The IPA Complete Guides to

Behavioral and Psychological Symptoms of Dementia

INTERNATIONAL PSYCHOGERIATRIC ASSOCIATION
www.ipa-online.org

BPSD

Specialists Guide

Specialists • Primary Care Physicians • Nurses

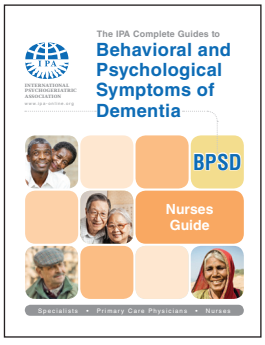
INTERNATIONAL PSYCHOGERIATRIC ASSOCIATION

www.ipa-online.org

The IPA Complete Guides to

Behavioral and Psychological Symptoms of Dementia (BPSD)

- **MODULE 1** An introduction to BPSD
- **MODULE 2** Clinical issues
- **MODULE 3** Etiology
- **MODULE 4** Role of family caregivers
- **MODULE 5** Non-pharmacological treatments
- **MODULE 6** Pharmacological management
- **MODULE 7** Cross-cultural and transnational considerations
- **MODULE 8** Long-term care (LTC)



The IPA Complete Guides to BPSD are available in three editions to meet a variety of practice needs.

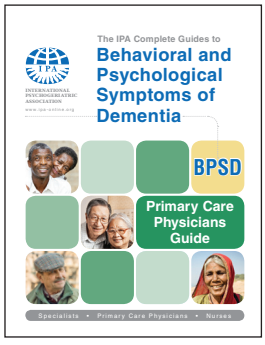


Photo Credits: Front Cover: (tl) © iStockphoto.com/Cliff Parnell; (c) © iStockphoto.com/YinYang; (bl) © iStockphoto.com/nyul; (br) © iStockphoto.com/Vikram Raghuvanshi Photography. Back Cover: (t) © iStockphoto.com/naphtalina; (c) © iStockphoto.com; (b) © iStockphoto.com/nyul.

The people on the front and back covers are shown for illustrative purposes only. They do not have any of the disorders identified in the book.

Design and Production: Symmetry

The *BPSD Educational Pack* was initially produced by the International Psychogeriatric Association (IPA) under an educational grant provided by Janssen-Cilag and Organon (1998, 2002). The 2010, 2012 and 2015 revisions to *The IPA Complete Guides to BPSD – Specialists Guide* were completed without sponsorship. The opinions expressed herein are those of the contributing authors and are not to be construed as the opinions or recommendations of the publishers or sponsors. Full prescribing information must be obtained for any of the drugs or procedures discussed herein.

Preface

The world's population is aging rapidly, and with it is coming a significant increase in the number of older people with dementia. This increase presents major challenges for the provision of healthcare generally and for dementia care in particular, for as more people have dementia, there will be more people exhibiting behavioral and psychological symptoms of dementia (BPSD).

BPSD exact a high price from both the patient and the caregiver in terms of the distress and disability they cause if left untreated. BPSD is recognizable, understandable and treatable. The recognition and appropriate management of BPSD are important factors in improving our care of dementia patients and their caregivers, and is central to the development of *The IPA Complete Guides to BPSD.*

The IPA Complete Guides to BPSD provide a comprehensive overview of the presentation and causes of BPSD, offering constructive guidance on treatment interventions, both pharmacologic and non-pharmacologic, along with information on caregiver education and support.

The IPA Complete Guides to BPSD – Specialists Guide was revised in 2015, based on the *BPSD Educational Pack* that was originally distributed in 1998 and updated in 2002 and in 2010. Further revisions in 2010 were based upon literature reviews by the contributors. *Module 8: Long-term care,* was added in 2012.

This guide draws on material presented at the consensus conferences of the International Psychogeriatric Association (IPA) Task Force on Behavioral Disturbances of Dementia (now the IPA Behavioral and Psychological Symptoms of Dementia Shared Interest Forum), held in the Spring of 1996, and the BPSD Update Conference in 1999.

Building on these significant forums, IPA has developed *The IPA Complete Guides to Behavioral and Psychological Symptoms of Dementia (BPSD).* As described in detail in the following pages, this series of three resource guides – *Specialists Guide, Nurses Guide* and *Primary Care Physicians Guide* – specifically addresses issues that are central to each perspective of care for the geriatric mental health patient, recognizing that each professional has a unique role and opportunity to provide care and support to the patient and caregiver.

This guide, *The IPA Complete Guides to Behavioral and Psychological Symptoms of Dementia (BPSD) – Specialists Guide,* is the most comprehensive in the series, with eight modules of extensive information that is of great value to all those in the geriatric healthcare profession, including physicians, nurses, psychologists, occupational therapists, social workers and others.

We suggest that readers make use of the reference and recommended reading lists provided in this document. Also, we especially hope the material will contribute to the improved management of dementia patients with BPSD and reduce some of the stress experienced by their caregivers and families.

Brian Draper, Project Editor 3rd and 4th Editions
School of Psychiatry
University of New South Wales
Euroa Centre
Prince of Wales Hospital
Randwick, New South Wales, Australia

Henry Brodaty, Project Editor 2nd Edition
School of Psychiatry
University of New South Wales
Euroa Centre
Prince of Wales Hospital
Randwick, New South Wales, Australia

Sanford I. Finkel, Project Editor 1st Edition
School of Psychiatry
University of Chicago Medical School
Chicago, Illinois USA

The IPA Complete Guides to BPSD

The only resource you need for all the members of your team!

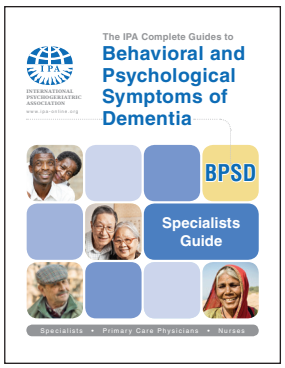
It is increasingly important that all professionals involved in the care and treatment of patients exhibiting signs of dementia have a thorough understanding of the *Behavioral and Psychological Symptoms of Dementia (BPSD)* and are provided with the best possible resources to guide them in developing effective courses of treatment.

