

Book reviews

EDITED BY SIDNEY CROWN, FEMI OYEBODE and ROSALIND RAMSAY

Schizophrenia (2nd edn)

Edited by Steven R. Hirsch & Daniel R. Weinberger. Oxford: Blackwell. 2003. 768 pp. £89.50 (hb). ISBN 0 632 06388 2

Eight years have passed since the first edition of this scholarly and definitive compendium of our knowledge of schizophrenia. I am not a psychiatrist, and my main credential for passing judgement on the book is sympathy for medical scientists working on an intractable problem, even if it is not in my own field. It is also an advantage in that a lay reviewer is in a good position to judge the clarity of the text and the persuasiveness of the arguments. Like its predecessor, the book succeeds superbly in the task of presenting the evidence rationally and with an agreeable preference for plain words rather than psychobabble. A highly commendable attribute is the full explanation of the scientific principles in areas such as molecular genetics, which characterise so much of the research effort of the intervening years. The plain black-and-white illustrations work surprisingly well in an era dominated by high-tech presentation, and remind readers that true masters of their craft need not rely on such adjuncts.

Essentially for the success of a new edition, the editors fulfil their intention that the revised text should incorporate the basic and clinical advances in this field since the first edition. Sensibly for a book to be consulted by readers of disparate interests it retains the original framework of four main sections: descriptive aspects, biological aspects, physical treatments and psychosocial aspects. The historical introduction is indispensable in an age in which so many students seem to believe that the history of their discipline began in the most recent issue of the relevant journal. It was a masterly touch in a book of this nature to cite John Locke's *Essay Concerning Human Understanding*, even if it was a little disconcerting to see 1959 given as the reference year (p. 3) although the reference 'to a later edition' is accurate. Of course, the reader's expectation is for new, incisive

information about aetiology and pathogenesis, leading to therapeutic efficacy. Regrettably but understandably, the authors have collated and analysed a mass of undoubtedly accurate observations which fail to convey understanding in the sense that Locke would have used the word. This is the fault of inscrutable nature, not obtuse scientists.

Uncertainty still seemingly extends even to the most basic issue, namely the definition of schizophrenia. In their chapter on the secondary schizophrenias, Hyde & Lewis state that 'schizophrenia is a behavioural disorder that is a diagnosis of exclusion'. Where does this leave Wing & Agrawal's painstaking and meticulous classification of the disease (or diseases), and Jablensky's conclusion (p. 223) that 'the clinical syndrome of schizophrenia is robust and can be identified reliably in different populations'? The section on biological aspects emphasises the conundrums concerning causes and effects. A host of tantalising clues appear in Jablensky's chapter 'The epidemiological horizon', complemented by and on occasion reiterated in McGrath & Murray's contribution on risk factors. Even 'stress', affirm Bebbington & Kuipers, can induce the disorder. Alas, psychiatrists still await the denouement when a latter-day Belgian detective makes sense of all these clues. As is so often the situation with chronic disorders, detailed genetic studies (reviewed in the chapter by Riley, Asherson & McGuffin on conventional linkage studies and in Egan, Leboyer & Weinberger's contribution on intermediate phenotypes) indicate polygenic risk factors, which may well be evidence of disease heterogeneity rather than multiple determinant loci.

The crucial role of dopamine in schizophrenia has been tacitly accepted by specialists and general observers. Indeed, in discussing drug treatment, Miyamoto *et al* assert that 'evidence has accumulated to suggest an important role for D₁-like dopamine receptors in the pathophysiology of schizophrenia' (p. 451). Yet O'Flynn and colleagues assure us that 'the dopamine

hypothesis... has long been the cornerstone of research into the pathophysiology of schizophrenia [but] has failed to provide a satisfactory explanation for the pathogenesis of schizophrenia' (pp. 89–90). Furthermore, in their review of neurochemical issues, Moghaddam & Krystal conclude that 'no single heuristic model involving one or two neurotransmitter systems can explain the pathophysiology of this syndrome'. Perhaps one's hope of progress is implicit in the article on brain imaging by Liddle & Pantelis. Consistent structural changes may give clues to the site – or, more probably, sites – of dysfunction. However, to an outsider it seems likely that understanding the malfunctioning brain depends on elucidating the most formidable problem in basic physiology, namely the way the normal brain works.

The section on treatment is comprehensive, so much so that it includes a 34-page discussion of the time-hallowed use of electroconvulsive therapy, about which there is still 'a lack of consensus' (p. 542) and for which its author (Sackeim) concedes that there is as yet no scientific rationale. A masterly advance on the first edition is a greatly expanded discussion of the practicalities and social implications of caring for patients with schizophrenia. It is enhanced by moving accounts from patients themselves; 'Grace's' remarks about her fear of drug side-effects is a telling comment on the continuing limitations of current treatment. There can be no better incentive for young scientists and clinicians seeking applications for their talents than to read this section.

This book faithfully and comprehensively recounts the current situation presented in all aspects by schizophrenia. However, the authors and editors fail to assert the authority warranted by their knowledge of their subject, in that some 190 of the book's 768 pages are devoted to references. Search technology ensures that even the tyro can amass a daunting array of seemingly legitimate information. This exercise does not confer understanding. It is the responsibility of the expert to weed the fields of indigestible superfluity, or at least to indicate the most prized blooms. Nevertheless, this book is a definitive, pleasingly readable and nicely presented source of information for anyone who wants to understand the whole problem or different aspects of it. The *Shorter Oxford English Dictionary* gives one definition of the word 'heuristic' (used by Moghaddam & Krystal,

as quoted earlier) as 'a system of education in which the pupil is trained to find out things for himself'. How apposite as a recommendation to read this book! An aphorism of the late Professor Eric Bywaters, doyen of rheumatologists, is that one consults textbooks to find out the things that no one knows.

