Forum of Nutrition

Vol. 63

Series Editor

Ibrahim Elmadfa  Vienna
Frontiers in Eating and Weight Regulation

Volume Editors

Wolfgang Langhans
ETH Zürich, Schwerzenbach

Nori Geary
ETH Zürich, Schwerzenbach

28 figures, 1 in color, and 4 tables, 2010
Library of Congress Cataloging-in-Publication Data

Frontiers in eating and weight regulation / volume editors, Wolfgang Langhans, Nori Geary.
   p. ; cm. -- (Forum of nutrition, ISSN 1660-0347 ; v. 63)
   Includes bibliographical references and indexes.
   ISBN 978-3-8055-9300-7 (hard cover : alk. paper)
QP136.F76 2010
612.3’9—dc22
2009043618

Bibliographic Indices. This publication is listed in bibliographic services, including Current Contents® and PubMed/MEDLINE.

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 2010 by S. Karger AG, P.O. Box, CH–4009 Basel (Switzerland)
www.karger.com
Printed in Switzerland on acid-free and non-aging paper (ISO 9706) by Reinhardt Druck, Basel
ISSN 1660–0347
Contents

VII List of Contributors
XI Preface
   Langhans, W.; Geary, N. (Schwerzenbach)

1 Introduction – Obesity and Food Intake: Basic and Clinical Approaches
   De Kloet A.D.; Woods, S.C. (Cincinnati, Ohio.)

9 Overview of the Physiological Control of Eating
   Langhans, W.; Geary, N. (Schwerzenbach)

54 Therapeutic Potential of Gut Peptides
   Wölnerhanssen, B.; Beglinger, C. (Basel)

64 Roles of Amylin in Satiation, Adiposity and Brain Development
   Lutz, T.A. (Zürich)

75 The Enterocyte as an Energy Flow Sensor in the Control of Eating
   Langhans, W. (Schwerzenbach)

84 Development of Hypothalamic Neural Networks Controlling Appetite
   Bouret; S.G. (Los Angeles, Calif./Lille)

94 Hypothalamic Nutrient Sensing and Energy Balance
   Moran, T.H. (Baltimore, Md.)

102 Blood-Brain Barrier as a Regulatory Interface
   Banks, W.A. (St. Louis, Mo.)

111 Do Leptin and Insulin Signal Adiposity?
   Hillebrand, J.J.G.; Geary, N. (Schwerzenbach)

123 Leptin–Signaling Pathways and Leptin Resistance
   Münzberg, H. (Baton Rouge, La.)

133 Hypothalamic-Brainstem Circuits Controlling Eating
   Blevins, J.E.; Baskin, D.G. (Seattle, Wash.)

141 Brainstem Integrative Function in the Central Nervous System Control of Food Intake
   Schwartz, G.J. (Bronx, N.Y.)
152 Gaining New Insights into Food Reward with Functional Neuroimaging
   Neary, M.T.; Batterham, R.L. (London)

164 Cortical Mechanisms of Human Eating
   Kringelbach, M.L. (Oxford/ Aarhus); Stein, A. (Oxford)

176 Genetic Variation in Dopaminergic Reward in Humans
   Stice, E.; Dagher, A. (Eugene, Oreg.)

186 Metabolic Imprinting in Obesity
   Sullivan, E.L.; Grove, K.L. (Beaverton, Oreg.)

195 Gene-Environment Interactions in Obesity
   Hetherington, M.M. (Leeds); Cecil, J.E. (St Andrews)

204 Author Index

205 Subject Index
List of Contributors

William A. Banks
VAMC/St. Louis University School of Medicine
Internal Medicine, Geriatrics
915 Grand Boulevard
St. Louis, MO
USA

Denis G. Baskin
Department of Veterans Affairs
University of Washington
VA Puget Sound Health Care System
1660 South Columbian Way
Seattle, WA
USA

Rachel L. Batterham
Centre for Diabetes and Endocrinology
Department of Medicine
University College London
Rayne Building
5 University Street
London
UK

Christoph Beglinger
Division of Gastroenterology
University Hospital
Basel
Switzerland

James E. Blevins
Department of Veterans Affairs
University of Washington
VA Puget Sound Health Care System
1660 South Columbian Way
Seattle, WA
USA

Sebastien G. Bouret
The Saban Research Institute,
Neuroscience Program
Childrens Hospital Los Angeles
University of Southern California
USC Childhood Obesity Center
Keck School of Medicine
4650 Sunset Boulevard, MS#135
Los Angeles, Calif.
USA

Joanne E. Cecil
Bute Medical School
University of St Andrews
St Andrews
UK

Alain Dagher
Montreal Neurological Institute
McGill University
3801 University Street
Montreal, Quebec
Canada

Annette D. De Kloet
Program in Neuroscience
University of Cincinnati
2170 East Galbraith Road
Cincinnati, OH
USA
Nori Geary
Physiology and Behaviour Group
Institute of Food, Nutrition and Health
ETH Zürich
Schorenstrasse 16
Schwerzenbach
Switzerland

Kevin L. Grove
Oregon National Primate Research Center
Oregon Health & Science University
505 NW 185th Avenue
Beaverton, OR
USA

Marion Hetherington
Institute of Psychological Sciences
University of Leeds
Leeds
England