It is for that need that the International Psychogeriatric Association (IPA) developed *The IPA Complete Guides to BPSD* which, although helpful to all geriatric healthcare providers, was prepared with a view toward the different perspectives of the many professions that encounter patients with BPSD.

To address your practice needs, *The IPA Complete Guides to BPSD* is designed to serve as a reference tool or as a training resource. When used for training, the individual guides of *The IPA Complete Guides to BPSD* series, as well as each module contained within *The IPA Complete Guides to BPSD – Specialists Guide,* can be used alone or together in a tailored approach to create your own customized program.

The IPA Complete Guides to BPSD is offered exclusively in electronic form. The advantages of a downloadable version include—

- Lower cost to you than a printed version
- Regular updating ensures you have the most recent information
- Easy to access and use anytime and anywhere you are around the world



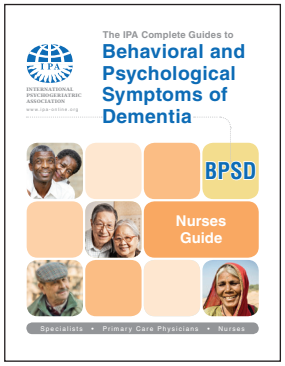
The IPA Complete Guides to BPSD – Specialists Guide is a comprehensive compilation of eight modules detailing the presentation and causes of BPSD, constructive guidance on pharmacological and non-pharmacological treatment interventions, and information on caregiver education and support. This is the most extensive in the *Guides* series, and while helpful for all geriatric healthcare professionals, it is especially instructive for geriatric mental healthcare specialists: physicians, nurses, psychologists, occupational therapists, social workers and others.

The Modules—

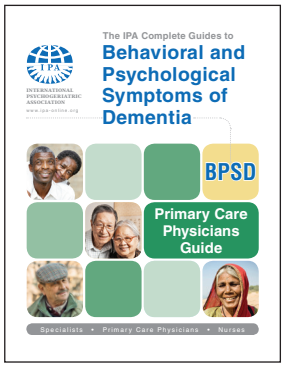
- Module 1 – An introduction to BPSD
- Module 2 – Clinical issues
- Module 3 – Etiology
- Module 4 – Role of family caregivers
- Module 5 – Non-pharmacological treatments
- Module 6 – Pharmacological management
- Module 7 – Cross-cultural and transnational considerations
- Module 8 – Long-term care

The IPA Complete Guides to BPSD

Each module includes an in-depth discussion and analysis of its subject area and concludes with a reference and recommended reading list. The content of *The IPA Complete Guides to BPSD – Specialists Guide* is designed to contribute to the improved management of dementia patients with BPSD and reduce some of the stresses experienced by caregivers and families of dementia patients.



The IPA Complete Guides to BPSD – Nurses Guide is intended for use by nurses and other professionals involved in nursing care to aid in the study and management of patients with BPSD, and is not for use by patients and their caregivers. The *Nurses Guide* focuses on the unique aspects involved in nursing, including care approaches and nursing interventions specific to BPSD, and the need to provide support to formal and informal caregivers. This guide should be seen as a complement to *The IPA Complete Guides to BPSD – Specialists Guide,* a more in-depth resource with its many different modules intended for all those healthcare professionals who have specialized in geriatric mental healthcare.



The IPA Complete Guides to BPSD – Primary Care Physicians Guide was written for primary care physicians, as many times they are the first point of contact for patients and their caregivers. In that role, it is vital that physicians and their staff are familiar with clinical manifestations and management of BPSD. This *Guide* is a valuable resource for the identification and early diagnosis of dementia that is so critical for patients and their caregivers. It is intended as a complement for Primary Care Physicians to *The IPA Complete Guides to BPSD – Specialists Guide.*

The IPA Complete Guides to BPSD, individually and as a series, provide the needed insight to help with early diagnosis and care for the patient and caregiver. With a disease that affects not just the patient, but also the family and the greater community and social systems, *The IPA Complete Guides to BPSD* series helps support all geriatric healthcare providers with both broad and specific information and care guidelines.

The International Psychogeriatric Association is committed to advancing geriatric mental health around the world through the creation of comprehensive and practical resources like *The IPA Complete Guides to BPSD* series. If you have a need to use *The IPA Complete Guides to BPSD* series in a language other than English, please contact the IPA Secretariat at the address listed on the acknowledgements page of this document to arrange a translation.

Acknowledgments

The production of *The IPA Complete Guides to Behavioral and Psychological Symptoms of Dementia (BPSD) – Specialist's Guide* has been made possible through the concerted effort of a number of experts in the field of dementia and associated behavioral and psychological symptoms.

Project Editors

Brian Draper (Australia) Henry Brodaty (Australia) Sanford I. Finkel (United States)

Module Editors

Module 1	An introduction to BPSD	Brian Draper (Australia) Sanford I. Finkel (United States) Larry Tune (United States)
Module 2	Clinical issues	George Grossberg (United States) Jay Luxenberg (United States) Larry Tune (United States)
Module 3	Etiology	Brian Draper (Australia) Martin Haupt (Germany) Michael Zaudig (Germany)
Module 4	Role of family caregivers	Henry Brodaty (Australia) Kim Burns (Australia)
Module 5	Non-pharmacological treatments	Daniel O'Connor (Australia) Peter Rabins (United States) Gregory Swanwick (Ireland)
Module 6	Pharmacological management	Dallas Seitz (Canada) Brian Lawlor (Ireland)
Module 7	Cross-cultural and transnational considerations	Huali Wang (PR China) Warachal Faison (United States) Akira Homma (Japan) Brian Draper (Australia)
Module 8	Long-term care	David Conn (Canada)

