Book reviews

In reaching his conclusions nearly every author who has graced the field of neurobiology is quoted, and a dazzling array of ideas are presented.

I would agree with the comments on the back cover by Albert Galaburda of Harvard, "This is a marvellous book,..."

M TRIMBLE

GABA and Mood Disorders: Experimental and Clinical Research (LERS Monograph Series Vol 4). Edited by G Bartholini, KG Lloyd, PL Morselli. (Pp 240; \$32.50.) New York: Raven Press, 1985.

For 25 years manipulation of monoaminergic synaptic function has provided the dominant pharmacological approach to the treatment of affective disorders. Inhibition of the uptake and further metabolism of noradrenaline or serotonin initially seemed to be important mechanisms of action of antidepressant drugs. However the time-course of these effects clearly does not correspond to the time course of therapeutic action of the drugs. More recent discoveries concerning receptor changes in rat brain following subacute administration of antidepressants have appeared likely to resolve this problem. Thus after 6–12 days "treatment" there is down-regulation of β -adrenoceptors, with desensitisation of the β -adrenoceptor-coupled adenylate cyclase, down-regulation of 5HT₂ receptors and biphasic changes in α_2 -adrenoceptors. However, many anomalous or contradictory findings have emerged making a comprehensive explanation of the mechanism of action of antidepressant drugs in terms of long-term changes in monoaminergic receptors untenable (for example, maprotiline does not down-regulate β -adrenoceptors and ECT produces an up-regulation in 5HT₂ receptors and function).

These considerations and some novel basic findings have lead to a renewed interest in the possible involvement of GABA in the aetiology and pharmacological management of affective disorders. Perhaps the most intriguing novel observation reported in this volume is the up-regulation of GABA_B (baclofen-sensitive) receptors in hippocampus and cortex following subacute administration of electroshock, or of antidepressant drugs of all major pharmacological types (for example desipramine, amitriptyline, viloxazine, nomifensine and citalopram). This effect is not seen after other psychotropic agents, but it is observed following subacute administration of pro-

gabide or of fengabine, agents thought to act directly or indirectly as GABAmimetics. Evidence from preliminary trials indicating that these compounds are effective antidepressants is presented in the second half of the book. Interestingly the subacute administration of progabide to rats lead to similar changes in 5HT₂ receptors as does repeated electroshock. Fengabine does not produce this effect. The proconvulsant action of antidepressant drugs is a well known clinical problem (both in patients receiving therapeutic doses, and in those taking overdoses). One contribution in this volume attempts to relate this phenomenon to an impairment of GABAergic inhibition. This remains to be established. However, the use of GABAmimetics, such as progabide, as antidepressants should offer a very real advantage in terms of producing an anti-convulsant "side effect".

The remarkable studies of Fred Petty on "learned helplessness" in rats provide evidence for a GABAergic mechanism (in the hippocampus and perhaps also the neocortex and lateral geniculate) in the initiation and prevention of this model of depression. They indicate that desipramine acts through a GABAergic mechanism when preventing learned helplessness.

The GABA related approach to the aetiology and therapy of depression can probably be integrated with the existing knowledge of (and lack of comprehension of) monoaminergic mechanisms. GABAmimetics accelerate the turnover of noradrenaline, and enhance the firing of noradrenergic neurons (probably by specific circuitry acting on the locus coeruleus). GABA agonists and GABA-transaminase inhibitors depress cerebral serotonergic transmission (apparently by a direct action in the nuclei of the dorsal raphe). GABA_B receptors modulate synaptic release of monoamines.

The clinical results reported for progabide and fengabine are somewhat preliminary. Three double blind studies of progabide in comparison with imipramine ($n = 11 + 11$), imipramine ($n = 38 + 37$) or nortriptyline ($n = 9 + 9$) show indistinguishable therapeutic outcomes. The true clinical effectiveness of fengabine can only be guessed at from the seven open studies (total $n = 76$) utilising 3 or 4 weeks of treatment and a variety of dosage schedules. Effects of progabide or fengabine in manic disorders are not reported. The well known studies of Emrich and of Post and colleagues on the antimanic effects of valproate, oxcarbazepine and carbamazepine are summarised. High doses of valproate or car-

bamazepine given acutely to rats reduce GABA turnover, but the exact relationship of changes in GABAergic function to therapeutic effect in mania is unknown.

This volume is beautifully produced. It has been edited to provide a highly coherent and readable text. Indeed the contributions tell a rather too consistent story. Contrary opinions are surprisingly absent. The repeated claims that fengabine is a GABAmimetic are taken on trust, but no evidence for an agonist action of GABA_A or GABA_B receptors is presented.

Synthelabo has rendered a valuable service by organising the meeting reported in this the 4th volume in their special monograph series with Raven Press. Scientists and clinicians are thus enabled to gain a rapid appreciation of current GABA-related approaches to understanding and treating depressive disorders. Their experience with monoamine theories will have taught them to temper their enthusiasm with appropriate scepticism.

BS MELDRUM

Upper Motor Neuron Functions and Dysfunctions. Recent Achievements in Restorative Neurology Series Volume 1. Edited by Sir John Eccles and Milan R Dimitrijevic. (Pp 346; £87.20.) Basel: S Karger AG, 1985.

