# CNS SPECTRUMS®

The International Journal of Neuropsychiatric Medicine

## ACADEMIC SUPPLEMENT

## Alzheimer's Disease Pathways to Practice: Assessing Diagnosis and Outcome Measures

Introduction

G.T. Grossberg

The Interplay of Neurotransmitters in Alzheimer's Disease

P.T. Francis

Formulating a Clinical Practice Care Plan for the Diagnosis and Assessment of Alzheimer's Disease

W.E. Faison

Utilizing Advanced Imaging and Surrogate Markers
Across the Spectrum of Alzheimer's Disease

M.A. Mintun

Rationalizing Therapeutic Approaches in Alzheimer's Disease

G.T. Grossberg

Behavioral and Neuropsychiatric Outcomes in Alzheimer's Disease

J.L. Cummings

Index Medicus/MEDLINE citation: CNS Spectr



#### Accreditation Statement

Mount Sinai School of Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide Continuing Medical Education for physicians.

Mount Sinai School of Medicine designates this Continuing Medical Education activity for a maximum of 3.0 Category 1 credit(s) toward the AMA Physician's Recognition Award. Each physician should claim only those credits that he/she actually spent in the educational activity.

It is the policy of Mount Sinai School of Medicine to ensure fair balance, independence, objectivity, and scientific rigor in all its sponsored activities. All faculty participating in sponsored activities are expected to disclose to the audience any real or apparent conflict-of-interest related to the content of their presentation, and any discussion of unlabeled or investigational use of any commercial product or device not yet approved in the United States.

This activity has been peer reviewed and approved by Eric Hollander, MD, professor of psychiatry, Mount Sinai School of Medicine. Review date: October 11, 2005.

#### Statement of Need and Purpose

Alzheimer's disease is a progressive disorder that negatively impacts cognitive, behavioral, and functional abilities. Alzheimer's disease currently affects ~4.5 million Americans, and the prevalence is expected to increase dramatically as the population ages. The clinical deterioration in Alzheimer's disease is, in part, a result of deficits involving several neurochemical pathways. The cholinergic system, which is the most consistently and dramatically affected neurotransmitter system in Alzheimer's disease, has been strongly implicated in the emergence of neuropsychiatric symptoms.

The pathogenesis of Alzheimer's disease is complex and not fully understood. Several factors, including amyloid plaques, neurofibrillary tangles, and inflammatory processes, are likely to contribute to the development of the disease. Acetylcholine and glutamate are involved in learning and memory and ongoing discoveries about the multiple pathophysiologic pathways involved in the development and progression of Alzheimer's has given rise to several plausible therapeutic targets. Emphasis has increasingly shifted to the accurate detection of the earliest phase of Alzheimer's. Identification of individuals with mild cognitive impairment who will develop Alzheimer's has improved via the use of neuropsychologic tests, neuroimaging, cerebrospinal fluid analysis, and other biomarkers.

New data on Alzheimer's disease therapies have become available since the publication of dementia treatment guidelines in 2001. Cholinesterase inhibitors (ChEIs) and memantine are well tolerated and have been shown to improve symptoms associated with Alzheimer's. Donepezil, galantamine, and rivastigmine are currently approved for the treatment of mild-to-moderate Alzheimer's disease.

As a consequence of global aging of the human population, the occurrence of cognitive impairment and dementia is rapidly becoming a significant burden for public health systems. Behavioral symptoms of Alzheimer's, in particular, cause great distress to caregivers, creating an emotional and financial burden that often prompts the caregiver to place the patient in a nursing facility. Primary and secondary prevention of dementia through individual and population-level interventions could reduce the burden of Alzheimer's disease. Physicians should be prepared to provide evidence-based answers to inquiries regarding treatment of Alzheimer's disease.

#### Target Audience

This activity is designed to meet the educational needs of psychiatrists and neurologists.

#### To Receive Credit for this Activity

Read this academic supplement, reflect on the information presented, and then complete the CME quiz found on pages 26 and 27. To obtain credits, you should score 70% or better. Termination date: November 30, 2007. The estimated time to complete this activity is 3 hours.

