Stahl's Essential Psychopharmacology

Third Edition

Stahl's Essential Psychopharmacology has become the definitive source of information on psychopharmacology and now continues as the established preeminent source of information in its field. This fully revised and expanded third edition enlists advances in neurobiology and recent clinical developments to explain with renewed clarity the concepts underlying drug treatment of psychiatric disorders. Clinical advances in antipsychotic and antidepressant therapy are discussed in detail; new, expanded material includes coverage of sleep disorders, obesity, addiction, chronic pain, and disorders of impulse control. The text also features four new chapters on psychiatric genetics, pain management, treatment of cognitive disorders, and treatment of sleep disorders. The text is also visually enhanced by art that has been increased by 100% and completely redrawn and a layout that has been completely redesigned for increased user friendliness. CME is also offered through questions available on the website of the Neuroscience Education Institute at neiglobal.com. *Stahl's Essential Psychopharmacology,* Third Edition, remains the essential text for students, scientists, psychiatrists, and other mental health professionals.

Stephen M. Stahl is Adjunct Professor of Psychiatry at the University of California at San Diego. He has conducted numerous research projects awarded by the National Institute of Mental Health, the Veterans Administration, and the pharmaceutical industry. Author of more than 350 articles and chapters, Dr. Stahl is an internationally recognized clinician, researcher, and teacher in psychiatry with subspecialty expertise in psychopharmacology.

Stahl's Essential Psychopharmacology

Neuroscientific Basis and Practical Applications

Third Edition

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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.

Contents

Preface to the Third Edition

Stahl's Essential Psychopharmacology in its third edition has doubled in number of words and figures compared with the second edition and has almost quadrupled compared with the first edition. In this period of time, the field of psychopharmacology has experienced incredible growth; it has also experienced a major paradigm shift from a limited focus on neurotransmitters and receptors to an emphasis on brain circuits, neuroimaging, genetics, and signal transduction cascades. The third edition of *Stahl's Essential Psychopharmacology* attempts to reflect this transformation in the field, and elements of this paradigm shift are incorporated into every chapter of this new edition. Other changes in the third edition include discussions about how numerous neurotransmitter systems and their circuits are hypothetically linked to current treatments in psychopharmacology. In recent years, many new drugs have been introduced, and many more are now in clinical testing. These are covered in this new edition.

Specifically, the basic neuroscience section at the beginning of the book has expanded from four chapters in the second edition to eight chapters. The clinical section has expanded from ten chapters to eleven and has been extensively reorganized, rewritten, and illustrated with roughly twice the number of figures in every chapter. However, the didactic style of the first and second editions has not changed and continues in this third edition.

The text is purposely written at a conceptual level rather than a pragmatic level and includes ideas that are simplifications and rules, while sacrificing precision and discussion of exceptions to rules. Thus, this text is not intended for the sophisticated subspecialist in psychopharmacology. Also, this book is not extensively referenced to original papers but rather refers to textbooks, reviews, and a few selected original papers, with only a limited reading list for each chapter. For those of you who are interested in specific prescribing information about the most common 100 or so psychotropic drugs, this information is available in the companion textbook, *Essential Psychopharmacology Prescriber's Guide*.

Now, you also have the option of going to Essential Psychopharmacology Online at www.essentialpsych.org. We are proud to announce the launch of this new website, which is due to premiere in the fall of 2008. This website will allow you to search within the entire Essential Psychopharmacology series that includes not only this third edition of *Stahl's Essential Psychopharmacology* but also *Essential Psychopharmacology Prescriber's Guide*. This site will be updated regularly and should therefore provide an up-to-date source for what you need to know about the essentials of psychopharmacology between publication of subsequent editions of these books.

Much of the new content is based on updated lectures, courses, slides, and articles I have written. Many of the new illustrations are now available as animations on the Neuroscience Education Institute's website, as are the lectures, slides, articles, continuing medical education (CME) credits, tests, certifications, and much more. Explore this interactive reference by visiting the Neuroscience Education Institute's website at www.neiglobal.com. If you are interested in comprehensive materials, you can choose to have access to both websites.