This book is based on the proceedings of a workshop held in Houston, Texas in October 1982, "to review achievements in restorative procedures that could modify the impaired functions in chronic neurological diseases". It contains an uneven mixture of basic science and clinical topics that is not restricted to upper motor neuron functions. Some authors present the results of their own work in detail while others have offered reviews, some brief and others wide-ranging and authoritative. Many of the clinical papers are disappointingly superficial, and the early part of the book records a number of procedures used for physiological testing and improving function in various brain and spinal cord disorders, in which claims of clinical usefulness are made but minimal evidence presented. This gives the reader a useful review of the range of techniques that have been tried but little feeling for their clinical value.

Some chapters stand out as particularly good, such as Jacquelin Perry's on the analysis that should be undertaken by orthopaedic surgeons before operating on spastic

lower limbs, and Evert Knutsson's on the different types of spastic restraint. The basic science contributions are more impressive, and include several excellent chapters on regeneration in the nervous system as well as an interesting account of the prevention of muscle atrophy after denervation by direct electrical stimulation in the rat.

This is a very expensive book which few individuals will wish to buy, but it is a useful source of ideas and references which would be valuable in any teaching hospital, medical school or basic science library.

DL MCLELLAN

Neurological Disturbances in Diabetes Mellitus. Revised 2nd Edition. By VM Prikhozhan. (Pp 528; £14.95.) Eastbourne: Bailliere Tindall/WB Saunders, 1985.

This book is mainly of interest in giving an insight into the clinical practice of medicine in Russia, since unfortunately our Russian colleagues are all too infrequently represented at international gatherings, and there is often difficulty in communication when they are there. It contains an obsessional documentation of all the neurological complications that can occur in diabetes. There is also an obsession with classification and wrangles over nomenclature. It is surprising to read that 30 to 39% of children born to diabetic mothers are mentally retarded and one wonders at the methods of diagnosis and definitions resulting in this statement. As a reminder that neurology is still a branch of neuropsychiatry in Russia, the importance of psychological factors in the precipitation of diabetes and the importance of psychotherapy in its management are discussed.

Although various theories of the aetiology of diabetic neuropathy that are under discussion in the western world, the sorbitol-myoinositol- Na^+K^+ ATPase story, the importance of intraneural microangiopathy and possible hypoxia of nerves are mentioned, they are given less prominence than by experts elsewhere and the experimental evidence which we consider relevant to this discussion is rarely cited.

In the section on therapy a list of spas providing physical treatment for diabetes is given with the particular characteristics of the water and mud available. The vogue of aldose reductase inhibition currently so popular in the west has not yet reached Russia. Vitamin therapy is given some prominence.

The book is very reasonably priced and is

recommended to anyone proposing to visit Russia or have contact with Russian colleagues to give a starting point for a dialogue.

PAMELA M LE QUESNE

Optic Neuritis. Edited by RF Hess and GT Plant. (Pp 310; £35.00.) Cambridge: Cambridge University Press, 1986.

Is it possible to enjoy reading a book and yet not recommend it?

This volume is based on a symposium held in November 1984 on the occasion of the centenary of Nettleship's publication on *Retroocular Neuritis*, an abridged version of which forms the appendix. There are 13 chapters, only two of which are clinically orientated (an excellent one by Heron on differential diagnosis, the other being on optic neuritis of childhood). There are two chapters on neurophysiology, two on psychophysics, two on electrophysiology and two on virus induced demyelination in the mouse optic nerve, all of a very high scientific calibre. There are first class chapters on pathogenesis (McDonald) and immunology (Compston) but these would sit as happily in a book entitled *Multiple Sclerosis*.

The final chapter entitled "The Interior Journey and Beyond: An Artist's view of Optic Neuritis" is intriguing. It begins with a quote from Robert Louis Stevenson's *Travels with a Donkey*: "For my part I travel not to go anywhere but to go"—not an inappropriate summary for this book with its idiosyncratic eclecticism of choice of topics that is more likely to appeal to physiologists than clinical neurologists. The bare title of *Optic Neuritis* is misleading and perhaps a qualifying sub-heading should have been added. For these reasons, the answer to the question at the beginning of the review has to be answered in the affirmative.

F CLIFFORD ROSE

Molecular Mechanisms of Ischemic Brain Damage (*Progress in Brain Research Vol 63*) Edited by K Kogure, K-A Hossmann, BK Siesjo, FA Welsh. (Pp 264; \$79.75.) Amsterdam: Elsevier Biomedical Press, 1985.

Hitherto, basic research in cerebrovascular disease has concentrated mainly on cerebral

blood flow and on the metabolism of oxygen and glucose. This led in turn to work on the disturbance of acid-base balance, ATP and cations produced by ischaemia. Despite immense effort and great advance in knowledge a therapeutic break-through has not followed. Workers are therefore turning to the study of cellular mechanisms in ischaemia in their search for the key.

One example will serve to emphasise the importance of this approach. The major role of mitochondria is to synthesise ATP in aerobic cells yet, when presented with free CA^{2+} $10\text{ }\mu\text{g}$ or more, isolated mitochondria cease to synthesise ATP and accumulate the cation. This is observed in isolated mitochondria. What is happening *in vivo*? All neurons do not exhibit the same susceptibility to ischaemia. They differ at the neurochemical, microphysiological and molecular levels.

The present volume presents a valuable survey of the present state of knowledge in the field. The status of the four editors and of many of the contributors has ensured that the volume is succinct, readable and authoritative. It will be of great value not only to those working at the molecular level but to those with a broader interest in cerebral ischaemia who wish to learn in a relatively painless fashion of the present state of the art.

JOHN MARSHALL

Notice

Ninth International Congress of Neurological Surgery. This will be held in New Delhi, India, 8–13th October 1989. Information may be obtained from Dr AK Banerji, Organising Secretary, Post Box No 4543, New Delhi 110016.