

Book reviews

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Anxiolytics

Edited by M. Briley & D. Nutt.
Berlin: Birkhäuser. 2000. 192 pp.
DM 188 (hb). ISBN 3 7643 6032 1

The drug treatment of anxiety, if not exactly in the doldrums, is being propelled by a very light wind indeed. Despite much activity in the research department, there is little evidence of major clinical gains being made with any of the new compounds. This book is one of a series, extravagantly entitled *Milestones in Drug Therapy*, and, despite having little to shout about, is welcome to illustrate the poverty of advance. The contributors range across three continents and include luminaries such as Rudolf Hoehn-Saric, Graham Burrows, David Baldwin, Stephen Stahl and Trevor Norman. Their contributions are well-knitted by Briley & Nutt, who introduce the book with the dilemma of the therapist wishing to treat anxiety with drugs, that "there are few clinically satisfactory alternatives to the benzodiazepines for the treatment of acute anxiety" and other drugs for more chronic anxiety "are still far from being ideal".

The chapters that follow give a good indication of why the wind no longer fills the sails of the anxiolytic barque. For the vessel to keep scudding across the waves you need a steady and reliable wind with no sudden changes in direction, a combination of excellent efficacy (anxiolysis implies a penicillin-like destruction of anxiety) and negligible adverse effects. We read that the powerful gusts created by benzodiazepines provide efficacy at the expense of potential dependence, that the absence of dependence with buspirone and other 5-HT_{1A} agonists is associated with uncertain efficacy despite "very active clinical research", that the reasonably steady wind generated by tricyclic antidepressants and selective serotonin reuptake inhibitors takes rather too long to fill the sails, and that neuropeptides, despite their revolutionary design, have hardly got our barque out of port.

It is sad to report that all this was known some years ago, and recent research has only clarified pharmacological and

pharmacokinetic details. Two chapters on 5-HT_{2C} receptor agonists and drugs that are subtype-selective with regard to benzodiazepine and GABA receptors give some possibilities for development, but the data are not inspiring. Where development might have led to real improvements, such as the introduction of reversible monoamine oxidase inhibitors (RIMAs) in place of irreversible ('suicide') inhibitors, we really have only a pale imitation of the original impressive anti-anxiety effects of phenelzine and iproniazid, and it is a shame that this therapeutic line has not been pursued more actively.

One major omission is discussion about the anxiolytic properties of venlafaxine and related selective serotonin and noradrenaline reuptake inhibitors. These may have more powerful anti-anxiety effects than other antidepressants and really deserve a separate chapter in a book of this nature. We surely need something to get the ship moving again, and while it is becalmed the psychological treatment alternatives are advancing rapidly, powered not only by natural winds but by the hearty puffs of our consumer society.

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The Neuropathology of Schizophrenia: Progress and Interpretation

Edited by Paul J. Harrison & Gareth W. Roberts. Oxford: Oxford University Press. 2000. 374 pp. £65.00 (hb). ISBN 0 19 262907 7

The subtitle of this book sums up the situation well. Immense progress has been made in delineating an association between schizophrenia and a multitude of neuropathological anomalies, yet much of the evidence is

inconclusive and the essential abnormality remains unknown. The excellent review of structural brain imaging studies by Hopkins & Lewis in Chapter 1 concludes that the median decrease in brain size in schizophrenia is 3%. Despite the fact that a decrease of brain tissue volume is reliably found in groups of patients, gross brain structure in most patients is within the normal range. A variety of microscopic anomalies have been reported, but too few of the observations have been replicated. The balance of evidence does not demonstrate a widespread loss of neurons, although there is tantalising evidence for loss of particular groups of neurons, such as interneurons from the anterior cingulate cortex. There are also many reports of abnormalities of the microstructural components that support neurotransmission (axons, synapses and synaptic proteins) but different investigators report different anomalies at different cerebral locations.

In the foreword, Janice Stevens expresses the hope that the studies described in the book might be a springboard for segregating patients into pathologically distinct cohorts. I remain sceptical that this will prove a fruitful path. The magnitude of virtually all reported anomalies in schizophrenia reported in this book, whether it be size of brain ventricles, density of neurons in the cingulate cortex or concentration of synaptic proteins, is distributed unimodally. This observation supports the alternative view that a variety of different pathoplastic factors generate multiple dimensions of variation in brain structure and function in schizophrenia. But this formulation