Jacquelien J. Hillebrand
Physiology and Behaviour Group
Institute of Food, Nutrition and Health
ETH Zürich
Schorenstrasse 16
Schwerzenbach
Switzerland

Morten L. Kringelbach
Department of Psychiatry
University of Oxford
The Queen’s College
UK

Wolfgang Langhans
Physiology and Behaviour Group
Institute of Food, Nutrition and Health
ETH Zürich
Schorenstrasse 16
Schwerzenbach
Switzerland

Thomas A. Lutz
Institute of Veterinary Physiology
Vetsuisse Faculty University of Zürich
Winterthurerstrasse 260
Zürich
Switzerland

Timothy H. Moran
Department of Psychiatry and Behavioral Sciences
Johns Hopkins University School of Medicine
Ross 618 720 Rutland Ave.
Baltimore, MD
USA

Heike Münzberg
Pennington Biomedical Research Center
Louisiana State University System
6400 Perkins Rd
Baton Rouge, LA
USA

Marianne T. Neary
Centre for Diabetes and Endocrinology
Department of Medicine
University College London
Rayne Building
5 University Street
London
UK

Alan Stein
Department of Psychiatry
University of Oxford
The Queen’s College
UK

Gary J. Schwartz
Departments of Medicine & Neuroscience
Albert Einstein College of Medicine
1300 Morris Park Ave., Golding 501
Bronx, NY
USA

Eric Stice
Oregon Research Institute
1715 Franklin Boulevard
Eugene, OR
USA

E.L. Sullivan
Division of Neuroscience
Oregon National Primate Research Center
Oregon Health & Science University
505 NW 185th Avenue
Beaverton, OR
USA
Bettina Wölnerhanssen
Department of Visceral Surgery
University Hospital
Basel
Switzerland

Stephen C. Woods
Obesity Research Center
University of Cincinnati
2170 East Galbraith Road
Cincinnati, OH
USA
Scientific interest in the physiology of eating and body weight regulation has grown rapidly in recent years. There are both purely scientific and wider, cultural reasons for this development. The scientific reason relates to the advent of molecular genetics. The discovery of the adipose tissue hormone leptin by Jeffrey Friedman and his colleagues at Rockefeller University just 16 years ago revealed an important new neuroendocrine signaling pathway involved in the control of eating, energy expenditure and weight regulation and, more generally, made clear the power of molecular genetic techniques to help illuminate brain-behavior relationships. The influence, and the promise, of applying these tools to the study of eating and body weight regulation can hardly be overestimated. The cultural reason relates to the ongoing pandemic of obesity and of obesity-related health problems. The scale of the individual and societal costs of this pandemic have became clear only in the last 10–15 years. Unfortunately, equally clear is the current lack of effective strategies to control eating and body weight. The development of preventive and therapeutic options is a tremendous challenge to the science of eating and weight regulation in all its forms, from basic physiology to cognitive and social psychology.

Like previous advances in scientific technique and thought, the explosive growth in knowledge during the initial years of the molecular genetic revolution has been followed by a somewhat more intellectually critical phase, characterized by attempts to integrate new data and concepts with existing approaches. This is evident in the increasing numbers of studies in which cutting-edge molecular methodologies are combined with sophisticated traditional behavioral or physiological methods or with other new techniques, for example, functional imaging. In our view, the science of eating control and body weight regulation seems to be well into this synthetic period. As a result, the current scene is not dominated by a single type of methodology or single mode of thought. Rather, the wide boundary of the unknown is being pushed back in different ways and at different levels, often most successfully when different sorts of methods are combined.
Our book attempts to capture the spirit of this exciting era in the physiology of eating and weight regulation as well as its significance to the alleviation of the affliction of obesity. Together with the editors at Karger Publishers, we conceived a fresh approach to the usual volume of a collection of review articles. Our concept has two novelities: First, the main content of the book is a collection of brief, expert descriptions of recent developments in 15 examples of the important research frontiers in the physiology of eating, especially as it relates to weight regulation and adiposity. The intent of this format is to reflect several exciting recent developments in our area in an accessible form, so as to help inform and influence research in the coming years. To highlight the necessity of this continuing research, the book begins with a brief, expert introduction to the currently employed strategies for the treatment of obesity and their mostly disillusioning outcomes. The book’s second unusual feature is that the frontier chapters are preceded by a general overview of the physiology of eating control and weight regulation. This overview chapter is meant both to provide requisite background information for the frontier chapters in an accessible way for readers for whom this is useful and to introduce an overarching conceptual and critical framework for the frontier chapters. As well, this chapter touches on several further active research areas that are not represented in the frontier chapters, such as new work on the satiating effect of glucagon-like peptide-1, advances in unraveling the complex role of brain serotonin in the control of eating, and the effects of bariatric surgery on physiological controls of eating and weight regulation, to name just three.

We hope that this approach has resulted in a book that is useful to students and newcomers to the field, to basic researchers engaged in the area, and to researchers and clinicians interested in the bidirectional translational dialog between bench and bedside. We have the optimistic view that the steady progress now visible in both basic and clinical research will generate increasingly effective treatments for disordered eating and body weight regulation. We hope that this book will facilitate this process. Last, but not least, we want to thank the editors at Karger Publishers for their patience and flexibility. Without their continuing support and understanding this book would not exist.

Wolfgang Langhans, Nori Geary
Schwerzenbach/Zürich