#### Disclaimer

This academic supplement is supported through an unrestricted educational grant by Forest Pharmaceuticals, Inc. Sponsorship of this review does not imply the sponsor's agreement with the views expressed herein. Although every effort has been made to ensure that drug doses and other information are presented accurately in this publication, the ultimate responsibility rests with the prescribing physician. Neither the publisher, the sponsor, nor the authors can be held responsible for errors or for any consequences arising from the use of information contained herein. Readers are strongly urged to consult any relevant primary literature. No claims or endorsements are made for any drug or compound currently under clinical investigation. This supplement may contain information concerning a use or dosage schedule that has not been approved by the US Food and Drug Administration.

## The International Journal of Neuropsychiatric Medicine

#### **EDITOR**

lack M. Gorman, MD Mount Sinai School of Medicine New York, NY

#### **ASSOCIATE AND FOUNDING EDITOR**

Eric Hollander, MD Mount Sinai School of Medicine New York, NY

#### **INTERNATIONAL EDITOR**

Joseph Zohar, MD Chaim Sheba Medical Center Tel-Hashomer, Israel

#### **ASSOCIATE INTERNATIONAL EDITORS EUROPE**

Donatella Marazziti, MD University of Pisa Pisa, Italy

#### **MID-ATLANTIC**

Dan J. Stein, MD, PhD University of Stellenbosch Cape Town, South Africa

#### **FAR EAST**

Shigeto Yamawaki, MD, PhD Hiroshima University School of Medicine Hiroshima, Japan

### **CONTRIBUTING WRITERS**

Jeffrey L. Cummings, MD Warachal Eileen Faison, MD Paul T. Francis, PhD George T. Grossberg, MD Mark A. Mintun, MD

### **MEDICAL REVIEWER**

David L. Ginsberg, MD

#### **CME EDITOR** Eric Hollander, MD

**SUPPLEMENT EDITORS** 

Eric Hollander, MD Joseph Zohar, MD

#### **BOARD OF ADVISORS NEUROLOGISTS**

Mitchell F. Brin, MD University of California, Irvine Irvine, CÁ

Jeffrey L. Cummings, MD University of California, Los Angeles Los Angeles, CA

Jerome Engel, Jr., MD, PhD University of California, Los Angeles Los Angeles, CA

Mark S. George, MD Medical University of South Carolina Charleston, SC

Deborah Hirtz, MD

National Institute of Neurological Disorders and Stroke, NIH Rockville, MD

Richard B. Lipton, MD Albert Einstein College of Medicine

Bronx, NY C. Warren Olanow, MD, FRCPC Mount Sinai School of Medicine New York, NY

Steven George Pavlakis, MD Maimonides Medical Center Brooklyn, NY

Stephen D. Silberstein, MD, FACP Thomas Jefferson University Philadelphia, PA

Michael Trimble, MD, FRCP, FRPsych National Hospital for Neurology and Neurosurgery London, United Kingdom

### **PSYCHIATRISTS**

Margaret Altemus, MD Cornell University Medical College New York, NY

Dennis S. Charney, MD Mount Sinai School of Medicine New York, NY

Dwight L. Evans, MD University of Pennsylvania Philadelphia, PA

Siegfried Kasper, MD University of Vienna Vienna, Áustria Martin B. Keller, MD Brown Medical School Providence, RI

**Lorrin M. Koran, MD**Stanford University School of Medicine

Stanford, CA Yves Lecrubier, MD

Hôpital de la Salpêtrière Paris, France

Herbert Y. Meltzer, MD Vanderbilt University Medical Center

Nashville, TN

Stuart A. Montgomery, MD St. Mary's Hospital Medical School London, United Kingdom

Charles B. Nemeroff, MD, PhD Emory University School of Medicine Atlanta, GA

Humberto Nicolini, MD, PhD National Mexican Institute of Psychiatry Mexico City, Mexico

Stefano Pallanti, MD, PhD University of Florence Florence, Italy

Katharine Phillips, MD Brown Medical School Providence, RI

Harold A. Pincus, MD Western Psychiatric Institute & Clinic RAND-University of Pittsburgh Health Institute, Pittsburgh, PA

Scott L. Rauch, MD Massachusetts General Hospital Charlestown, MA

Alan F. Schatzberg, MD Stanford University School of Medicine Stanford, CA

Thomas E. Schlaepfer, MD University of Bonn Bonn, Germany

Stephen M. Stahl, MD, PhD University of California, San Diego La Jolla, CA

Norman Sussman, MD, DFAPA New York University Medical School New York, NY

Karen Dineen Wagner, MD, PhD The University of Texas Medical Branch Galveston, Texas