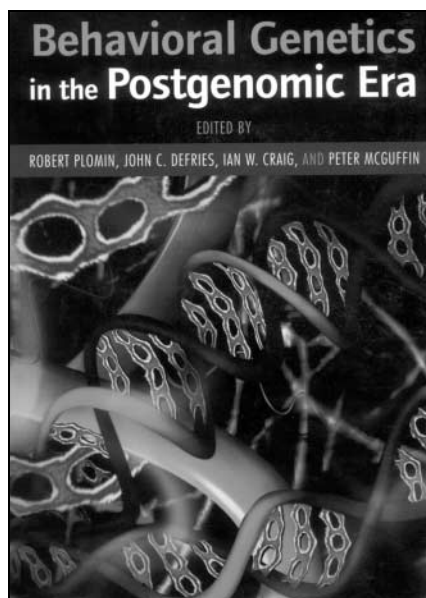
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Behavioral Genetics in the Postgenomic Era

Edited by Robert Plomin, John C. DeFries, Ian W. Craig & Peter McGuffin.

Washington, DC: American Psychological Association. 2003. 608 pp. US\$49.95 (members), \$59.95 (non-members) (hb). ISBN 1 55798 926 5

The closing years of the 20th century saw molecular genetic approaches prove successful in identifying genes involved in a large number of rare disorders and traits that show a simple, Mendelian pattern of inheritance. In the opening years of the new millennium human geneticists are applying the powerful approaches and knowledge emanating from the human genome project to tackle the more challenging problem of genetically complex disorders and traits – common (or universal) characteristics that show substantial variation within human populations, and that do not have a simple pattern of inheritance; these are disorders and traits that are likely to follow some form of multifactorial model in which a combination of susceptibility genes and environmental factors act and interact to determine the expression of the trait. Most clinical psychiatrists will immediately recognise that many psychiatric disorders fall into this category; furthermore, so do most normal behavioural traits (including general and specific cognitive abilities and personality variables). As the media frequently remind us, the human genome project continues to deliver increasingly powerful resources and tools that can be used to investigate such disorders – including a working draft of the sequence of DNA in the human genome, detailed catalogues of the common variants in the DNA sequence and increasing numbers of annotated genes (i.e. identified DNA sequences



that code for genes for which the expression profile and protein product are known and characterised). This will make the coming years an exciting time for all researchers and clinicians interested in psychiatric and behavioural disorders, because application of this knowledge will lead to the identification of genes and environmental factors influencing these traits.

The publication of *Behavioral Genetics in the Postgenomic Era* is therefore timely. This nicely presented, edited volume arose from a meeting coordinated by the Wellcome Trust: the authors include many of the leading clinical and basic scientists within the field of behavioural genetics, and its scope appropriately represents current research within this area. According to the flyleaf, this book sets itself the goal of assessing the current status and likely future directions in genetic research on behaviour. This goal is met within its 600 pages, and a broad range of theoretical and trait-specific topics are covered. The book focuses on behavioural traits rather than on psychiatric disorders. It is arranged in 26 chapters, divided into nine sections. The first six chapters provide orientation and theoretical background information regarding molecular, statistical and design aspects relevant to behavioural genetics. This is followed by sections on learning and memory in mice, human cognitive abilities, cognitive disabilities, psychopharmacology, personality, and a limited coverage of psychopathologic topics – chapters on attention-deficit hyperactivity disorder, schizophrenia, mood disorders and dementia. A helpful glossary is included for the non-specialist.

A minor criticism is that the style and degree of specialisation of chapters are variable; consequently it will be easier to use the book for reference to individual topics rather than to read it sequentially as an overview. Undoubtedly, it would be an excellent addition to any psychiatric library. Consistent with the title, the coverage of the main psychiatric disorders is relatively limited, and readers mainly interested in psychiatric genetics will find more extensive coverage and focus on disorders in *Psychiatric Genetics and Genomics* (McGuffin *et al*, 2002).

McGuffin, P., Owen, M. J. & Gottesman, I. I. (eds) (2002) *Psychiatric Genetics and Genomics*. Oxford: Oxford University Press.

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Pharmacogenetics of Psychotropic Drugs

Edited by Bernard Lerer. Cambridge: Cambridge University Press. 2002. 446 pp. £95 (hb). ISBN 0 521 80617 8

Students and teachers of psychopharmacology have a sense that the most difficult topic to teach and to remember is that of pharmacokinetics. Since many aspects of pharmacokinetics are genetically determined, I approached this book with hope of enlightenment. New discoveries and techniques in molecular genetics should eventually cast light on such questions as why individual patients respond (or do not respond) to drugs, and why some experience more side-effects than others.

The editor's introduction gives a compelling account of the potential importance of pharmacogenetics, but also sounds an ominous note of caution about the complexity of the subject. More than a million single-nucleotide polymorphisms have been discovered that might be relevant. Many of the claimed associations of allelic variations with drug responses have failed attempts at replication. Psychopharmacology is likely to be more difficult than other branches of therapeutics to disentangle through molecular genetics because of the difficulty in identifying drug responders from placebo