

A NEW ERA OF CATECHOLAMINES IN THE LABORATORY AND CLINIC

..... EDITED BY

LEE E. EIDEN

Series Editor S. J. Enna



ADVANCES IN
PHARMACOLOGY



VOLUME SIXTY EIGHT

ADVANCES IN PHARMACOLOGY

A New Era of Catecholamines in the
Laboratory and Clinic

Edited by

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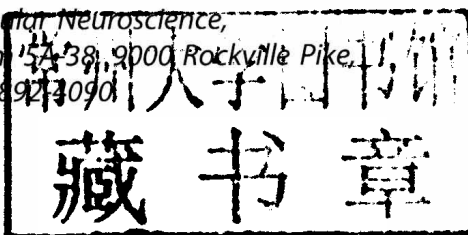
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Academic Press is an imprint of Elsevier
525 B Street, Suite 1800, San Diego, CA 92101-4495, USA
225 Wyman Street, Waltham, MA 02451, USA
32, Jamestown Road, London NW1 7BY, UK
The Boulevard, Langford Lane, Kidlington, Oxford, OX5 1GB, UK
Radarweg 29, PO Box 211, 1000 AE Amsterdam, The Netherlands

First edition 2013

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British Library Cataloguing-in-Publication Data

A catalogue record for this book is available from the British Library

Library of Congress Cataloging-in-Publication Data

A catalog record for this book is available from the Library of Congress

ISBN: 978-0-12-411512-5

ISSN: 1054-3589

For information on all Academic Press publications
visit our website at store.elsevier.com

Printed and bound in United States in America

13 14 15 10 9 8 7 6 5 4 3 2 1



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PREFACE

The Tenth International Catecholamine Symposium (XICS) was held at the Asilomar Conference Grounds in Pacific Grove, California, during September 9–13, 2012. The Conference Grounds afforded a beautiful seaside setting, but one without distractions. This was the first international symposium focused on catecholamines in the twenty-first century and, for physiologists, pharmacologists, and clinicians, there was a lot of catching up to do. The impetus for this symposium was provided primarily by David Goldstein, the founding Chief of the Clinical Neurocardiology Section, NINDS, and the President of the Eighth International Catecholamine Symposium in 1996. The Organizing Committee for the XICS, in addition to Dr. Goldstein, included Daniel O'Connor, Professor of Medicine and Pharmacology at the Institute for Genomic Medicine, University of California San Diego, and President of the Catecholamine Society; David Sibley, Chief of the Molecular Neuropharmacology Section, NINDS, Bethesda, MD; Esther Sabban, Professor of Biochemistry and Molecular Biology, New York Medical College; and the editor of this volume.

The comprehensive conference proceedings are published under separate cover and include abstracts and extended abstracts of virtually all papers and posters presented at the symposium. This volume of *Advances in Pharmacology* is devoted to in-depth coverage by thought leaders in the field of catecholamine research in attendance at the XICS, and to aspects of the field, including mechanisms of catecholamine biochemistry, cell biology, systems biology, and clinical diagnosis and treatment, which have developed dramatically over the past decade. The 21 chapters of the book are divided into 4 sections. The first is devoted to recent advances in the understanding of the basic cell biology of the catecholaminergic neuron. Areas in which new developments are prominent include elucidation of a highly integrative cellular signaling network for tyrosine hydroxylase regulation in the human brain that extends to phosphorylation ‘memory’ (see contributions from Nakashima et al. and Dickson and Briggs), co-factor regulation (see chapter by H. Ichinose), brain catecholamine ‘endocrine’ functions during development (M. Ugrumov), interactions between catecholamines and granins during storage and release (Bartolomucci and colleagues), and modulation of catecholamine release and action at the synapse by co-released peptide transmitters. The second section contains

four chapters that examine complementary aspects of CNS catecholamine circuitry in which either new aspects of functional neuroanatomy (see chapters by Kobayashi et al. and Itoi et al.) or catecholamine interactions with other neurotransmitter systems (see contribution from Hensler and colleagues) have created a substantively improved basic ‘matrix’ for understanding catecholamine neurotransmission in the mammalian brain. The chapter by Bonoldi and Howes, in particular, reassesses the role of dopamine in schizophrenia in a way that is especially timely given recent progress in stitching together prefrontal and ventral striatal dopaminergic mechanisms with genetic evidence for association between dopamine metabolism and cognitive endophenotypes that characterize this psychiatric illness. Section 3 focuses on neurological diseases associated with defects in catecholamine biosynthesis. Contributions in this section underscore the important clinical fact that understanding the deficiencies associated with these human diseases illuminates disease mechanisms, provides markers for disease detection, diagnosis, progression, and prognosis, and offers targets for gene therapy and pharmacological intervention. Recent progress on all these fronts is illustrated for Menkes and Parkinson’s diseases (see chapters by Kaler and Holmes, and D. Goldstein), genetic AADC deficiency (chapter by Hwu and colleagues), and pheochromocytoma (Richter et al.). Schafer et al. provide neuroanatomical evidence for the expression of VMAT2 in human (but not rodent) endocrine pancreas, making the high-affinity VMAT2 ligand tetrabenazine a candidate marker for beta cell mass in human type I diabetes, based on optimization of this PET ligand for VMAT2 in human CNS. This section concludes with a contribution from A. Emery that highlights implications of biased ligand signaling, high-throughput screening, and recent advances in x-ray crystallographic analysis of catecholamine (beta-adrenergic) receptors for drug discovery. The final section of this volume comprises contributions on catecholamines and stress. Research on catecholamine involvement in the systemic response to stress is part of the foundation of modern pharmacology, and our understanding of the dynamics of these responses continues to be refined (see chapter by Kvetnansky et al.). In addition, as for the well-established importance of biogenic amine neurotransmission in schizophrenia, depression, hypertension, and Parkinson’s disease, the role of catecholamines in stress is currently being integrated into a much more coherent view of stress transduction circuitry in both the central and peripheral nervous system that emphasizes linkages between noradrenergic inputs to peptidergic stress response centers in the brain (Khan and Watts), peptidergic modulation of noradrenergic centers that affect the gain

and sensitivity of stress responses (Van Bockstaele), and peptidergic inputs to catecholamine effector cells of the adrenal medulla, as well as the hypothalamic centers controlling corticosterone secretion from the adrenal cortex, in the stress response (T. Mustafa).

This volume of *Advances in Pharmacology* should provide the reader who is interested in monitoring the translational harvest of the most recent decade of catecholamine research an excellent basis for judging what this is likely to be, how soon it is likely to occur, and what new opportunities for pharmacological investigation and targeting of human disease are likely to arise in the coming decade.

David Goldstein, Dan O'Connor, Esther Sabban, and David Sibley sacrificed considerable time and effort in the organization of the XICS, for which the catecholamine field owes them a considerable debt. I also acknowledge them as silent partners in the editing of this volume, completed under the auspices of the Series Editor S.J. Enna, and the guidance and assistance of the Editorial Manager Lynn LeCount.

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Volume 68 Editor

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