Contributors

Ricardo Allegri (Argentina)
Caroline Arasaratnam (Australia)
Takashi Asada (Japan)
Olusegun Baiyewu (Nigeria)
Lesley Blake (United States)
Cassio Bottino (Brazil)
Sarah Brisbin (Canada)
Alistair Burns (United Kingdom)
Gerard Byrne (Australia)
Eric Caine (United States)
WC Chan (Hong Kong SAR PR China)
Vijay Chandra (India)

Acknowledgments *continued*

Georgina Charlesworth (United Kingdom)
Mian-Choon Chong (Taiwan)
David Conn (Canada)
Carolyn Cooler (United States)
Jeffrey Cummings (United States)
Abhilash Desai (United States)
Davangere Devariand (United States)
Robin Eastwood (United Kingdom)
Barry Edelstein (United States)
Engin Eker (Turkey)
Lee Fay-Low (United Kingdom)
Monica Ferriera (South Africa)
Vinod Gangoli (India)
Serge Gauthier (Canada)
Maggie Gibson (Canada)
Ingalill Hallberg (Sweden)
Suzanne Hanser (United States)
Martin Haupt (Germany)
Edward Helmes (Australia)
Hugh Hendrie (United States)
Timothy Howell (United States)
Ali Javadpour (Iran)
Daniel Krause (United States)
Linda Lam (Hong Kong SAR PR China)
James Lindesay (United Kingdom)
Jacobo Mintzer (United States)
Wendy Moyle (Australia)
Nancy Pachana (Australia)
David Resnikoff (Mexico)
Karen Ritchie (France)
Barry Rovner (United States)
Ken Sakauye (United States)
Richard Schultz (United States)
Dallas Seitz (Canada)
Martin Smalbrugge (Netherlands)
Guk-Hee Suh (Republic of Korea)
Masatoshi Takeda (Japan)
Linda Teri (United States)
Meinhardt Tropper (Israel)
Huali Wang (China)
Joy Webster (United States)
R.B. Wetzels (Netherlands)
Peter Whitehouse (United States)
Steven Zarit (United States)
Sytse Zuidema (Netherlands)

The International Psychogeriatric Association wishes to acknowledge the support received from Janssen-Cilag and Organon for the development, production, and distribution of the first two editions of the *IPA BPSD Educational Pack*.

About IPA

The **International Psychogeriatric Association** (IPA), founded in 1982, is a unique and diverse professional healthcare community promoting better geriatric mental health—across disciplines, across borders, and across geriatric issues. Psychiatrists, scientists, neurologists, geriatricians, primary care physicians, epidemiologists, nurses, psychologists, occupational therapists, social workers, and many other healthcare professionals come to the IPA community from all over the globe to discuss, learn, share, and research information about behavioral and biological aspects of geriatric mental health. IPA promotes research and education, facilitates an international exchange of ideas on psychogeriatric issues, and fosters cross-cultural understanding of the latest developments in the field.

For more information, contact:
International Psychogeriatric Association (IPA)
550 Frontage Road, Suite 3759, Northfield, IL, 60093 United States
Tel: +1.847.501.3310; Fax: +1.847.501.3317
E-mail: info@ipa-online.org
Website: http://www.ipa-online.org

Abbreviations in BPSD

ABC	Antecedents Behavior Consequences
AD	Alzheimer's disease
ADAS-cog	Alzheimer's Disease Assessment Scale (cognitive portion)
ADCS	Alzheimer's Disease Cooperative Study
ADI	Alzheimer's Disease International
ADL	Activities of Daily Living
ADRC	Alzheimer's Disease Research Center
ALMA	Association Against Alzheimer's Disease and Related Disorders of Argentina
APOE	Apolipoprotein E
ARDSI	Alzheimer's and Related Disorders Society of India
BEHAVE-AD	Behavioral Pathologic Rating Scale for Alzheimer's disease
BPSD	Behavioral and Psychological Symptoms of Dementia
CAM	Confusion Assessment Method
CAMDEX	Cambridge Examination for Mental Disorders of the Elderly
CASI	Cognitive Abilities Screening Instrument
CATIE-AD	Clinical Antipsychotic Trials of clinical effectiveness—Alzheimer's disease
CBI	Caregiver Burden Inventory
CBT	Cognitive Behavioral Therapy
CDR	Clinical dementia rating
CERAD	Consortium to Establish a Registry for Alzheimer's Disease
CERAD-BRSD	Behavior Rating Scale for Dementia of the Consortium to Establish a Registry for Alzheimer's Disease
ChAT	Choline acyltransferase
CIDI	Composite International Diagnostic Interview
CIND	Cognitive Impaired Not Demented
CMAI	Cohen-Mansfield Agitation Inventory
COMT	Cathecol-O-methyltransferase
CSDD	Cornell Scale for Depression in Dementia
CSID	Community Screening Instrument for Dementia
DAT	Dementia of Alzheimer's type
DBDS	Dementia Behavior Disturbance Scale
DLB	Dementia with Lewy bodies
DIS	Diagnostic Interview Schedule
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders (fourth edition)
ECT	Electroconvulsive therapy
EPS	Extrapyramidal side effects
FTD	Frontotemporal dementia

