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978-0-521-88663-5 - Depression and Bipolar Disorder: Stahl's Essential Psychopharmacology,

Third Edition

Stephen M. Stahl

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## Depression and Bipolar Disorder

The best-selling *Stahl's Essential Psychopharmacology* – fully revised and updated throughout – continues its tradition of being the preeminent source of information in its field. This third edition of *Depression and Bipolar Disorders* draws from the revised chapters in *Stahl's Essential Psychopharmacology* to form a resource that is essential reading for all clinicians involved in the treatment of depression and bipolar disorder. Straightforward reading for both professionals treating these conditions and students learning the mechanisms of drug reactions, this eminently readable book can be read cover to cover by experts and novices alike.

**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.

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# Depression and Bipolar Disorder

## Stahl's Essential Psychopharmacology

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**Third Edition**

Stephen M. Stahl

University of California at San Diego

With Illustrations by  
Nancy Muntner

Editorial Assistant  
Meghan M. Grady



**CAMBRIDGE**  
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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.

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## Preface to the Third Edition

This booklet is a set of the three chapters from the third edition of *Stahl's Essential Psychopharmacology* that deal exclusively with depression and bipolar disorders and their treatment with modern psychopharmacological agents. The knowledge base of psychopharmacology for depression and bipolar disorders has exploded since the publication of the second edition of *Essential Psychopharmacology*, and this third edition attempts to reflect these changes.

Some would argue that antidepressants have become the therapeutic market that is the largest and has the most prescribers anywhere in the world, and in fact, anywhere in medicine. Since all specialties prescribe these medications, with psychiatrists in fact a minority of prescribers, there is intense interest in this area of therapeutics. This therapeutic area of psychopharmacology occupies the largest single section of the full textbook, and since many readers may be interested in this area alone, we offer the three chapters on depression, bipolar disorders, antidepressants, and mood stabilizers as a stand-alone spinoff of the third edition of *Stahl's Essential Psychopharmacology*.

Psychopharmacology has not only experienced incredible growth since publication of the second edition of this textbook; it has also experienced a major paradigm shift from a limited focus on neurotransmitters and receptors to an emphasis as well 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 each of these chapters in this booklet. Many new antidepressants and mood stabilizers have been introduced in recent years, and many more are now in clinical testing, and these are covered in this new edition. These three chapters on mood disorders and their treatments have been extensively reorganized, rewritten, and illustrated with roughly twice the number of figures in every chapter. However, what has not changed is the didactic style of the first and second editions, which 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 is not a text intended for the sophisticated subspecialist in psychopharmacology. Also, it is not extensively referenced to original papers, but rather to textbooks and reviews and a few selected original papers, with only a limited reading list for each chapter. For those of you interested in specific prescribing information about the most common one hundred or so psychotropic drugs, this information is available in the companion textbook, *Essential Psychopharmacology Prescriber's Guide*. A spinoff of this

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book just on antidepressants is also available, called *Essential Psychopharmacology Prescriber's Guide of Antidepressants*. Mood stabilizers are available in a second spinoff, called *Essential Psychopharmacology of Antipsychotics and Mood Stabilizers*.

Now, you also have the option of going to Essential Psychopharmacology Online at [www.essentialpsych.org](http://www.essentialpsych.org). We are proud to announce the launch of this new website, which is due to premiere in the fall of 2008. Access to 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 in this text is based on updated lectures, courses, slides, and articles by the author. Many of the new illustrations are now available as animations on the Neuroscience Education Institute's website, as are the lectures, slides and articles, continuing medical education (CME) credits, tests, certifications, and much more. I invite you to explore this interactive reference by visiting the Neuroscience Education Institute's website at [www.neiglobal.com](http://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 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 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 it 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. After the text has been read, the entire book can be rapidly reviewed again merely 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](http://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. Also, you can search topics in the field covered in the Essential Psychopharmacology book series on Essential Psychopharmacology Online.

This mechanism of using the materials will create a certain amount of programmed learning by incorporating the elements of repetition, as well as interaction with visual learning through graphics. Hopefully, the visual concepts learned via graphics will reinforce abstract concepts learned from the written text, especially for those of you who are primarily "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. Following review of the complete text, it should be simple to review the entire book by going through the graphics once again. 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.

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For those of you interested in the specific updates made in the third edition, the mood disorder chapter expands the descriptions of unipolar and bipolar disorders and discusses the entire bipolar spectrum. Included are 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. The chapter on mood stabilizers 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.

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.

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## 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 such as mood disorders 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 as well 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 in mood disorders

### 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.

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The Neuroscience Education Institute designates this educational activity for a maximum of 24.0 *AMA PRA Category 1 Credits*<sup>™</sup>. 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 that are being 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 24 hours.

### Instructions for CME Credit

To receive a certificate of CME credit or participation, please complete the posttest (you must score at least 70% to receive credit) and 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 the posttest (certificate included) for non-NEI members.

### NEI Disclosure Policy

It is the policy of the Neuroscience Education Institute to ensure balance, independence, objectivity, and scientific rigor in all 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, Eli Lilly, Forest, GlaxoSmithKline, Janssen, Jazz Pharmaceuticals, Labopharm, Lundbeck, Neurocrine Biosciences, NeuroMolecular, Neuronetics, Novartis, Organon, PamLab, Pfizer, Pierre Fabre, sanofi-aventis, Schering-Plough, Sepracor, Shire, SK Corporation, Solvay, Somaxon, Takeda, Tethys, Tetrigenix, Vanda Pharmaceuticals, and Wyeth.

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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 FDA. 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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