

Cambridge University Press

978-0-521-76058-4 - Next Generation Antidepressants: Moving Beyond Monoamines to Discover Novel Treatment Strategies for Mood Disorders

Edited by Chad E. Beyer and Stephen M. Stahl

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Next Generation Antidepressants

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Frontmatter

[More information](#)

Contents

List of contributors page vi

Preface ix

Chad E. Beyer

List of abbreviations x

-
- | | | | |
|---|---|---|--|
| 1 | Current depression landscape: a state of the field today 1
Laurence Mignon and Stephen M. Stahl | 5 | Defining depression endophenotypes 70
Lisa H. Berghorst and Diego A. Pizzagalli |
| 2 | Novel therapeutic targets for treating affective disorders 12
Eliyahu Dremencov and Thomas I. F. H. Cremers | 6 | Genetic and genomic studies of major depressive disorder 90
Roy H. Perlis |
| 3 | Developing novel animal models of depression 28
Lotte de Groote, Malgorzata Filip, and Andrew C. McCreary | 7 | Medicinal chemistry challenges in the design of next generation antidepressants 102
David P. Rotella |
| 4 | Translational research in mood disorders: using imaging technologies in biomarker research 45
Jul Lea Shamy, Adam M. Brickman, Chris D. Griesemer, Anna Parachikova, and Mark Day | 8 | Application of pharmacogenomics and personalized medicine for the care of depression 119
Keh-Ming Lin, Chun-Yu Chen, and Yu-Jui Yvonne Wan |
| | | | <hr/> <i>Index</i> 132 |

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Preface

As the World Health Organization estimates that depression will become the second leading cause of death by the year 2020 – due primarily to complications arising from stress and the cardiovascular system – the need to develop novel and more effective treatment strategies for patients suffering with mood disorders has never been more paramount. Current treatment options for depressed patients include a variety of molecules designed to exclusively elevate central nervous system levels of monoamines such as serotonin (5-HT). These classes include the monoamine oxidase inhibitors and tricyclics and are exemplified by the selective serotonin reuptake inhibitors (SSRIs) and the dual serotonin/norepinephrine reuptake inhibitors (SNRIs). While these medicines are moderately effective in some patient populations, there are still considerable limitations associated with all commercially available antidepressants. These drawbacks include, but are not limited to, delayed onset of efficacy, treatment resistance in many patients, and deleterious side effects such as emesis and sexual dysfunction. The focus of this book is to review the current landscape and state of the field for depression research with an eye towards shedding light on where the future of mood disorders research is headed in terms of novel therapeutic targets, preclinical model development, exploring depression endophenotypes, and medicinal chemistry strategies. Undoubtedly all of these disciplines, as well as others including genetics and translational medicine approaches, will need to successfully collaborate to help build a better understanding of disease etiology, patient stratification, and treatment. As depression research has evolved over the past 50 years, the next decade will be instrumental in facilitating a move beyond our current understanding and pharmacological treatment options, and strive to discover and develop more personalized and effective treatment options for the millions of patients suffering from chronic and debilitating mood disorders.

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Abbreviations

5HIAA, 5-hydroxy-indole-acetic acid
ACTH, adrenocorticotrophic hormone
BBB, blood–brain barrier
BD, bipolar disorder
BDI, Beck Depression Inventory
BDNF, brain-derived neurotrophic factor
BNST, bed nucleus of the stria terminalis
BOLD, blood oxygen level-dependent
CANTAB, Cambridge Neuropsychological Test Automated Battery
CBF, cerebral blood flow
CBV, cerebral blood volume
CNV, copy-number variation
CRF, corticotropin-releasing factor
CSF, cerebrospinal fluid
DA, dopamine
DAT, dopamine transporter
DRN, dorsal raphe nucleus
DST, dexamethasone suppression test
ECT, electro-convulsive therapy
ERP, event-related potential
FDG, fluorine-18-labeled deoxyglucose
FLAIR, fluid attenuated inverse recovery
fMRI, functional magnetic resonance imaging
FST, forced swim test
GWAS, genomewide association study
HPA, hypothalamic–pituitary–adrenal
IAT, Implicit Association Test
LC, locus coeruleus
MAOI, monoamine oxidase inhibitor
MDD, major depressive disorder
MED, minimal effective dose
MTD, maximal tolerated dose
MRN, median raphe nucleus
MRS, magnetic resonance spectroscopy
MTHF, L-5-methyl-tetrahydrofolate
NE, norepinephrine
NET, norepinephrine transporter
NK, neurokinin
PET, positron emission tomography
PFC, prefrontal cortex
phMRI, pharmacological MRI
POC, proof-of-concept

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SERT, serotonin transporter

SNP, single nucleotide polymorphism

SNRI, serotonin/norepinephrine reuptake inhibitor

SP, substance P

SSRI, selective serotonin reuptake inhibitor

STAR*D, Sequenced Treatment Alternatives to Relieve Depression study

SXR, steroid and xenobiotic receptor

T3, triiodothyronine

TCA, tricyclic antidepressant

TCI, Temperament and Character Inventory

TST, tail suspension test

vACC, ventral anterior cingulate cortex

VTA, ventral tegmental area

WCST, Wisconsin Card Sorting Test

WGTA, Wisconsin General Testing Apparatus

WMH, white matter hyperintensities