In general, this text attempts to present the fundamentals of psychopharmacology in a simplified and readily readable form. Thus, this material should prepare the reader to consult more sophisticated textbooks as well as the professional literature. The organization of the information 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 review only the color graphics and the legends for these graphics. Virtually everything covered in the text is also covered in the graphics and icons. Next, read the text from the beginning, while reviewing the graphics at the same time. After the text has been read, the entire book can be rapidly reviewed by referring to the various color graphics in the book. Finally, as a member of the Neuroscience Education Institute, you can utilize the content available online at www.neiglobal.com to obtain continuing medical education credits for this activity or as a helpful interactive reference. Many of the graphics are animated and available on this site. Topics in the field covered in the Essential Psychopharmacology book series can be searched on Essential Psychopharmacology Online.

This mechanism of using the materials will create a certain amount of programmed learning because it incorporates the elements of repetition and interaction with visual learning through graphics. I hope that the visual concepts learned via graphics will reinforce abstract concepts learned from the written text, especially for "visual learners" (i.e., those who retain information better from visualizing concepts than from reading about them).

For those of you who are already familiar with psychopharmacology, this book should provide easy reading from beginning to end. Going back and forth between the text and the graphics should provide interaction. After the complete text has been read, reviewing the entire book by going through the graphics once again should be simple. In addition, the Neuroscience Education Institute's website further expands the *Essential Psychopharmacology* learning experience, and Essential Psychopharmacology Online allows quick searches of topics in this field.

For those of you who are interested in the specific updates made in the third edition, the first section on basic science expands its coverage of the structure and function of neurons, synaptogenesis, signal transduction cascades, ion channels, psychiatric genetics, brain circuits, neuroimaging, and disease models of malfunctioning brain circuits that result in psychiatric symptoms in psychiatric disorders.

The second section on clinical science has been extensively revised, with much expanded coverage of psychosis and antipsychotics, especially of the neurotransmitter glutamate, including the NMDA (N-methyl-d-aspartate) receptor hypofunction hypothesis of schizophrenia and genetic advances in schizophrenia. Several new antipsychotics are also included, as is extensive coverage of cardiometabolic risks and sedation related to antipsychotics.

The mood disorder chapter expands the descriptions of unipolar and bipolar disorders and discusses the entire bipolar spectrum. All clinical chapters include sections on matching the symptoms of the disorder under discussion to various hypothetically malfunctioning brain circuits. The antidepressant chapter includes extensive coverage not only

of new drugs and several agents in late-stage testing, but also expanded coverage of "old" (and often neglected) drugs that remain valuable therapeutics but are off-patent and not promoted commercially. In this chapter are new sections on antidepressants and women; on trimonoamine modulators and brain stimulation therapies that may augment antidepressants; and a discussion of "symptom-based" antidepressant selection algorithms for combining antidepressants to treat residual symptoms and attain remission in major depressive disorder. A chapter specifically on mood stabilizers has been added and explains not only the mechanism of action of agents used to treat bipolar disorder but also the use of drugs in combinations to treat this disorder.

The chapter on anxiety disorders now includes coverage of fear conditioning, fear extinction, and stress biology as well as various anxiety disorders and their treatments with anxiolytics and with new drugs on the horizon that have novel mechanisms. Sleep disorders, including not only insomnia but also disorders of wakefulness (excessive daytime sleepiness) and their treatments, are now greatly expanded as a new, separate chapter, which also introduces histamine, a new neurotransmitter system.

A new chapter on chronic pain and fibromyalgia and their treatments has also been added. Attention deficit hyperactivity disorder, in both children and adults, covering both stimulants and nonstimulants, is now a separate chapter. Dementia is also a separate chapter and emphasizes disease-modifying treatments on the horizon. The final chapter is a greatly expanded chapter on reward, emphasizing drug abuse but also covering other disorders of reward, such as disorders of sexual function, eating disorders, and disorders of impulsivity.

This is an incredibly exciting time for the fields of neuroscience and mental health, creating fascinating opportunities for clinicians to utilize current therapeutics and to anticipate future medications that are likely to transform the field of psychopharmacology. Best wishes for your first step on your journey into this fascinating field of psychopharmacology.

