

agencies that deal with the topic of advertising prescription drugs. Sales representatives who work for major pharmaceutical companies should consider reading this book, as it will give them a better understanding of the issues that must be considered before they are supplied with the promotional materials that are necessary for them to effectively do their job. In contrast, individuals not involved with regulatory affairs, drug promotion, or drug advertising (such as scientists performing basic drug research) will likely find the book to be too dry to hold their interest. Unfortunately, there is little that can be done to make FDA regulations exciting and interesting to individuals not already involved in these areas.

Reviewed by:
William E. Heydorn,
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PSYCHOPHARMACOLOGY: The Fourth Generation of Progress

Floyd E. Bloom and
David J. Kupfer, Eds.
Raven Press, New York, NY, 1995.
ISBN 078170166X, \$175.00.

The Fourth Edition of this popular reference work is a massive compilation of information in both the basic science and clinical applications of psychopharmacology. Many of the 163 chapters have helpful summaries, diagrams, explicit attempts to link preclinical and clinical findings, and prognoses for further progress. However, as observed by Plotsky et al. (Chapter 84), the basic science has provided us with "an embarrassment of riches" that have not yet been integrated into the concepts of normal and abnormal CNS function. This volume, with its wealth of accessible summaries, should promote such interactions.

The preclinical section, edited and summarized (Chapter 1) by Floyd Bloom, is divided into three subsections. The first is a critical analysis of methods, which provides helpful summaries of molecular genetics, electrophysiology and behavioral techniques. Not only are the techniques described, but their advantages and disadvantages are summarized.

The major thrust of this section consists of reviews of the amino acid, amine and peptide neurotransmitters. These reviews range from integrated, stimulating conceptual pro-

gressions to comprehensive, but relatively shallow, summaries of results.

Some of the conceptual narratives are especially well-crafted. For example, the review of dopamine biochemical pharmacology by Roth and Elsworth (Chapter 21) integrates a wide range of data into a systematic comparison of the diverse mesotelencephalic projections; it also suggests means of exploiting this diversity in the quest for more specific drug treatments. Another engaging chapter, "Serotonin and Behavior" (Chapter 41, by Jacobs and Fornal) immediately catches the readers' interest: "Serotonin is an enigma. It is at once implicated in virtually everything, but responsible for nothing." The authors present primarily electrophysiological evidence suggesting that widely projecting serotonin neurons facilitate rhythmic movements and inhibit "irrelevant" sensory input.

The review of hypothalamic dopamine systems begins with the surprising statement that diencephalic dopamine neurons outnumber those in the substantia nigra. The authors outline several similarities and differences between these and the more familiar midbrain dopamine neurons. Several chapters review the molecular biology of receptor subtypes and transporters, as well as second messenger systems through suggested clinical implications. In this edition, unlike the previous one, receptor subtypes and cellular effects of neurotransmitters are covered in chapters adjacent to those on the transmitters themselves. This arrangement leads to a more integrated conceptual progression.

In addition to the classical neurotransmitters, several classes of novel putative messenger molecules are reviewed. These include arachidonic acid, nitric oxide, purines, growth factors, and factors produced by proto-oncogenes. Each chapter includes a brief history of the discovery of the molecule's functions, as well as a brief discussion of its numerous known or suspected roles. This section is a reminder of the major conceptual discoveries in the past eight years: none of these molecules was the subject of a chapter in the previous edition. Snyder and Dawson (Chapter 54) observe that one might assume that the nervous system could accomplish its tasks with perhaps as few as two transmitters—one excitatory and one inhibitory. Yet, in recent years, we have discovered not only more horses in the stable, but more stables,

each with numerous inhabitants.

The preclinical section ends with 12 chapters that discuss integrative concepts ranging from energy metabolism, development and plasticity, to neuroendocrine and neuroimmune interactions, stress, drug addiction, sexual behavior and animal models of psychiatric disorders. These are useful overviews that draw together preclinical findings related to specific problems that are then further elaborated in the clinical section.

The clinical section, edited and introduced (Chapter 70) by David Kupfer, is divided into reviews of methods, discussions of psychiatric disorders and presentations of integrative concepts. The methods section includes discussions of classification of disorders, treatment strategies, pharmacokinetics and various types of imaging, electrophysiological and magnetic techniques.

Nineteen chapters are devoted to mood disorders; these include discussions of the roles of numerous neurotransmitters, hormones, immune responses and biological rhythms in mood disorders as well as updates on common treatments. Perhaps the most interesting chapters were those summarizing the roles of the various neurotransmitters in affective disorders (Chapters 79 to 82) and interactions with neuropeptides, hormones and the immune system (Chapters 83 to 85).

Eleven chapters cover new developments in schizophrenia, including the proposed roles of dopamine, glutamate and serotonin in its etiology, and updates on its treatment. Most of these were summaries of treatment results or symptomatology. However, the chapter on "Neurodevelopmental Perspectives in Schizophrenia" (Weinberger, Chapter 98) presents especially interesting evidence favoring the recent conceptual shift towards developmental deficits. It also explains how early anomalies might remain relatively unrecognized until adulthood, when schizophrenia is usually diagnosed.