Herman G.M. Westenberg, MD University Hospital Utrecht Utrecht, The Netherlands Stuart C. Yudofsky, MD Baylor College of Medicine Houston, TX

#### **MBL COMMUNICATIONS** Corporate Staff

**CEO & PUBLISHER** Darren L. Brodeur

**ASSOCIATE PUBLISHER** Elizabeth Katz

MANAGING EDITOR Christopher Naccari

**SENIOR EDITOR Deborah Hughes** 

NATIONAL ACCOUNT MANAGER Kathleen J. Skae, MBA

**SALES & MARKETING ASSOCIATE** Jennifer Gomez

**DEPUTY SENIOR EDITOR** José R. Ralat

**ACQUISITIONS EDITORS** Lisa Arrington Shoshana Bauminger

ASSOCIATE EDITOR-ENDURING MATERIALS **Shelley Wong** 

**ASSOCIATE EDITORS** Peter Cook

Dena Croog INTERN Stephanie Spano

ART DIRECTOR Derek Oscarson

**GRAPHIC DESIGNER Brad Evans** 

CONTROLLER John Spano

**OFFICE MANAGER** Manuel Pavón

INFORMATION TECHNOLOGY Clint Bagwell Consulting

**CORPORATION COUNSEL** Lawrence Ross, Esq. Bressler, Amery, and Ross

# CNS SPECTRUMS®

## The International Journal of Neuropsychiatric Medicine

## **Table of Contents**

November 2005 Volume 10 – Number 11 – Supplement 18

- 5 Introduction—Alzheimer's Disease Pathways to Practice: Assessing Diagnosis and Outcome Measures
  - By George T. Grossberg, MD
- The Interplay of Neurotransmitters in Alzheimer's Disease

  By Paul T. Francis, PhD
- 10 Formulating a Clinical Practice Care Plan for the Diagnosis and Assessment of Alzheimer's Disease By Warachal Eileen Faison, MD
- 13 Utilizing Advanced Imaging and Surrogate Markers Across the Spectrum of Alzheimer's Disease By Mark A Mintun, MD
- 17 Rationalizing Therapeutic Approaches in Alzheimer's Disease
  By George T. Grossberg, MD
- 22 Behavioral and Neuropsychiatric Outcomes in Alzheimer's Disease
  By Jeffrey L. Cummings, MD
- 26 CME QUIZ

The quiz on Alzheimer's disease is CME-accredited by Mount Sinai School of Medicine for 3.0 credit hours.

Founded in 1996, CNS Spectrums is an Index Medicus journal and is available on MEDLINE under the citation CNS Spectr. It is available online at www.cnsspectrums.com. CNS Spectrums is also distributed to all CINP members and is accredited for international CME by EACIC.

CNS Spectrums (ISSN 1092-8529) is published monthly by MBL Communications, Inc., 333 Hudson Street, 7th Floor, New York, NY 10013.

One-year subscription rates: domestic \$140; foreign \$195; in-training \$85. For subscriptions: Phone: 212-328-0800; Fax: 212-328-0600; Web: www.cnsspectrums.com.

Postmaster: Send address changes to *CNS Spectrums c*/o MMS, Inc, 185 Hanson Court, Suite 110, Wood Dale, IL 60191-1150.

For editorial inquiries, please fax us at 212-328-0600 or e-mail us at dh@mblcommunications.com. For bulk reprint purchases, please contact: Christopher Naccari at cdn@mblcommunications.com.

Opinions and views expressed by authors are their own and do not necessarily reflect the views of the publisher, MBL Communications, Inc., or the editorial advisory board. Advertisements in CNS Spectrums are accepted on the basis of adherence to ethical medical standards, but acceptance does not imply endorsement by CNS Spectrums or the publisher.

CNS Spectrums is a registered trademark of CNS Spectrums, LLC, New York, NY. Permission to reproduce articles in whole or part must be obtained in writing from the publisher.

BPA member since July 2005.





Copyright ©2005 by MBL Communications, Inc. All rights reserved. Printed in the United States.