Abbreviations in BPSD *continued*

GABA	Gamma-aminobutyric-acid
GDS	Geriatric Depression Scale
GDS	Global Deterioration Scale
GMS	Geriatric Mental Status
GRACE	Genetics, responses, and cognitive enhancers
HPA	Hypothalamic-pituitary-adrenal
ICD-10	International Classification of Diseases (tenth revision)
IPA	International Psychogeriatric Association
LTC	Long term care
MCI	Mild cognitive impairment
MDS	Minimum Data Set
MHPG	3-methoxy-4-hydroxy-phenylglycol
MIMIC	Multiple Indicators Multiple Causes
MMSE	Mini-Mental State Examination
MPHW	Multi-purpose health workers
NIA	National Institute on Aging
NHBPS	Nursing Home Behavior Problem Scale
NINCDS-ADRDA	National Institute of the Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease-Related Disorders Association*
NMDA	N-methyl d-aspartate
NOSIE	Nurses' Observation Scale for Inpatient Evaluation
NPI	Neuropsychiatric Inventory
NPI-D	Neuropsychiatric Inventory—Distress Subscale
NRS	Neurobehavior Rating Scale
PAS	Pittsburgh Agitation Scale
PD	Parkinson's disease
PDD	Parkinson's disease dementia
RAGE	Rating Scale for Aggression in the Elderly
REACH	Resources for Enhancing Alzheimer's Carer Health
RMBPC	Revised Memory Behavior Problem Checklist
RUDAS	Rowland Universal Dementia Assessment Scale
SCAG	Sandoz Clinical Assessment Geriatric Scale
SSRI	Selective serotonin reuptake inhibitors
TCA	Trycyclic antidepressants
VaD	Vascular dementia
WHO	World Health Organization
ZBI	Zarit Caregiver Burden Interview

* Now known as the Alzheimer's Association

Contents

MODULE 1 An introduction to BPSD **1.1**

Key messages 1.2
Importance of identifying and treating BPSD 1.2
Development of specific therapies for BPSD 1.8
Future directions: research 1.10
IPA educational programs for BPSD 1.10
Appendix: Rating scales for BPSD 1.11
References and recommended reading 1.13

MODULE 2 Clinical issues **2.1**

Key messages 2.2
BPSD 2.2
Specific symptomatology: psychological 2.5
Specific symptomatology: behavioral 2.12
Assessment tools 2.14
Delirium: a differential diagnosis from BPSD 2.14
Appendix 1. Diagnostic classification of signs and symptoms in patients with dementia: a historical review 2.16
Appendix 2. Rating scales for BPSD in clinical settings 2.17
References and recommended reading 2.19

MODULE 3 Etiology **3.1**

Key messages 3.2
Introduction 3.2
Genetic abnormalities in dementia—relationship to BPSD 3.3
Neurotransmitter changes in dementia—relationship to BPSD 3.4
Neuropathologic changes in dementia—relationship to BPSD 3.8
Structural neuroimaging 3.8
Functional neuroimaging 3.9
Circadian rhythms—relationship to BPSD 3.10
Other clinical contributors to BPSD 3.10
Conclusion 3.14
References and recommended reading 3.14

Contents *continued*

MODULE 4 Role of family caregivers **4.1**

Key messages 4.2
Introduction 4.2
What is caregiver burden? 4.3
Measuring caregiver burden 4.3
Factors associated with caregiver burden 4.4
The impact of BPSD on family caregivers 4.8
The impact of family caregivers on BPSD 4.9
Caregiver interventions for BPSD 4.10
Other interventions 4.11
Barriers to caregivers seeking assistance 4.12
Elements of success 4.12
Recommendations for caregivers 4.13
Conclusion 4.14
References and recommended reading 4.14

MODULE 5 Non-pharmacological treatments **5.1**

Key messages 5.2
Introduction 5.2
Understanding BPSD 5.2
Underlying principles 5.3
Assessment methods 5.4
Treatment principles 5.5
Individual treatments 5.6
Treatment of particular symptoms 5.8
Physical environment 5.9
Conclusions 5.10
References and recommended reading 5.10

MODULE 6 Pharmacological management **6.1**

Key messages 6.3
General principles 6.3
Drug classes and target symptoms 6.4
Miscellaneous drug classes 6.18
Electroconvulsive therapy for BPSD and depression 6.19
Special populations 6.20
References and recommended reading 6.22

Contents *continued*

MODULE 7 Cross-cultural and transnational considerations 7.1

Key messages 7.3
Introduction 7.3
Aspects of BPSD likely to vary across cultures 7.3
BPSD in minority elders in the United States 7.12
BPSD in the Middle East 7.16
BPSD in Asia 7.19
BPSD in Latin America 7.32
BPSD in Africa 7.37
References and recommended reading 7.38

MODULE 8 Long-term care 8.1

Key messages 8.2
Introduction 8.3
Principles of good care 8.3
Environmental design 8.4
Screening and behavioral assessment 8.4
Non-pharmacological interventions 8.7
Pharmacological interventions 8.9
Optimizing the use of psychotropic medications 8.11
Role of the interdisciplinary team 8.15
Education and training 8.19
Guidelines 8.20
References and recommended reading 8.22

INTERNATIONAL PSYCHOGERIATRIC ASSOCIATION

www.ipa-online.org

MODULE 1

An introduction to BPSD

The IPA Complete Guides to Behavioral and Psychological Symptoms of Dementia

BPSD

Specialists Guide

Specialists • Primary Care Physicians • Nurses

MODULE 1: An introduction to BPSD

CONTENTS

Key messages	**1.2**
Importance of identifying and treating BPSD	**1.2**
The aging of the world's population	1.2
BPSD in classic descriptions of dementia	1.3
Emerging recognition of BPSD	1.4
Modern definition of BPSD—a consensus statement	1.4
Frequency and impact of BPSD	1.5
Development of specific therapies for BPSD	**1.8**
Quality-of-life assessment	1.9
Pharmacoeconomic assessment	1.9
Future directions: research	**1.10**
IPA educational programs for BPSD	**1.10**
Appendix: Rating scales for BPSD	**1.11**
References and recommended reading	**1.13**

Key messages

- With the aging of the world's population, a significant increase in the absolute number of older people with Alzheimer's disease (AD) and other dementias is now occurring.
- Dementia is associated with progressive cognitive decline, a high prevalence of behavioral and psychological symptoms of dementia (BPSD) such as agitation, depression and psychosis, stress in caregivers, and costly care.
- BPSD are an integral part of the disease process and present severe problems to patients, their families and caregivers, and society at large.
- BPSD are treatable and generally respond better to therapy than other symptoms or syndromes of dementia.
- Treatment of BPSD offers the best chance to alleviate suffering, reduce family burden, and lower societal costs in patients with dementia.

