

## Lamotrigine Update and Its Use in Mood Disorders

Stephen C Hurley

**OBJECTIVE:** To provide a qualitative, systematic update and review of the pharmacology, pharmacokinetics, efficacy in mood disorders, adverse effects, and costs of lamotrigine.

**DATA SOURCES:** Citations obtained from MEDLINE searches (1985–September 2001) using lamotrigine as a text word, articles identified in reference lists of pertinent articles, abstracts presented at conferences, and research data from GlaxoSmithKline.

**DATA EXTRACTION:** English-language articles were considered for possible inclusion. Each title and abstract was examined to determine whether the publication contained up-to-date information relevant to the objective. Twenty clinical trials that provided data on response rates in mood disorders were tabulated.

**DATA SYNTHESIS:** Lamotrigine's primary action is to modulate voltage-gated sodium channels. Evidence suggests that it decreases glutamate transmission, directly reduces calcium influx, mildly blocks transmitter reuptake, and alters intracellular mechanisms of resting transmitter release. The average half-life of lamotrigine is approximately 24 hours, but decreases to approximately 7.4 hours when used concurrently with phenytoin, and increases to approximately 59 hours with valproic acid. Seven of the 20 clinical trials were randomized, double-blind, and controlled. Existing data are inadequate to evaluate lamotrigine use in major depression. The pooled response rates for patients with depressed, manic, mixed, and rapid cycling bipolar disorder were similar, ranging from 52% to 63%. Adverse effects are infrequent when the drug is used alone, but become more frequent when lamotrigine is combined with other anticonvulsants. While most rashes are mild, approximately 1 in 500 patients develops exfoliative dermatitis. A slow upward dose titration is recommended to reduce the incidence of serious rash, but this may delay the attainment of adequate dosage for 6 weeks. Lamotrigine has positive effects on cognitive function, but occasionally produces insomnia. Lamotrigine costs 2–4 times more than lithium, carbamazepine, and generic valproic acid.

**CONCLUSIONS:** When efficacy, adverse effects, and cost are considered, lamotrigine should probably be reserved as a second-line agent for bipolar depression.

**KEY WORDS:** lamotrigine, mood disorders.

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Although a number of medications have been successfully used for mood stabilization, the need for better outcomes was emphasized in a recent prospective study.<sup>1</sup> Eighty-two patients, diagnosed with bipolar disorder and maintained on lithium, carbamazepine, or valproic acid, were evaluated after an average follow-up of 4.2 years. During this period, 68% of the patients experienced 2 or more relapses. Kaplan-Meier survival analysis indicated that the probability for a recurrence of mania or depression within 1 year was 37%.

Since carbamazepine and valproate are antiepileptic drugs (AEDs), it is not surprising that newly developed seizure medications are studied for their effects on mood.

Lamotrigine is one of the newer AEDs for partial epilepsy. In 1993, a battery of psychological tests designed to measure drug effects on health-related quality of life found little difference between lamotrigine and placebo.<sup>2</sup> However, patient scores on the Affect Balance (or happiness) scale, which is designed to measure positive aspects of mental health, increased by 94% ( $p = 0.003$ ). The next year, an abstract<sup>3</sup> presented at the annual meeting of the American Psychiatric Association reported that lamotrigine produced sustained clinical improvement in 2 patients with refractory bipolar disorder. In the ensuing years, a number of reports have been published on lamotrigine treatment of mood disorders.

Lamotrigine was available in 12 other countries before it was approved by the Food and Drug Administration in December 1994. At this time, >1 million patients have

Author information provided at the end of the text.

