

Essential Psychopharmacology of Antipsychotics and Mood Stabilizers

Updated from the best-selling second edition of *Essential Psychopharmacology*, in this new book Stephen Stahl has revised the chapters covering antipsychotics and mood stabilizers. New material includes discussion of two new theories about dopaminergic modulation of receptors by new antipsychotic drugs: firstly, the “fast dissociation” (hit and run) hypothesis for how the atypical antipsychotics act, and secondly, a whole new class of antipsychotic agent, known as dopamine system stabilizers, with the prototypical agent aripiprazole. Also covered is the use of anti-convulsant agents to treat manic psychosis and the newest atypical antipsychotic ziprasidone. The antipsychotics chapter has increased by a third, with nearly fifty new images to illustrate the stunning advances in antipsychotic and mood stabilizer treatments since the publication of the second edition. This book will be essential reading for all professionals treating psychosis, and students who need to know the mechanisms of drug actions. CME self-assessment tests are included.

Reviews of *Essential Psychopharmacology*, First Edition

“Essential reading ... I would thoroughly recommend this book to anyone who works with psychotropic drugs – or who has the task of teaching others about them!”

American Journal of Psychiatry

“Firmly grounded in contemporary neuroscience ... an excellent and comprehensive account of the pharmacology of drugs currently used to treat psychiatric disorders.”

Psychological Medicine

“This masterful production will benefit a broad spectrum of readers, from students to knowledgeable and experienced psychopharmacologists.”

Psychiatric Times

“Finally, an elegant and beautiful psychopharmacology text written by a basic scientist who is also a clinician.”

Journal of Clinical Psychiatry

Stephen M. Stahl is Adjunct Professor of Psychiatry at the University of California, San Diego. He has conducted numerous research projects awarded by the National Institute of Mental Health, the Veterans Administration, and the pharmaceutical industry. The author of more than 200 articles and chapters, Dr. Stahl is an internationally recognized clinician, researcher, and teacher in psychiatry with subspecialty expertise in psychopharmacology.

Cambridge University Press

978-0-521-89074-8 - Essential Psychopharmacology of Antipsychotics and Mood Stabilizers

Stephen M. Stahl

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PSYCHOPHARMACOLOGY OF
ANTIPSYCHOTICS AND
MOOD STABILIZERS

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PUBLISHED BY THE PRESS SYNDICATE OF THE UNIVERSITY OF CAMBRIDGE
The Pitt Building, Trumpington Street, Cambridge, United Kingdom

CAMBRIDGE UNIVERSITY PRESS
The Edinburgh Building, Cambridge CB2 2RU, UK
40 West 20th Street, New York, NY 10011-4211, USA
477 Williamstown Road, Port Melbourne, VIC 3207, Australia
Ruiz de Alarcón 13, 28014 Madrid, Spain
Dock House, The Waterfront, Cape Town 8001, South Africa
<http://www.cambridge.org>

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First published 2002

Printed in the United States of America

Typeface Adobe Garamond 10/12 pts *System* QuarkXPress™ [HT]

Library of Congress Cataloging in Publication Data is available

A catalog record for this book is available from the British Library

ISBN 0521 89074 8 paperback

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In memory of Daniel X. Freedman, mentor, colleague, and scientific father.

To Cindy, my wife, best friend and tireless supporter.

To Jennifer and Victoria, my daughters, for their patience and understanding of the demands of authorship.

PREFACE

This book is an update of the two chapters from the second edition of *Essential Psychopharmacology* that deal exclusively with psychosis, schizophrenia, and their treatment with antipsychotic drugs. The knowledge base of psychopharmacology for psychosis and schizophrenia has expanded considerably in the two years since the publication of the second edition of *Essential Psychopharmacology*, and this updated edition attempts to reflect these changes. In most developed countries, antipsychotics have become the highest value therapeutic market, not only for psychiatry, but for medical therapeutics in general. Since prescribers are rapidly expanding their utilization of the newer antipsychotics for the treatment of disorders other than psychosis, such as for the treatment of cognition in Alzheimer disease and for mood stabilization in bipolar disorders, it is particularly important to understand how the drugs categorized here as “antipsychotics” work.

Before discussing what the specific contents of this book have to offer in the area of psychosis and schizophrenia and antipsychotic drugs, it may be useful to point out that this text attempts to present the fundamentals of psychopharmacology in a simplified and readily readable format. Therefore, this material should aid the reader when consulting more sophisticated textbooks as well as the professional literature. The organization of the information here also applies principles of programmed learning for the reader, namely repetition and interaction, which has been shown to enhance retention.

Therefore, it is suggested that novices first approach this text by going through the material from beginning to end, reviewing only the color graphics and the legends for these graphics. Virtually everything covered in the text is also covered in the graphics and icons. Once having gone through all the color graphics in these chapters, it is recommended that the reader then go back to the beginning of the book and read the entire text, reviewing the graphics at the same time. Finally, after the text has been read, the entire book can be rapidly reviewed again merely by reexamining the various color graphics in the book. This use of the materials

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will aid in programmed learning by the use of repetition and interaction with visual learning through graphics. Hopefully, the visual concepts learned by reviewing the graphics will reinforce the written concepts learned from the text. For those of you who are already familiar with psychopharmacology, this book should provide a good review from beginning to end.

The text for this book has been written at a conceptual level rather than at a pragmatic level and includes ideas that are simplifications and rules. Thus, this is not a text for the sophisticated subspecialist in psychopharmacology. Another feature of this book is that it is not extensively referenced to original papers but rather to textbooks and reviews, including several written by the author.

Some of the specific information the reader can expect from this book in the first chapter includes an explanation of psychosis in general, and of the disorder schizophrenia in particular. The various dimensions of symptoms of schizophrenia are discussed as well as the hypotheses for the etiology of schizophrenia, including neurodevelopmental and neurodegenerative theories. Included is an extensive description of two neurotransmitter systems: dopamine and glutamate.

The use of antipsychotic drugs is covered in the second chapter. This includes the classical neuroleptics, more than a dozen agents also known as conventional antipsychotics, and the new so-called “atypical” antipsychotics, as well as a new class of antipsychotic agents termed dopamine system stabilizers. The conventional antipsychotics have been well known for decades, but are falling out of use as modern treatment shifts to the use of atypical antipsychotics. The atypical antipsychotics are rapidly expanding into therapeutic use throughout the world and include the original atypical antipsychotic clozapine, and the newer agents risperidone, olanzapine, quetiapine, and ziprasidone, as well as several other agents in clinical development. The major atypical antipsychotics are differentiated from each other as members of the same class that nevertheless can be distinguished by their efficacies in different symptom dimensions and their side effect profiles. The mechanisms of action of both conventional and atypical antipsychotics are explained here with icons and color graphics, including explanation of two new theories about dopaminergic modulation of receptors by antipsychotics. These include the concept of fast dissociation or “hit and run” actions of atypical antipsychotics on dopamine receptors by atypical antipsychotics, as well as the introduction of a new class of antipsychotic agent, the dopamine system stabilizers, with the prototype aripiprazole. Also examined is the use of anticonvulsant agents as treatments for mania and as adjuncts to the treatment of psychosis and schizophrenia with antipsychotics. Finally, drug metabolism by the cytochrome P450 system and the interaction of these drugs with cholinergic, dopaminergic, and serotonergic neuronal systems are covered.

Best wishes for your first step on your journey into this fascinating field of psychopharmacology.

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