Importance of identifying and treating BPSD

The aging of the world population

The number of older people in the world is rising rapidly. For example, in 2000, there were 600 million people aged 60 and over; it is estimated there will be 1.2 billion by 2025 and 2 billion by 2050. In 2009 about two thirds of older people were living in the developing world, and by 2025 there will be 75%—a reflection of the improvements in healthcare and nutrition that are enjoyed by much of the world's population in the second half of the twentieth century. In the developed world, the very old (age 80+) is the fastest growing population group (World Health Organization, 2009).

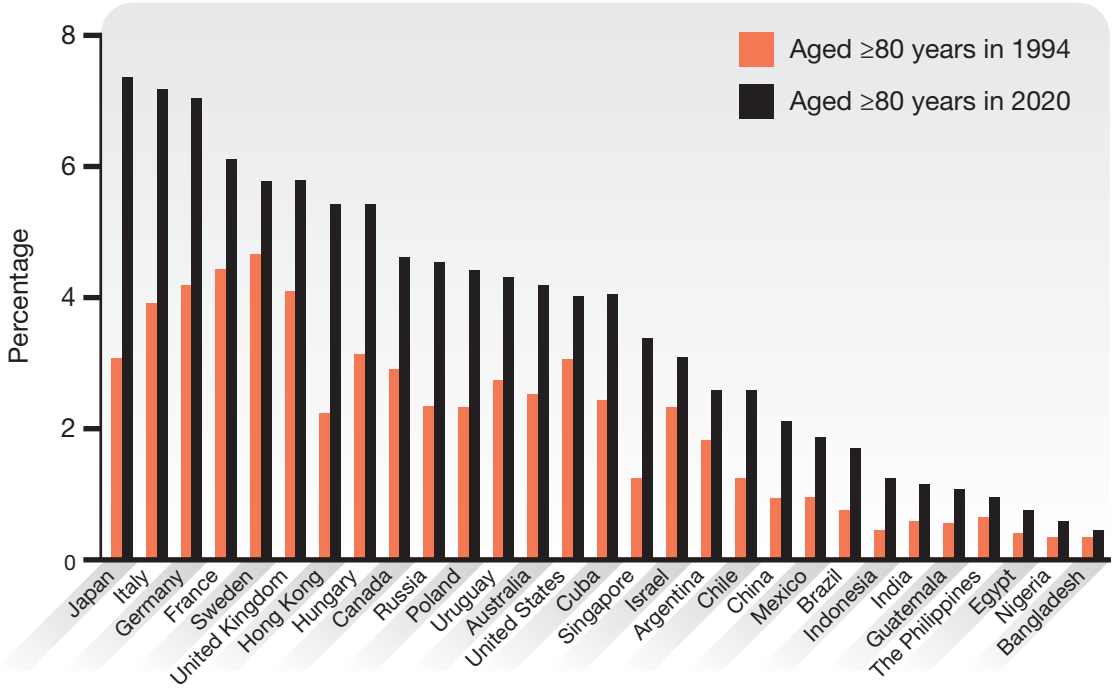


Figure 1.1: Estimations of the increasing size of the elderly population

As these numbers increase (Figure 1.1), there will be a dramatic rise in the number of people with dementia. This increase will be disproportionately higher in low- and middle-income countries than in high-income countries. The *2009 World Alzheimer Report* estimated that there were 35.6 million people with dementia in 2010, the numbers nearly doubling every 20 years, to 65.7 million in 2030 and 115.4 million in 2050. The majority of people with dementia currently live in low- and middle-income countries (58% in 2010) and this will rise to 71% by 2050 (Alzheimer's Disease International, 2009).

Disabilities and dementias increase markedly in the over 80-year-old population. Over the age of 75 years, the annual incidence of AD is about 1%, increasing to approximately 10% at age 85 (Bachman et al., 1990; Brayne, 2006). The prevalence of dementia has been reported to be between 5% and 8.5% in those over the age of 60 years, while in the very elderly, the prevalence is between 28.7% and 63.9% in those over the age of 90 years (Alzheimer's Disease International, 2009).

These increases have major implications for the provision of healthcare generally and for dementia care in particular. If more people have dementia, there will be more people exhibiting behavioral and psychological symptoms of dementia. This implication constitutes the greatest burden to caregivers. This module describes these important aspects of dementia, as well as their frequency and impact.

BPSD in classic descriptions of dementia

BPSD have been identified as integral parts of dementing disorders from the earliest descriptions of these conditions. For example, in defining the 'demence senile' in 1838, Esquirol noted that it is a condition that may be accompanied by emotional disturbances (Esquirol, 1838). Alois Alzheimer, in his classic early twentieth-century case description of the disease now universally associated with his name, noted behavioral symptoms as prominent manifestations in his brief case description (Alzheimer, 1906). The symptoms included:

- Paranoia
- Delusions of sexual abuse
- Hallucinations
- Screaming

Vascular dementia (previously called multi-infarct dementia) also has emotional instability and BPSD as prominent features. BPSD, particularly visual hallucinations and depression, are seen in Lewy body dementia. The behavioral variant of frontotemporal dementia, as its name implies, has predominant early behavioral changes that can include apathy, altered eating behavior, socially and sexually inappropriate behaviors, irritability and compulsive behaviors.

Consensus definitions of AD have generally included behavioral descriptions. The American Psychiatric Association's Fifth Edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM5)* describes major neurocognitive disorder with or without behavioral disturbance but does not provide a code for the specific type of behavior. In addition, rating scales such as the Blessed Dementia Scale and the Sandoz Clinical Assessment Geriatric Scale (SCAG) that have traditionally been used for the assessment of dementia have incorporated BPSD as elements of the condition.