# Research In Mood Disorders An Update

**Gin S. Malhi, Marc Masson, Frank  
Bellivier**



## **Research In Mood Disorders An Update:**

**Research in Mood Disorders** Hanns Hippus, Franz Müller-Spahn, 1994 This book is about depression it critically reviews both the latest results and the most recent advances in clinical therapy techniques The first part of the book provides a clear and concise overview of all the important new results concerning the course of affective psychoses discussing them against the background of comprehensive and quite interesting genetic studies The pathogenetic findings provide the framework for presenting recent studies on chronobiology neuroendocrinology and personality research The second part of the book provides a clearly structured overview of the most effective forms of clinical therapy for depressive disorders known to date The focus here is on practical cognitive and pharmacological approaches especially in the context of therapy resistance Also featured are the latest results concerning electroconvulsive therapy The editors themselves world class authorities in this field have brought together a group of internationally renowned experts to make this book as solid practical and interesting as possible for clinicians looking to improve their skills as therapists and also for students and researchers wanting to keep up on the most effective techniques This volume appears under the auspices of the International PTD Committee

**Genetics and Epigenetics of Psychiatric Diseases, 2nd Edition** Cunyou Zhao, Weihua Yue, Zhexing Wen, 2020-10-09 Psychiatric diseases have a highly complex etiology aggregating in families but not segregating in a traditional Mendelian manner Recent approaches to understanding the causes of psychiatric disease have focused on describing the genetic contribution to major psychiatric illnesses the use of large scale genome wide association studies GWAS and exome sequencing has enabled a systematic exploration of genetic risk factors and identified over 100 independent genomic loci significantly associated with psychiatric diseases however there remains uncertainty about the causal genes involved in disease pathogenesis and how their function is regulated Since many GWAS variants reside in non coding regions the disease associated common variants might be enriched in regulatory domains including enhancers and regions of active chromatin state These lead us to focus on the possible role of non sequence based genomic variation in health and disease Of particular interest are epigenetic modifications that regulate gene expression through modifications to DNA RNA histone proteins and chromatin The availability of high throughput profiling methods for quantifying epigenomic modifications in large numbers of samples has enabled us to perform epigenome wide association studies EWAS aimed at screening methylomic variations associated with environmental exposure and disease Thus systematic integration of genetic epigenetic and epidemiological approaches will contribute to improving our understanding of the molecular mechanisms underlying disease phenotypes

**An Update on Neurocognitive Impairment in Schizophrenia and Depression** Kenneth Hugdahl, Vince D. Calhoun, 2012-05-01 Despite all research that has been devoted to schizophrenia over the last years the understanding of the biological bases of the disorder is still fragmentary Adding to the complexity is the realization that basic cognitive functions are seriously distorted and that removal of symptoms does not necessarily ameliorate the

cognitive deficits It has also been shown that cognitive deficits can occur before clinical symptoms in a prodromal phase of the disorder pointing to a possible causal relationship between cognitive deficits and outbreak of the disorder However it is still not possible to diagnose a patient from cognitive deficits alone or from a combination of clinical symptoms and cognitive deficits and structural and functional neuroimaging data although promising have also not found the way to routine clinical practice The aim of the Research Topic is therefore to provide an update on research on cognitive and brain imaging research for the understanding of cognitive deficits in schizophrenia The suggested contributors are all internationally recognized experts in their respective fields The suggested contributions will cover the field from the use of standardized neuropsychological tests to establish cognitive response profiles in patients with schizophrenia to the use of advanced new techniques for the analysis of brain imaging data

**Clinical Trial Design Challenges in Mood Disorders** Mauricio Tohen, Charles Bowden, Andrew A. Nierenberg, John Geddes, 2015-01-24 Poor clinical trial designs result in failed studies wasting research funds and limiting the advancement of cures for disorders Clinical Trial Design Challenges in Mood Disorders outlines classic problems researchers face in designing clinical trials and discusses how best to address them for the most definitive and generalizable results Traditional trial designs are included as well as novel analytic techniques The book examines information on high placebo response the generalizability of studies conducted in the developing world the duration of maintenance studies and the application of findings into clinical practice With representation from contributors throughout the world and from academia industry regulatory agencies and advocacy groups this book will contribute toward improved clinical trial design and valid precise and reliable answers about what works better and faster for patients Summarizes common trial design problems and their solutions Encompasses funding subject selection regulatory issues and more Identifies best practices for definitive and generalizable results Includes traditional trial designs and novel analytic techniques Represents academia industry regulatory agencies and advocacy groups

