Book review

Mitochondrial inhibitors and neurodegenerative disorders, by P.R. Sanberg, H. Nishino, C.V. Borlongon, (eds.), Humana Press, New Jersey, 1999. ISBN 0-896-03805-X, pp. 313, \$125.00.

It is only in the past one or two decades that the essential role of the mitochondrion in the pathogenesis of neurodegenerative diseases has been recognised. In the 1980's the effects of MPTP, an inadvertent contaminant of a "designer" drug of abuse, did much to stimulate interest in the role of mitochondrial electron transport disruption in neurodegenerative disease. MPTP, following its oxidation to MPP⁺, is taken up into dopaminergic neurons to inhibit oxidative phosphorylation at complex I of the electron transport chain to induce an irreversible parkinsonian syndrome. These observations did much to re-stimulate biological research into the aetiologies and possible pathogenic mechanisms of Parkinson's disease.

Other neurotoxins have long been known to have effects on mitochondrial metabolism, notably heavy metals including mercury and manganese. Recently attention has also turned to other inhibitors of mitochondrial function and their possible contribution to experimental models, if not to the pathogenesis, of other neurodegenerative diseases. One of these is 3-nitropropionic acid (3NP), a potent inhibitor of complex II (succinic dehydrogenase) found naturally in a fungal contaminant of sugar cane. 3NP, particularly when introduced systemically, has been shown to induce lesions of the striatum in animals and humans. This has, of course, made 3NP useful in producing animal models of Huntington's disease (HD), in which a degenerative loss of striatal neurons underlies the dyskinetic motor symptoms. And despite the undoubted advances provided by transgenic and related models following identification of the

HD gene, systemic 3NP toxicity still provides the best animal correlate of the disease.

However, it is perhaps debatable whether 3NP deserves quite the number of chapters in this multi-author book which address its mechanisms and effects. A few other mitochondrial neurotoxicity models of neurodegenerative diseases have been covered; these include malonate (another striatal neurotoxin) and MPTP. Hypoxia and azide are also discussed as are, interestingly, the effects of aging and metabolic challenges on membrane components.

A stronger editorial influence would have been valuable to provide better integration of the component chapters; it is frustrating to re-read, at the beginning of most chapters on 3NP, the description of its human neurotoxicity following ingestion of mildewed sugarcane. However the book is well-produced with most chapters providing useful figures and a comprehensive literature survey. The content certainly reflects much of the interests and research directions of the editors; nevertheless a breadth of technique and approach is described, from mammalian models of disease, in which therapeutic neuronal transplantation, neuroprotective strategies and behavioural consequences can be tested, to basic neurochemistry and tissue culture models.

One would have to have a very specialised enthusiasm for 3NP neurotoxicity to buy this book – and I would guess that the authorship accounts for the majority of 3NP aficionados. For the other neuroscientists or neurologists who recognise the growing importance of mitochondrial dysfunction in neurology, this book provides a broad, if imbalanced, overview of current research approaches.

G.P. Reynolds