Emerging recognition of BPSD

The focus on BPSD began in earnest only in the 1980s. Some investigators attributed BPSD to neurotransmitter or neuropathological changes whereas others have focused more on personality contributions and psychosocial factors (see Module 3).

It is clear that BPSD need to be assessed as part of an evaluation of dementia. Since 1986, there have been a number of scales developed to evaluate BPSD (see the box below for some examples and this module's Appendix for a full list).

1986
The Cohen-Mansfield Agitation Inventory (CMAI) focused specifically on behaviors such as hitting, pacing and screaming (Cohen-Mansfield et al., 1989; Cohen-Mansfield, 1996).

1987
The Behavioral Pathologic Rating Scale for Alzheimer's disease (BEHAVE-AD) focused on specific symptoms in AD, different from those seen in other neuropsychiatric disorders, such as the delusion that people are stealing things, fear of being left alone and fragmented sleep (Reisberg et al., 1996).

1994
The Neuropsychiatric Inventory (NPI) has frequency and severity scales for behaviors common to AD, but also includes scales for other dementias (Cummings et al 1994).

1995
The Consortium to Establish a Registry in AD (CERAD) Behavioral Scale focused on both behavioral and psychological symptoms (Tariot et al., 1995; Tariot, 1996).

2008
The Cambridge Behavioural Inventory—Revised—designed to distinguish FTD from AD and other degenerative dementias (Wear et al, 2008)

Modern definition of BPSD—a consensus statement

In 1996, the International Psychogeriatric Association (IPA) convened the Consensus Conference on the Behavioral Disturbances of Dementia for two purposes: to review current knowledge on behavioral disturbances of dementia and to reach some consensus of opinion in four critical areas:

- Definition of the symptoms
- Causes of the symptoms
- Description of clinical symptoms
- Research directions

The 1999 Update Consensus Conference provided additional knowledge and new research directions:

> The consensus group, consisting of some 60 experts in the field, from 16 countries, produced a statement on the definition of BPSD: "The term *behavioral disturbances* should be replaced by the term *behavioral and psychological symptoms of dementia* (BPSD), defined as: symptoms of disturbed perception, thought content, mood or behavior that frequently occur in patients with dementia." (Finkel and Burns, 1999)

There are many ways in which BPSD can be grouped. The participants of the Consensus group recognized that for certain purposes it might be useful to group them into specific symptom clusters (e.g., depressive syndrome, psychotic syndrome). A simple method of grouping is shown in the following box.

Behavioral symptoms
Usually identified on the basis of observation of the patient, including physical aggression, screaming, restlessness, agitation, wandering, culturally inappropriate behaviors, sexual disinhibition, hoarding, cursing and shadowing.

Psychological symptoms
Usually and mainly assessed on the basis of interviews with patients and relatives; these symptoms include anxiety, depressive mood, hallucinations and delusions. A psychosis of Alzheimer's disease has been accepted since the 1999 conference.

The European Alzheimer's Disease Consortium also noted that the term *BPSD* is not a unitary concept and recommended that it should be divided into several or more groups of symptoms (e.g., apathy, mood/agitation, psychosis) each possibly reflecting a different prevalence, course over time, biological correlate and psychosocial determinants (Robert et al., 2005). One grouping based upon factor analysis of the CMAI suggested four groups—aggressive behavior, physically non-aggressive behavior, verbally agitated behavior, and hiding and hoarding (Rabinowitz et al., 2005). A Multiple Indicators Multiple Causes (MIMIC) model identified four factors—psychosis, moods, agitation, and behavioral dyscontrol (Proitsi et al., 2009). Clearly more research is required to better characterize BPSD syndromes, although current knowledge about variations of BPSD between individuals and psychosocial circumstances emphasizes the importance of a tailored approach to treatment and care. The clinical presentation of BPSD is covered in detail in Module 2.

Frequency and impact of BPSD

BPSD can result in suffering, premature institutionalization, increased costs of care, and significant loss of quality-of-life for people with dementia and their families and caregivers (Finkel et al., 1996). A number of studies looking at the occurrence of BPSD in nursing home and community populations have found these symptoms to occur in up to 97% of patients. The *Medical Research Council Cognitive Function and Ageing Study in England and Wales* found that 11 of 12 symptoms of BPSD were more common in 587 participants with dementia than

in 2,050 participants without dementia—the exception being sleep problems (Savva et al., 2009). The Cache County study has reported the point- and 5-year-period prevalence of BPSD on the Neuropsychiatric Inventory (NPI) in an incident sample of 408 dementia participants (Steinberg et al., 2008). Details of the study are presented in Table 1.1. BPSD tend to persist; for example, at 18-month follow-ups in the Cache County study, delusions persisted in 65.5% of individuals, depression in 58.3%, and aberrant motor behavior in 55.6% (Steinberg et al., 2004).

Table 1.1: Point and 5-year Prevalence of BPSD in the Community as measured by the Neuropsychiatric Inventory (NPI)

NPI BPSD items	Point Prevalence at Baseline (%)	Five-year period prevalence (%)
Delusions	18	60
Hallucinations	10	38
Agitation/Aggression	14	45
Depression/Dysphoria	29	77
Apathy/Indifference	20	71
Elation/Euphoria	1	6
Anxiety	14	62
Disinhibition	7	31
Irritability/Lability	20	57
Aberrant Motor Behavior	7	52
Any Symptom	56	97

(Steinberg et al., 2008, reproduced with permission)

Rates of BPSD are high in nursing homes around the world regardless of which behavioral scales are used. For example, in Australia 92% of nursing home residents were reported to have at least one type of BPSD as measured by the BEHAVE-AD (Brodaty et al., 2001), in the Netherlands 81% had clinically significant neuropsychiatric symptoms on the NPI-NH, and 85% showed at least one symptom of agitation on the Cohen-Mansfield Agitation Inventory (CMAI) (Zuidema et al., 2007). In Norway 84% of residents had clinically significant neuropsychiatric symptoms on the NPI (Selbæk et al., 2008); and in the United States 69% had behavioral symptoms on the Patient Assessment Instrument when residents with comorbid psychiatric disorders were excluded (McCarthy et al., 2004). More details of specific behaviors as measured by the BEHAVE-AD and CMAI are noted in Tables 1.2 and 1.3.