**Psychology in Modules** David G. Myers, C. Nathan DeWall, 2015-01-12 In this version of Psychology Twelfth Edition David Myers and Nathan DeWall break down the new edition's 16 chapters into 53 modules assignable in any sequence and brief enough to be read in one sitting It is a format favored by a wide range of students and instructors one that is supported by substantial research showing that students working with shorter reading assignments develop a deeper understanding of the material The new edition of Modules includes the same new features and content of Psychology Twelfth Edition including hundreds of new citations and new infographics And like Psychology Twelfth Edition is more than ever a fully integrated text media learning package with the modular edition's LaunchPad now featuring dozens of new Concept Practice activities

**Psychoneuroscience** Gerhard Roth, Andreas Heinz, Henrik Walter, 2023-03-13 The textbook builds a bridge between the neurosciences theoretical and experimental neurobiology neurology and the psychosciences psychology psychiatry psychotherapy and aims to help provide the other disciplines with the most important and scientifically validated knowledge in an understandable form The question

of how mental experience and brain processes relate to each other has long been considered mysterious In this book you will learn based on the latest scientific findings that the two areas form an indissoluble unity even if we experience and study them differently We present this unity in concrete terms in psychological neurobiological theory and psychiatric psychotherapeutic practice We treat the principles of neurobiological excitation and information processing the structure and function of the limbic system the development of the personality and the interaction of genetic epigenetic factors and prenatal and postnatal environmental influences which may be favourable or unfavourable On this basis the exemplary presentation of important mental disorders such as addictive disorders schizophrenic disorders affective disorders and anxiety disorders takes place Finally following in the footsteps of the eminent psychotherapist Klaus Grawe the concept of neuropsychotherapy is introduced and it is shown why psychotherapy and neurobiology belong together and can enrich each other Our psychoneuroscientific approach paints a picture of man that is not based on opposites but on an integration of psyche brain behavior and experience

**The Oxford Handbook of Mood Disorders** Robert J. DeRubeis, Daniel R. Strunk, 2017-04-24 The most comprehensive volume of its kind The Oxford Handbook of Mood Disorders provides detailed coverage of the characterization understanding and treatment of mood disorders Chapters are written by the world's leading experts in their respective areas The Handbook provides coverage of unipolar depression bipolar disorder and variants of these disorders Current approaches to classifying the mood disorders are reviewed and contemporary controversies are placed in historical context Chapter authors offer a variety of approaches to understanding the heterogeneity of the experiences of those who meet criteria for mood disorders both within and across cultures The role of genetic and environmental risk factors as well as premorbid personality and cognitive processes in the development of mood pathology are detailed Interpersonal neurobiological and psychological factors also receive detailed consideration The volume reviews mood disorders in special populations e.g. postpartum and seasonal mood disorders as well as common comorbidities e.g. anxiety substance use disorders Somatic and psychosocial treatment approaches receive in depth coverage with chapters that describe and review empirical evidence regarding each of the most influential treatment approaches The depth and breadth offered by this Handbook make it an invaluable resource for clinicians and researchers as well as scholars and students

*Clinical Handbook for the Management of Mood Disorders* J. John Mann, Patrick J. McGrath, Steven P. Roose, 2013-05-09 Provides a one stop evidence based guide to the management of all types of mood disorders

**Neuroprogression in Psychiatric Disorders** A. Halaris, B.E. Leonard, 2017-07-25 In this volume international experts critically review cutting edge advances in neuroprogression research The relevance of these findings to psychiatric and neurological disorders is clarified Potential etiopathological mechanisms of neuroprogression are described in detail Special emphasis is placed on the role of the immune system in stress and stress related disorders and brain immune interactions The epigenetic consequences of adverse experiences in early childhood which may prelude major psychiatric disorders are

also considered Recent research has not only provided evidence of neuroprogression in psychiatric and neurological disorders but has shown that pharmacologic interventions have the potential to arrest this process Advances in testing and imaging will lead to timely diagnosis and earlier treatment Identification of neurological mechanisms alongside epi genetic vulnerability markers will create truly personalized treatment programs This book is a valuable resource for everyone who wishes to gain insight into the essential features of the neuroprogressive course of major psychiatric and neurological disorders In particular psychiatrists neuroscientists and neurologists as well as immunologists pharmacologists and molecular biologists will find very informative chapters of direct relevance to their field

