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


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 adenylyl cyclase, down-regulation of 5HT₂ receptors and biphasic changes in 5₂-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, maproline 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 GABA₆ (baclofen-sensitive) receptors in hippocampus and cortex following subacute administration of electroshock, or of antidepressant drugs of all major pharmacological types (for example desipramine, amitryptiline, vloxazine, nomifensine and citalopram). This effect is not seen after other psychotropic agents, but it is observed following subacute administration of pro- 

gebide or of fengabine, agents thought to act directly or indirectly as GABAmimetics. Evidence from preliminary trials indicating that these compounds are effective anti-depressants 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 anti-depressant 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. GABA-mimetics 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 serotoninergic transmission (apparently by a direct action in the nuclei of the dorsal raphe). GABA₆ 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 nortryptiline (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 GABA-mimetic are taken on trust, but no evidence for an agonist action of GABA₆ or GABA₇ 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


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 Jacqueline Perry's on the analysis that should be undertaken by orthopaedic surgeons before operating on spastic