Book review

The GABA Receptors (2nd edition) edited by S.J. Enna and N.G. Bowery, Humance, 1997. $125 (x + 332 pages) ISBN 0 89603 458 5

This timely new edition gives a comprehensive overview of the substantial developments made in the understanding of the physiology and pharmacology of GABA-receptors since the first edition in 1983. It is now clear that GABA-receptors exist as many different subtypes, which are grouped into $GABA_A$, $GABA_B$ and $GABA_C$ receptors, the latter in reality being a distinctive subtype of the $GABA_A$ receptor with a unique pharmacology. The book is organized around this subdivision and provides a thorough treatment for each receptor type.

The GABA Receptors gives a very thorough account of the way in which $GABA_A$ receptor subtypes are sculptured from the potential 17 known subunits, to cater for the specific functional requirements of distinct neuronal circuits. There is a seemingly never-ending list of potential modulators at these receptors, to an extent that somewhat tests any faith in distinct modulatory sites on particular subunits. Nevertheless, the actions of benzodiazepines and various modulators at these sites, as well as anaesthetic actions on $GABA_A$ receptors, are well covered. It is a pity that the section on the transport systems for GABA reuptake does not include an explicit account of uptake inhibitors and the particular transporters (GAT 1–4) they act on. Some of this information is found elsewhere, but it is an oversight. Prof. Krogsgaard-Larsen provides an in-depth account of the contributions of medicinal chemistry to the analysis and understanding of $GABA_A$ receptors, much of which has come from his own work around the isoxazoles.

$GABA_B$ receptors have come a long way from the earliest demonstration by Norman Bowery, some 20 years ago, that autonomic terminals are modulated through bicuculline-insensitive GABA-receptors that are clearly not of the $GABA_A$ type. His subsequent demonstration of this $GABA_B$ receptor in the central nervous system provided a considerable challenge to neurochemists and neurophysiologists. How well this challenge has been met is clearly brought out in three chapters on the functional pharmacology, electrophysiology and neurochemistry of the $GABA_B$ receptor type. It is both puzzling and to a degree disappointing that molecular biology has not proved as bountiful in the $GABA_B$ field as it has with the $GABA_A$–$GABA_C$ group. Indeed $GABA_B$ receptors have not yet been sequenced, which is an impediment in the identification of suggested subtypes of this receptor. It also makes the related medicinal chemistry more difficult, despite the spectacularly successful development of highly potent $GABA_B$ agonists and antagonists by the Ciba-Geigy chemists, who have provided a splendid chapter on the relevant medicinal chemistry.

Perforce, the chapter on $GABA_C$ receptors is less developed, as this topic is only now at the stage that $GABA_B$ receptors had reached about ten years ago. Nevertheless, the present knowledge of the $GABA_A$–$GABA_C$ duo provides a fine illustration of the power and impact of molecular biology in modern pharmacology.

Overall, the book provides a good read for all who are interested in the medicinal chemistry and pharmacology of these important receptors.

David I.B. Kerr
Department of Anaesthesia & Intensive Care
The University of Adelaide
Adelaide, South Australia 5005