**Treatment-Resistant Mood Disorders** André F Carvalho, Roger S McIntyre, 2015-03-26 Treatment resistant major depression and bipolar disorder are highly prevalent and disabling conditions associated with substantial morbidity and mortality The assessment and management of refractory patients with mood disorders is a major clinical challenge for mental health providers Part of the Oxford Psychiatry Library OPL series this pocketbook provides a concise view of the current definitions assessment and evidence based management of treatment resistant mood disorders and reviews novel therapeutic targets for mood disorders which may enhance the therapeutic armamentarium of clinicians in the near future The pocketbook serves as a useful guide for mental health practitioners including psychiatrists clinical psychologists trainees and interested primary care physicians

*The Wiley-Blackwell Handbook of Mood Disorders* Mick Power, 2013-06-26 The Wiley Blackwell Handbook of Mood Disorders 2 e reflects the important and fast changing advancements that have occurred in theory and practice in unipolar and bipolar mood disorders There is no other current reference that gathers all of these developments together in a single book Every chapter is updated to reflect the very latest developments in theory and practice in unipolar and bipolar mood disorders Includes additional chapters which cover marital and family therapy medical disorders and depression and cross cultural issues Contributions are from the world s leading authorities and include psychiatrists and clinical psychologists with experience in both research and in practice Focuses on innovations in science and clinical practice and considers new pharmacological treatments as well as psychological therapies

**Handbook of Diagnosis and Treatment of Bipolar Disorders** Terence A. Ketter, 2009-08-26 This readable guide to the assessment and management of patients with bipolar disorder can help physicians keep abreast of dramatic and rapid advances of recent years and integrate them into their practice Handbook of Diagnosis and Treatment of Bipolar Disorders emphasizes recent controlled studies and FDA approved indications and translates these data into the real world of clinical practice The contributions of the eleven chapter authors from Stanford University reflect more than a decade of clinical research and treatment undertaken at that institution including advances in diagnosis and interventions supported by controlled studies They provide crucial information regarding diagnosis pharmacotherapy psychotherapy and treatment of patients from special populations such as children women and older adults and patients with particular challenging illness course such as rapid cycling This is the first book to provide

quantitative assessment of potential benefit number needed to treat and risk number needed to harm for all approved treatments for bipolar disorder providing clinicians with information needed to balance benefits and risks in order to render individualized state of the art evidence based care It describes all FDA approved indications reviewing efficacy safety tolerability pharmacokinetics illness phase specific dosing and drug interactions A chapter on multiphase treatment strategy explains crucial illness transition points and describes how these have been integrated with knowledge of illness phase in mood disorders The book then demonstrates the relevance of this approach to therapeutics by providing An overview of pharmacotherapy that covers the emergence of evidence based pharmacotherapy and number needed to treat and harm analyses Guidelines to managing acute manic and mixed episodes that include evidence based assessments of lithium divalproex carbamazepine and second generation antipsychotics Coverage of acute major depressive episodes in bipolar disorders that outlines four tiers of treatment for this most pervasive illness phase with the fewest approved treatments Discussion of the longer term management of bipolar disorders including reviews of controlled trials of recently approved pharmacotherapies such as lamotrigine olanzapine aripiprazole and adjunctive quetiapine A review of the use of mood stabilizers and second generation antipsychotics often in combinations as well as the controversial role of adjunctive antidepressants in treating patients with rapid cycling bipolar disorders Description of important advances in evidence based adjunctive psychotherapeutic interventions in bipolar depression and bipolar maintenance treatment Comprehensive in scope yet readily accessible for application to clinical practice the book includes summary tables quick reference lists of clinical pearls and case studies to make its content more relevant Handbook of Diagnosis and Treatment of Bipolar Disorders is the ideal source for integrating recent research into everyday practice     Psychiatry Review and Canadian Certification Exam Preparation Guide James Bourgeois,Usha Parthasarathi,Ana Hategan,2012 The first comprehensive psychiatry review textbook designed expressly for the Canadian market Psychiatry Review and Canadian Certification Exam Preparation Guide is the resource residents and psychiatrists need to master the qualifying examinations in psychiatry of the Royal College of Physicians and Surgeons of Canada These exams are required for certification both for graduating residents and most foreign trained psychiatrists seeking to practice in Canada This new volume based on The American Psychiatric Publishing Board Review Guide for Psychiatry has been carefully edited to include only material relevant to the Canadian exam References have been taken from both the U S and Canadian psychiatric literature and laboratory units medication names and doses and the language used have been edited to be consistent with Canadian psychiatry The volume takes the reader from the basic sciences comprising the foundation of psychiatry through the psychiatric interview and other diagnostic topics to syndrome specific chapters paralleling DSM IV TR and finally to current treatment options Rounding out the review is a 200 question practice exam that reflects the structure of the actual board examinations Although no substitute for quality medical and residency training Psychiatry Review and Canadian Certification Exam Preparation Guide will help the prospective exam