Table 1.2: Prevalence of BPSD in 11 Sydney Nursing Homes

BEHAVE-AD BPSD items	Prevalence (%)
Delusions	54
Hallucinations	33
Psychosis (Delusions + Hallucinations)	60
Activity Disturbance	53
Aggression	77
Behavioral Disturbance (Activity Disturbance + aggression)	82
Diurnal Disturbance	47
Affective Disturbance	60
Anxiety and Phobias	69
BEHAVE-AD Total	92

(Brodaty et al., 2001; reproduced with permission)

Table 1.3: Prevalence of BPSD in 59 Dutch Dementia Special Care units

CMAI BPSD Items with prevalence ≥ 10%	Prevalence (%) at least weekly
General restlessness	44
Cursing or verbal aggression	33
Constant request for attention	32
Negativism	31
Repetitious sentences/questions	30
Pacing	29
Performing repetitious mannerisms	28
Complaining	26
Grabbing	24
Making strange noises	20
Inappropriate robing/disrobing	18
Handling things inappropriately	18
Get to different place	16
Hitting	13
Screaming	13
Hoarding things	12
Hiding things	10

(Zuidema et al., 2007; reproduced with permission)

The 10/66 Dementia Research Group pilot studies in low- and middle-income countries from Latin America, India, China, and South East Asia, and Nigeria found that 71% of carers reported at least one problem behavior. The people with dementia were also assessed, and significant psychological symptoms were detected in 50% (Ferri et al., 2004)

Various BPSD occur at different phases of illness. Research has indicated that these symptoms either:

- appear to occur increasingly as the dementing disorder progresses; or
- may occur more commonly during specific periods in the dementing disorder.

Untreated BPSD contribute to:

- Premature institutionalization (Colerick and George, 1986; Morriss et al., 1990; Steele et al., 1990; O'Donnell et al., 1992; de Vugt et al., 2005)
- Increased financial cost (Cohen-Mansfield, 1995; Herrmann et al., 2006)
- Decreased quality of life for both the caregiver and the patient (Deimling and Bass, 1986; Burgio, 1996);
- Significant caregiver stress (Rabins et al., 1982)
- Stress to nursing staff in residential facilities (e.g., Rodney, 2000; Draper et al., 2000)
- Excess disability (Brody, 1982; Hinton et al., 2008), i.e., people with BPSD function at a lower level than those without. Once symptoms are ameliorated or removed, functional level improves (reducing patient and caregiver distress and improving quality of life)

Development of specific therapies for BPSD

Since the 1990s there has been increased interest in specific therapies for BPSD for several reasons:

- BPSD are recognized as major sources of burden for caregivers of people with dementia and are frequently cited by caregivers as reasons for institutionalization of their relatives.
- Determination of the impact of pharmacological and non-pharmacological interventions in treating BPSD became an area of active scientific research and investigation.
- Previously, clinicians had attempted to treat BPSD with various medications in the absence of data regarding their efficacy.

There are many reasons why good research data were previously lacking. Older people with dementia were considered a 'difficult' study population because of their age, frailty, and the nature of their illnesses. Until the 1990s there were no good methods to assess individuals with dementia. Subsequently, governments, the pharmaceutical industry, and research foundations have become interested in BPSD. Efforts to measure the outcome of treatment in terms of quality of life and cost-effectiveness are increasing. The research has yielded mixed results, confirming that antipsychotic drugs have modest efficacy in the treatment of agitation, aggression, and psychosis associated with dementia but with an increased risk of cerebrovascular adverse events and mortality. There are no proven alternative psychotropic agents for BPSD, although many are being investigated (Jeste et al., 2008). There are also some promising indications that non-psychotropic agents such as analgesics might be effective for BPSD (Husebo et al., 2011) (See Module 6).

Similarly, while there are some promising non-pharmacological treatments for BPSD such as aromatherapy, ability-focused carer education, preferred music therapy, and muscle relaxation training, effect sizes are modest, and there is still considerable need for more research (O'Connor et al, 2009a, b). (See Module 5).

While some of these BPSD treatment outcome studies have yielded disappointing results, the importance of tailoring pharmacological and/or non-pharmacological interventions to fit the needs of individuals with behaviors that have complex multifactorial etiologies has become clearer (Meares and Draper, 1999; Bird et al., 2007). In addition, non-pharmacological interventions should generally be employed before pharmacotherapy. In a 4-week open-label brief psychosocial intervention that was employed as the first stage of a RCT of the treatment of clinically significant agitation in Alzheimer's disease, 43% of the participants improved by 30% on the CMAI (Ballard et al., 2009). The challenge is to better identify which interventions work best for specific behaviors in individuals in various contexts.

Quality-of-life assessment

Recently, there have been attempts to measure quality of life in older persons with dementia. Such assessments include evaluation of the following items:

- Health status (including health-associated disabilities)
- Environment (including restrictions, stigma, opportunity for choice)
- Subjective perceptions of mood, physical discomfort and frustration
- Behavioral observation of activity, affect and social involvement
- Caregiver reporting of behavior and mood

Pharmacoeconomic assessment

Pharmacoeconomic assessment of treatment interventions (a kind of cost effectiveness measurement) is an important part of decision-making in healthcare. This is particularly true for BPSD because the increased demand for effective interventions has significant consequences for private and public healthcare budgets.

