

## Anxiety Disorders

# **Modern Trends in Pharmacopsychiatry**

**Vol. 29**

Series Editor

**B.E. Leonard** Galway



# Anxiety Disorders

Volume Editors

**D.S. Baldwin** Southampton/Cape Town

**B.E. Leonard** Galway

8 figures, 2 in color, and 5 tables, 2013

**KARGER**

Basel · Freiburg · Paris · London · New York · New Delhi · Bangkok ·  
Beijing · Tokyo · Kuala Lumpur · Singapore · Sydney

## Modern Trends in Pharmacopsychiatry

(Formerly published as 'Modern Problems in Pharmacopsychiatry')

---

### Prof. David S. Baldwin

University of Southampton  
Faculty of Medicine  
University Department of Psychiatry  
Southampton (UK)

---

### Prof. Brian E. Leonard

Department of Pharmacology  
National University of Ireland  
Galway (Ireland)

#### Library of Congress Cataloging-in-Publication Data

Anxiety disorders (Baldwin)

Anxiety disorders / volume editors, D.S. Baldwin, B.E. Leonard.

p. ; cm. -- (Modern trends in pharmacopsychiatry, ISSN 1662-2685 ;  
vol. 29)

Includes bibliographical references and index.

ISBN 978-3-318-02463-0 (hard cover : alk. paper) -- ISBN 978-3-318-02464-7

(electronic version)

I. Baldwin, David S., editor of compilation. II. Leonard, B. E., editor of  
compilation. III. Title. IV. Series: Modern trends in pharmacopsychiatry ;  
v. 29. 1662-2685

[DNLM: 1. Anxiety Disorders--therapy. W1 MO168P v.29 2013 / WM 172]

RC531

616.85'22--dc23

2013029183

**Bibliographic Indices.** This publication is listed in bibliographic services, including Current Contents® and Index Medicus.

**Disclaimer.** The statements, opinions and data contained in this publication are solely those of the individual authors and contributors and not of the publisher and the editor(s). The appearance of advertisements in the book is not a warranty, endorsement, or approval of the products or services advertised or of their effectiveness, quality or safety. The publisher and the editor(s) disclaim responsibility for any injury to persons or property resulting from any ideas, methods, instructions or products referred to in the content or advertisements.

**Drug Dosage.** The authors and the publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new and/or infrequently employed drug.

All rights reserved. No part of this publication may be translated into other languages, reproduced or utilized in any form or by any means electronic or mechanical, including photocopying, recording, microcopying, or by any information storage and retrieval system, without permission in writing from the publisher.

© Copyright 2013 by S. Karger AG, P.O. Box, CH-4009 Basel (Switzerland)

www.karger.com

Printed in Germany on acid-free and non-aging paper (ISO 9706) by Kraft Druck, Ettlingen

ISSN 1662-2685

e-ISSN 1662-4505

ISBN 978-3-318-02463-0

e-ISBN 978-3-318-02464-7

# Contents

## **VII Preface: Concerted Efforts to Improve the Understanding and Treatment of Anxiety Disorders**

Angst, J. (Zurich); Baldwin, D.S. (Southampton/Cape Town)

### **1 On the Nature of Obsessions and Compulsions**

de Haan, S.; Rietveld, E.; Denys, D. (Amsterdam)

### **16 The Origin of Anxiety Disorders – An Evolutionary Approach**

Willers, L.E.W.G.; Vulink, N.C.; Denys, D. (Amsterdam); Stein, D.J. (Cape Town)

### **24 Genetic Factors in Anxiety Disorders**

Domschke, K. (Würzburg); Maron, E. (London/Tartu)

### **47 Neuroimaging in Anxiety Disorders**

Fredrikson, M.; Faria, V. (Uppsala)

### **67 Potential Neuroimmunological Targets in the Treatment of Anxiety Disorders**

Hou, R. (Southampton); Tang, Z. (Suzhou); Baldwin, D.S. (Southampton/Cape Town)

### **85 Anxiety and Cardiovascular Disease**

Davies, S.J.C. (Toronto, Ont./Bristol); Allgulander, C. (Stockholm)

### **98 The Early Phases of Anxiety Disorders: From Prevention to Treatment**

Vázquez-Bourgon, J.; Herrán, A.; Vázquez-Barquero, J.L. (Santander)

### **111 Duration of Untreated Illness and Duration of Illness in Anxiety Disorders: Assessment and Influence on Outcome**

Altamura, A.C.; Camuri, G.; Dell'Osso, B. (Milan)

### **119 Pharmacotherapy of Generalized Anxiety Disorder**

Allgulander, C. (Stockholm); Baldwin, D.S. (Southampton/Cape Town)

### **128 Pharmacological Treatment of Panic Disorder**

Bandelow, B. (Göttingen); Baldwin, D.S. (Southampton/Cape Town); Zwanzger, P. (Münster)

### **144 Pharmacological Treatment of Social Anxiety Disorder**

Masdrakis, V.G. (Athens); Turic, D. (Southampton); Baldwin, D.S. (Southampton/Cape Town)

### **154 Pharmacotherapy of Posttraumatic Stress Disorder**

Koller, A.; Stein, D.J. (Cape Town)

**164 Evidence-Based Treatment Pathways for Translational Studies in  
Obsessive-Compulsive Disorders**

Fineberg, N.A. (Welwyn Garden City/Hatfield/Cambridge); Pallanti, S. (Florence/  
New York, N.Y.); Reghunandanan, S. (Welwyn Garden City)

**178 Author Index**

**179 Subject Index**

# Preface

## **Concerted Efforts to Improve the Understanding and Treatment of Anxiety Disorders**

Anxiety disorders are common, usually have an early onset, often take a prolonged course, cause much personal distress, impair everyday function, lower quality of life, and carry a considerable economic burden. They are often ‘co-morbid’ with other forms of mental disorder – including major depression, bipolar disorder, schizophrenia, substance misuse – and with physical illness, and many anxiety disorders are associated with an increased risk of self-harm. It is hard not to regard anxiety disorders as a significant public health problem which requires the attention of health professionals and health policy makers [1].

