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Guest Editors' Note

GABA-A receptors are the major inhibitory transmitter receptors in the mammalian central nervous system. They are chloride ion channels that can be opened by γ-aminobutyric acid (GABA) and are the targets of action of a variety of pharmacologically and clinically important drugs. To date, 16 human GABA-A receptor cDNAs have been cloned. However, these bare facts do not do justice to the major discoveries and insights into brain function that research on these receptors, and particularly their subtypes, have provided over the last 20 years. Researchers in this field have embraced new and emerging technologies to precisely delineate the mechanism of action of GABA-A receptors which have suggested new treatments for epilepsy, anxiety, sleep disturbance, cognition impairment and psychosis. In doing so, their work on the role of GABA-A receptor subtypes in modulating neurotransmission and their consequence influence on behaviour have provided some of the most elegant research produced in the field of neuroscience in the last 10 years. Consequently, it has been a particular pleasure for us to edit this special edition of PBB on GABA-A receptors which highlights some of the best research in this field by those who have dedicated much of their career to it. Studies employing genetic manipulation of different GABA-A receptor subunits in mice (Dixon et al and Morris et al) or different mouse strains (Mathiasen et al) in combination with standard benzodiazepines and subtype-selective drugs yield interesting insights into the mechanism of action of anxiolytic drugs (reviewed by Reynolds). Lovick extends this topic by examining the changes in anxiety levels in females across the oestrus cycle and demonstrates changing expression profiles GABA-A receptor subtypes. Additionally, Bailey et al describe a human volunteer experimental medicine model in which the effects of subtype-selective GABA-A drugs may be explored and perhaps provide an insight into the development and maintenance of anxiety in humans. A review by Mohler et al and experimental evidence from Morris et al highlights the interactions of the GABA system with other neurotransmitter systems such as dopamine and glycine and how these can modulate behaviour, including in disease states such as psychoses. These themes are further explored by Kohut & Ator and Licata & Rowlett who probe the abuse potential of benzodiazepines in primates in a series of experiments designed to determine whether particular subunits mediate the abuse potential of benzodiazepines. GABA-A receptors also mediate the effects of alcohol, a drug that is frequently abused. Lobo & Harris and Enoch review which GABA-A receptor subtypes mediate the many and various effects of alcohol and their role in the development of alcoholism. Bonin & Orser discuss another area of GABA-A receptor function: the role of different subtypes in mediating general anaesthesia. Finally, GABA-A receptor subtypes also played a role in the discovery of a new use for an old drug, gaboxadol. Ebert describes the interesting hypnotic profile of gaboxadol and the lack of tolerance to sleep EEG and its sedative effects. We would like to thank Prof. Dai Stephens for inviting us to be guest editors and extend our sincere gratitude to all of the authors who have contributed to this special edition of PBB.

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