taker ameliorate weaknesses and enhance strengths in preparation for a successful exam experience

**Mental Disorders in Primary Care** André F. Carvalho, Roger S. McIntyre, 2017-02-09 Mental disorders are highly prevalent in the primary care setting yet are frequently misdiagnosed and often inappropriately treated The presence of unrecognized or misdiagnosed mental disorders is associated with increased service utilization and health care costs and can significantly impact the patient's quality of life and risk of suicide Written by experts from around the world Mental Disorders in Primary Care offers readers with a comprehensive and evidence based guide to the diagnosis and treatment of mental disorders in the primary care setting Containing 21 chapters on a variety of psychiatric disorders such as depressive disorders and substance use disorders and key topics for discussion such as drug interactions and collaborative care Mental Disorders in Primary Care is essential reading for clinicians treating patients in a primary care setting Fully up to date to reflect DSM 5's taxonomy of psychiatric disorders this resource provides readers with a global and comprehensive guide to the diagnosis and treatment of patients with mental disorders

**The Treatment of Bipolar Disorder** André F. Carvalho, Eduard Vieta, 2017-03-01 Bipolar disorder is a chronic and debilitating mental illness affecting a significant proportion of the world's population It is associated with significant impairments in health related quality of life and psychosocial functioning and has significant illness related morbidity and heightened mortality rates due to medical comorbidities and suicide The management of this disorder requires a complex combination of pharmacological and psychosocial interventions which can be challenging for clinicians Written by world experts in the field of bipolar disorder The Treatment of Bipolar Disorder Integrative Clinical Strategies and Future Directions provides readers with a concise and comprehensive guide to the integrative management of bipolar disorder This resource contains 31 chapters on the various management choices available from both established and novel treatment areas such as psychoeducation psychotherapeutic interventions neuromodulatory approaches and novel therapeutic targets The complexity and diversity of the management choices available makes this a continually evolving field and necessitates forward thinking By both discussing the current management of bipolar disorder and the future developments available this resource provides all clinicians working with patients with bipolar disorder an up to date and reflective guide to its management and what the future holds

**The Oxford Handbook of Adult Cognitive Disorders** Michael L. Alosco, Robert A. Stern, 2019-05-07 The prevalence of adult cognitive disorders will dramatically rise over the next 25 years due to the aging population Clinical research on adult cognitive disorders has rapidly evolved including evidence of new adult cognitive disorders and greater insight into the clinical presentation mechanism diagnosis and treatment of established diseases The Oxford Handbook of Adult Cognitive Disorders is an up to date scholarly and comprehensive volume covering most diseases conditions and injuries resulting in impairments in cognitive function in adults Topics covered include normal cognitive and brain aging the impact of medical disorders and psychiatric illnesses on cognitive function adult neurodevelopmental disorders and various neurological conditions This Handbook also provides a section on unique

perspectives and special considerations for clinicians and clinical researchers covering topics such as cognitive reserve genetics diversity and neuroethics Readers will be able to draw upon this volume to facilitate clinical practice including differential diagnosis treatment recommendations assessment practices and to obtain an in depth review of current research across a wide spectrum of disorders provided by leaders in their fields The Oxford Handbook of Adult Cognitive Disorders is a one of a kind resource appropriate for both clinicians and clinical researchers from advanced trainees to seasoned professionals