Knowledge of the underlying causes of anxiety disorders is incomplete, and this hinders reliable diagnosis and accurate prediction of prognosis, and the refinement of treatment approaches. Many individuals with recognisable anxiety disorders do not present to health professionals, or do present but are not diagnosed correctly. Even when recognised as having an anxiety disorder, the standard of care received by many patients is less than ideal. Unfortunately, the effectiveness and acceptability of current pharmacological and psychological treatments in real-world clinical practice is often disappointing. It is reasonable to contend that one way to address the current unmet public health, clinical and research needs in anxiety disorders is through the development of independent collaborative networks [2].

There are many world-leading centres of research excellence within Europe, some with clinical and research databases that are sufficiently large and detailed to have already led to step-changing insights into anxiety disorders. But methodologies vary across centres, and this reduces the ability to confirm or refute new findings. There seems much scope for developing multi-centre collaborative patient databases and for harmonising research methodologies, to bring new insights and other perspectives on current debates about the diagnosis and treatment of mental disorders. The European College of Neuropsychopharmacology (ECNP) has been concerned to support the development of such independent collaborative

international research networks of basic scientists and practising clinicians, has established the ECNP Network Initiative (ECNP-NI) to help meet this goal, and has adopted and supported the Anxiety Disorders Research Network (ADRN) [1].

There is a parallel need for similar networks in low- and middle-income countries. South Africa offers many opportunities to gain additional insights into the mechanisms that underlie and maintain anxiety disorders. These include access to a range of clinical groups that allow important questions about anxiety to be explored in more detail: such as the influence of HIV/AIDS, the effect of traumatic experiences and societal deprivation, and role of common South African substances of abuse in precipitating and maintaining anxiety symptoms. Through its Marie Curie Actions International Research Staff Exchange Scheme funding stream, the European Union is supporting the Joint European South African Research Network in Anxiety Disorders (EUSARNAD) programme to strengthen existing links and foster new collaborative research configurations, and to enhance the relevance of translational research activity jointly conducted within Europe and South Africa to other developed and developing societies [3].

Contributors to this book are drawn from participating centres within the ADRN: many chapters include authors from a range of centres, including the University of Cape Town in South Africa, reflecting the collaborative and international nature of the ADRN. The early chapters provide updates on the nature and origin of anxiety and related symptoms and insights from genetic and neuroimaging research, and from investigations of cardiovascular and immunological factors; subsequent chapters consider the early phases of anxiety disorders, and the effects of prolonged illness before undergoing treatment; the later chapters provide succinct but comprehensive accounts of the evidence-based pharmacological treatment of generalised anxiety disorder, panic disorder, social anxiety disorder, post-traumatic stress disorder and obsessive-compulsive disorder.

The development of new treatments for patients with mental disorders is often described as being 'in crisis'. An ECNP Summit on the future of neuropsychopharmacological research in Europe recommended that research efforts and productivity could be enhanced by setting up and supporting specialist centres of excellence in clinical neuroscience, experimental medicine research, and brain imaging, in which early-phase trials could be conducted, with the accumulation of experience and training of new researchers [4]. We believe that research networks such as the ADRN can play a role in meeting these recommendations, whilst providing a framework for the training of the next generation of pre-clinical and clinical researchers.

*Jules Angst, Zurich*  
*David S. Baldwin, Southampton/Cape Town*



## Acknowledgements

The Anxiety Disorders Research Network is part of the European College of Neuropsychopharmacology Network Initiative (ECNP-NI) and receives financial support from the ECNP to support its development. Current (July 2013) centres within the ADRN are located in Amsterdam, Athens, Bristol, Florence, Göttingen, Gothenburg, Groningen, Leiden, London, Milan, Münster, Paris, Pisa, Santander, Southampton, Stockholm, Tartu, Tel Aviv, Uppsala, Welwyn Garden City, Würzburg, and Zurich. Administrative support to the ADRN is provided by Miss Magda Nowak, through a grant from the ECNP-NI; she provided invaluable assistance to the Editors in the development of this book.

## References

- 1 Baldwin DS, Allgulander C, Altamura AC, Angst J, Bandelow B, den Boer J, Boyer P, Davies S, Dell'Osso B, Eriksson E, Fineberg N, Fredrikson M, Herran A, Maron E, Metspalu A, Nutt D, van der Wee N, Vázquez-Barquero JL, Zohar J: Manifesto for a European anxiety disorders research network. *Eur Neuropsychopharmacol* 2010;20:426–432.
- 2 Baldwin DS, Pallanti S, Zwanzger P: Developing a European research network to address unmet needs in anxiety disorders. *Neurosci Biobehav Rev* DOI: 10.1016/j.neubiorev.2013.01.009.
- 3 Baldwin DS, Stein DJ: A joint European and South African research network in anxiety disorders (editorial). *Hum Psychopharmacol* 2012;27:4–5.
- 4 Nutt D, Goodwin G: ECNP Summit on the future of CNS drug research in Europe 2011: report prepared for ECNP by David Nutt and Guy Goodwin. *Eur Neuropsychopharmacol* 2011;21:495–499.