Six chapters on anxiety disorders discuss neuroimaging studies, the role of the serotonin_{1A} receptor, environmental factors and treatments. The chapter on "Anxiety and the Serotonin_{1A} Receptor" (Coplan et al., Chapter 110) stands out as a summary of possible mechanisms differentiating generalized anxiety disorders from panic attacks and obsessive compulsive disorders.

Eleven chapters cover geriatric disorders. These present the genetics,

possible biological mechanisms, neuropsychological assessments, biological and brain imaging markers and treatments of Alzheimer's disease, as well as other geriatric disorders. Additional chapters cover Parkinson's disease, tardive dyskinesia, other neurological and personality disorders, eating, sleep and childhood disorders, and substance abuse. Three chapters on integrative concepts end this section, discussing genetics, multimodal research and statistical methodology.

A final section covers Special Topics, including new techniques for drug design, ethical issues and economics of drug development and treatment. It is not clear why the chapter on violence and aggression is placed here, rather than with the other psychiatric disorders.

In summary, this is indeed a most comprehensive and extremely useful resource for both preclinical and clinical researchers in psychopharmacology. However, it is unlikely that it will serve as a text in many courses, because of its sheer bulk (2002 pages, 11 lbs.) and expense (\$175). On the other hand, at less than 10 cents per page, it may be the bargain of the decade. It is highly recommended for anyone dedicated to research or clinical treatment of psychological disorders.

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ADVANCED COMPUTER-ASSISTED TECHNIQUES IN DRUG DISCOVERY

Hans van de Waterbeemd, Editor
VCH, Basel, 1994.
ISBN 3-527-29248-9, \$140.00

This volume covers 3D quantitative structure-activity relationships, rational use of chemical and sequence databases, advanced statistical techniques, and neural networks and expert systems. While many chapters are not reviews of the subject, but instead emphasize the authors' approach with no reference made to other highly related work, all are well-written and informative.

After an overview by the editor, Pitea et al. discuss chemometrics and molecular modeling to perform 3D QSAR. They illustrate their approach with several examples. Next, David

describes his CoMFA approach, illustrated with calcium channel agonists. Cruciani and Clementi explain GOLPHE, the variable-selection refinement of partial least-squares, and illustrate it with two applications.

Johnson et al. describe using 2D or 3D molecular similarity to select compounds for testing, to prepare structure-activity maps and to display 3D properties. They also describe the mathematical procedures to apply these concepts. Downs and Willett discuss compound selection based on clustering of chemical structure databases. They review clustering methods and provide examples of applications. Lewi and Moereels describe receptor mapping and phylogenetic clustering based on the amino acid sequence of 71 G-protein coupled receptors.

Continuum regression is presented by Malpass et al. as a general technique that encompasses multiple linear regression, partial least squares and principal components regression. They discuss its theoretical basis and its performance compared to the other methods. Dore and Ojasoo present correspondence factorial analysis, which shows the relationships between compounds and their responses in several biological tests, using the affinities of 187 steroids to five different receptors. Rose et al. discuss k-nearest neighbor and single-class discrimination to analyze biologically active compounds surrounded by active compounds in descriptor space. Schaper describes fuzzy adaptive least squares using examples of four different biological end-points. Additionally, Clare discusses alternating conditional expectations in QSAR, which detects the form of nonlinear relationships between properties and bioactivity. Manallack and Livingstone discuss the advantages and disadvantages of neural networks compared to statistical methods. They propose experimental guidelines to prevent overtraining. Lastly, A-Razzak and Glen discuss the artificial intelligence technique of rule induction to discover the relationships between biological activity and chemical properties. They propose it as a complement to conventional statistical and pattern-recognition techniques.

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BRIEFLY NOTED

THE NEUROPHARMACOLOGY OF POLYAMINES

Chris Carter, Editor
Academic Press, London, 1994.
ISBN 0-12-161640-1, \$44.00

The polyamines putrescine, spermine and spermidine are ubiquitous in distribution and function. They have received particular attention for their roles in cell growth and differentiation. These roles have, and will continue to have, major implications for the oncology field. This book, however, deals with the roles of the polyamines in neuropharmacology.

The twelve chapters cover formation and metabolism, transport pathways, neurotransmitter/neuro-modulator function, NMDA receptors, radioligand binding sites, polyamine binding sites, arthropod polyamine toxins, electrophysiology, interaction at neuronal Ca²⁺ channels, roles in cerebral ischemia, brain polyamines and ornithine decarboxylase.

These chapters and the contributing authors provide a useful and comprehensive coverage of the neuronal roles of the polyamines. The book is most timely in light of recent reports that nanomolar concentrations of intracellular polyamines may serve to provide the endogenous voltage-dependent block of K⁺ channels.

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