Stephen M. Stahl, MD, PhD

CME Information

Release/Expiration Dates

Original release date: March 2008
CME credit expiration date: original expiration February 2011 (if this date has passed, please contact NEI for updated information)

Target Audience

This activity was designed for health care professionals, including psychiatrists, neurologists, primary care physicians, pharmacists, psychologists, nurses, and others, who treat patients with psychiatric conditions.

Statement of Need

The content of this educational activity was determined by rigorous assessment, including activity feedback, expert faculty assessment, literature review, and new medical knowledge, which revealed the following unmet needs:

- Psychiatric illnesses have a neurobiological basis and are primarily treated by pharmacological agents; understanding each of these, as well as the relationship between them, is essential in order to select appropriate treatment for a patient
- The field of psychopharmacology has experienced incredible growth; it has also experienced a major paradigm shift from a limited focus on neurotransmitters and receptors to an emphasis on brain circuits, neuroimaging, genetics, and signal transduction cascades

Learning Objectives

Upon completion of this activity, you should be able to:

- Apply neurobiologic and mechanistic evidence when selecting treatment strategies in order to match treatment to the individual needs of the patient
- Utilize new scientific data to modify existing treatment strategies in order to improve patient outcomes

Accreditation and Credit Designation Statements

The Neuroscience Education Institute is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The Neuroscience Education Institute designates this educational activity for a maximum of 90.0 *AMA PRA Category 1 Credits*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Activity Instructions

This CME activity is in the form of a printed book and incorporates instructional design to enhance your retention of the information and pharmacological concepts presented. You are advised to go through the figures in this activity from beginning to end, followed by the text, and then complete the posttests and evaluations. The estimated time for completion of this activity is 90 hours.

Instructions for CME Credit

Certificates of CME credit or participation are available for each topical section of the book (total of twelve sections). To receive a section-specific certificate, please complete the relevant posttest (you must score at least 70% to receive credit) and section evaluation available online only at http://www.neiglobal.com/ep3. If a score of 70% or more is attained, you can immediately print your certificate. There is a fee for each certificate (varies per section).

NEI Disclosure Policy

It is the policy of the Neuroscience Education Institute to ensure balance, independence, objectivity, and scientific rigor in its educational activities. The Neuroscience Education Institute takes responsibility for the content, quality, and scientific integrity of this CME activity.

All faculty participating in any NEI-sponsored educational activity and all individuals in a position to influence or control content development are required by NEI to disclose to the activity audience any financial relationships or apparent conflicts of interest that may have a direct bearing on the subject matter of the activity. Although potential conflicts of interest are identified and resolved prior to the activity, it remains for the audience to determine whether outside interests reflect a possible bias in either the exposition or the conclusions presented.

Neither the Neuroscience Education Institute nor Stephen M. Stahl, MD, PhD has received any funds or grants in support of this educational activity.

Individual Disclosure Statements

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Dr. Stahl has been a consultant, board member, or on the speakers bureau for the following pharmaceutical companies within the last three years: Acadia, Alkermes, Amylin, Asahi Kasei, Astra Zeneca, Avera, Azur, Biovail, Boehringer Ingelheim, BristolMyers Squibb, Cephalon, CSC Pharmaceuticals, Cyberonics, Cypress Bioscience, Dainippon,

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No other financial relationships to disclose.

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No other financial relationships to disclose.

Disclosed financial relationships have been reviewed by the Neuroscience Education Institute CME Advisory Board to resolve any potential conflicts of interest. All faculty and planning committee members have attested that their financial relationships do not affect their ability to present well-balanced, evidence-based content for this activity.

Disclosure of Off-Label Use

This educational activity may include discussion of unlabeled and/or investigational uses of agents that are not approved by the U.S. Food and Drug Administration. Please consult the product prescribing information for full disclosure of labeled uses.

Disclaimer

Participants have an implied responsibility to use the newly acquired information from this activity to enhance patient outcomes and their own professional development. The information presented in this educational activity is not meant to serve as a guideline for patient management. Any procedures, medications, or other courses of diagnosis or treatment discussed or suggested in this educational activity should not be used by clinicians without evaluation of their patients' conditions and possible contraindications or dangers in use, review of any applicable manufacturer's product information, and comparison with recommendations of other authorities. Primary references and full prescribing information should be consulted.

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