**Mood Disorders** A. J. Rush, Brian E. Leonard, 1997 This volume provides up to date scientifically based alternative treatment algorithms for various kinds of mood disorders It is one of the first publications to enunciate stepwise specified pharmacological management procedures recommended for major depressive bipolar and dysthymic disorders In addition it indicates the role for special forms of treatment for depression including light and electroconvulsive therapies based on published peer reviewed scientific literature and extensive in depth clinical experience It will be of particular interest to psychiatric residents internists family physicians general practitioners nurses medical students and other mental health professionals who are committed to a scientifically based approach to the management of patients with mood disorders

Research highlights from the first 100 accepted articles in Frontiers in Sleep Stuart F. Quan, Colin Shapiro, Dalva Poyares, Judith Owens, Stephen Sheldon, Ambra Stefani, John Winkelman, Marie-Pierre St-Onge, Luis Buenaver, Patricia L. Haynes, 2024-03-11 Frontiers in Sleep is committed to advancing developments in the field of sleep research by communicating scientific knowledge to researchers and the public alike to enable the scientific breakthroughs of the future In particular the journal welcomes submissions that support and advance the UN s Sustainable Development Goals SDGs notably SDG 3 good health and well being A better understanding of the impact of deficient and poor quality sleep and sleep disorders on physical and mental health and performance is highly relevant with as many as 45% of the world s population currently affected Here we are pleased to introduce this Theme book entitled Research Highlights from the first 100 accepted articles in Frontiers in Sleep edited by our Chief Editors of Frontiers in Sleep This ebook aims to celebrate the milestone of the first 100 accepted articles in our journal by recognizing highly deserving authors and their outstanding research projects The work presented here spotlights the broad diversity of exciting research performed across the journal We hope you enjoy our selection of key articles We also thank all authors editors and reviewers of Frontiers in Sleep for their contributions to our journal and look forward to another exciting year in 2024

**Clinician's Guide to ADHD Comorbidities in Children and Adolescents** Joseph Sadek, 2018-09-26 The diagnosis and management of ADHD co occurring with other disorders such as anxiety depression tics and substance use remain major challenges for clinicians treating all age groups This book guides clinicians through each step in the diagnosis and management of the comorbidity through essential case studies describing psychiatric disorders that frequently occur with child ADHD are well described in every case Each case includes a diagnosis section and management section and is accompanied by questions and answers

concerning the most important aspects in diagnosing and managing of both ADHD and the comorbid disorders Drawn from actual clinical encounters the case studies also feature ample current and valid references     The Science and Practice of Lithium Therapy Gin S. Malhi, Marc Masson, Frank Bellivier, 2016-11-24 This book provides a clear and comprehensive guide to the clinical prescription of lithium that draws upon evidence based knowledge of its mechanisms of action The book is divided into two parts on the science of lithium and the practice of lithium therapy The former covers aspects such as the properties of the lithium ion pharmacokinetics and pharmacodynamics impact on neurotransmission and gene expression modulation The section on practice includes discussion of variability in response to lithium use of lithium in the treatment of bipolar disorders its value in suicide prevention administration during pregnancy and in the pediatric age group and side effects Lithium is arguably the only true mood stabilizer and its multifaceted effects across many clinical domains have given rise to a resurgence of interest in recent years fuelled by both researchers and clinicians Nevertheless its use remains constrained by exaggerated concerns about potential side effects In reality lithium is a simple molecule that is relatively straightforward to administer and monitor and has potentially profound benefits at a fraction of the cost of contemporary agents This book dispels the many myths and concerns that surround its use and will be of interest for clinicians and researchers worldwide and those that are recipients of lithium therapy

## Reviewing **Research In Mood Disorders An Update**: Unlocking the Spellbinding Force of Linguistics

In a fast-paced world fueled by information and interconnectivity, the spellbinding force of linguistics has acquired newfound prominence. Its capacity to evoke emotions, stimulate contemplation, and stimulate metamorphosis is really astonishing. Within the pages of "**Research In Mood Disorders An Update**," an enthralling opus penned by a highly acclaimed wordsmith, readers set about an immersive expedition to unravel the intricate significance of language and its indelible imprint on our lives. Throughout this assessment, we shall delve to the book is central motifs, appraise its distinctive narrative style, and gauge its overarching influence on the minds of its readers.

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