries of visual vertigo (factitious, to boot), while Benvolio's advice to Romeo in *Romeo and Juliet*, '…turn giddy, and be holp by backward turning…', would do equally well as a remedy for lovesickness or positional vertigo. Patients, by and large, do not know what they mean by dizziness, which would not be so bad if doctorswere good at finding out. In truth, however, the complaint of dizziness is still apt to make medical hearts sink much as they must have done in Hippocrates' time.

The reasons for this are all too obvious. As a presenting symptom, dizziness is not only among the most notoriously difficult to describe, it comes trailing in its wake a fearsome retinue of anatomy and physiology – abstruse, intricate and precise. The vestibular apparatus is yoked to the brainstem, cerebellum and eye muscles, territory where even neurologists tread with trepidation. And it does not stop with the central nervous system. A host of diseases affecting quite different and remote organ systems can just as well produce it. Added to this is the well-known propensity of dizziness to send patients mad, encouraging spirited and probably futile debate as to which came first: the psyche or the balance organs. What is needed is a road map to see our hapless patients and their medical attendants safely between the Hill of Difficulty and the Slough of Despond. Fortunately, such a map is at hand, in the form of Adolfo Bronstein's and Thomas Lempert's book.

The book is one of a burgeoning family of Cambridge Clinical Guides, and bodes well for the series as a whole. It begins with a clear and concise review of the essential anatomy and physiology, and core examination techniques. This gives the authors the opportunity to anticipate and debunk some of the standard excuses offered by busy clinicians for not properly assessing dizzy patients in clinic: no longer will a badly positioned couch get you off the hook! After this initial scene setting, Bronstein and Lempert wisely elect to pursue a symptom-led approach (after all, patients do not come along to clinic neatly labelled with a diagnosis, as many a weightier