To obtain an accurate picture of the true costs and benefits of an intervention (e.g., pharmacological or non-pharmacological treatments, environmental alterations), pharmacoeconomic studies must measure many factors. These include increased length of hospitalization for older medically ill people with dementia, premature institutionalization in a nursing home, and improvement or deterioration in symptoms.

Clinicians in most countries now find they must consider the economic costs and benefits of particular drugs as well as the drug's effectiveness and safety. New medications with benefits in terms of improved tolerability and safety profiles but with higher drug purchase costs often change the cost-benefit assessments. Current studies are focusing on these issues in dementia and will inform clinicians about which treatments are most appropriate for specific symptoms.

Future directions: research

Advances in understanding BPSD depend on investigating their phenomenology, origins, courses, pathophysiology, social and environmental influences, and responses to treatment interventions.

Opportunities for research on BPSD are exciting because of new techniques and methods for the assessment of people with dementia, as well as the availability of measurement scales specifically developed for this population. Research resources are unevenly distributed and unavailable in many countries. More research is needed to ensure a strong and productive research program.

Research now needs to address the following areas:

- Development of cross-culturally applicable methods for the assessment of BPSD
- Further exploration of the relationship of types of BPSD to the environments in which they occur
- Understanding of the etiological biological and psychological substrates of types of BPSD
- Longitudinal evaluation of the incidence and prevalence of BPSD in different types of dementia
- Determination of the clinical and social impact of BPSD on the patient, family, healthcare professionals, healthcare systems, and society
- Development of a well-defined profile of treatment methods with specific reference to different types of BPSD and the response of those BPSD to non-pharmacological and pharmacological interventions

IPA educational programs for BPSD

The continuing discussion and need to define and understand BPSD in patients has led to the formation of IPA's ***Shared Interest Forum*** on BPSD. The mission of the BPSD Special Interest Group is "the promotion of research, training, and dissemination of information on behavioral and psychological symptoms of dementia [BPSD] to healthcare professionals and caregivers."

The goals of the BPSD educational programs are to:

- Inform psychiatrists, neurologists, geriatricians, related healthcare providers and caregivers of the behavioral and psychological symptoms of AD and other dementias; inform about the relationship between the symptoms and the course of the illness
- View the symptoms both individually and collectively in developing a specific plan for intervention; describe what is known about current treatments and management
- Describe and understand the specific needs of caregivers in relation to these symptoms
- View cross-cultural and translation variations.

Educational modalities include the following:

- Publication in journals
- Establishment of an international speakers' bureau slides
- An internet web site

Appendix: Rating scales for BPSD

This Appendix lists commonly used rating scales for the assessment of BPSD. A reprint of these scales can be found either in the original reference given or in the Appendix to a special issue of *International Psychogeriatrics* 1996; 8 (Suppl 3).

Behavioral and Emotional Activities Manifested in Dementia (BEAM-D)
Sinha, D., Zemlan, F.P., Nelson, S., et al. A new scale for behavioral agitation in dementia. *Psychiatry Research* 1992; 41: 73–88.

Behavioral Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD)
Reisberg, B., Borenstein, J., Salob, S.P., Ferris, S.H. Behavioral symptoms in Alzheimer's disease: Phenomenology and treatment. *Journal of Clinical Psychiatry* 1987; 48 (Suppl): 9–15.

Blessed Dementia Scale
Blessed, G., Tomlinson, B.E., Roth, M. The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. *British Journal of Psychiatry* 1968; 114: 797–811.

Brief Agitation Rating Scale (BARS)
Finkel, S.I., Lyons, J.S., Anderson, R.L. A brief agitation rating scale (BARS) for nursing home elderly. *Journal of the American Geriatrics Society* 1993; 41: 50–52.

Cambridge Behavioural Inventory—Revised
Wear, H.J., Wedderburn, C.J., Mioshi, E., et al. The Cambridge Behavioural Inventory revised, *Dementia & Neuropsychologia*, 2008: June 2(2): 102–107.

Caretaker Obstreperous Behavior Rating Assessment (COBRA)
Drachman, D.S., Swearer, J.M., O'Donnell, B.F., et al. The Caretaker Obstreperous Behavior Rating Assessment (COBRA) scale. *Journal of the American Geriatrics Society* 1992; 40: 463–480.

CERAD Behavior Rating Scale for Dementia
Tariot, P.N., Mack, J.L., Patterson, M.B., et al. The behavior rating scale for dementia of the consortium to establish a registry for Alzheimer's disease. The behavioral pathology committee of the consortium to establish a registry for Alzheimer's disease. *American Journal of Psychiatry* 1995; 152(9): 1349–1357.

Cohen-Mansfield Agitation Inventory (CMAI)
Cohen-Mansfield, J., Marx, M.S., Rosenthal, A.S. A description of agitation in a nursing home. *Journal of Gerontology* 1989; 44: M77–M84.

Cornell Scale for Depression in Dementia (CSDD)
Alexopoulos, G.S., Abrams, R.C., Young, R.C., Shamoian, C.S. Cornell Scale for Depression in Dementia. *Biological Psychiatry* 1988; 23: 271–284.

Dementia Behavior Disturbance Scale (DBD)
Baumgarten, M., Backer, P., Gauthier, S. Validity and reliability of the Dementia Behavior Disturbance Scale. *Journal of the American Geriatrics Society* 1990; 38: 221–226.

Dementia Mood Assessment Scale (DMAS)
Sunderland, T., Alterman, I., Yount, D., et al. A new scale for the assessment of depressed mood in dementia subjects. *American Journal of Psychiatry* 1988; 145: 955–959.

Dysfunctional Behavior Rating Instrument (DBRI)
Molloy, D.W., McIlroy, W.E., Guyatt, G.H., Lever, J.A. Validity and reliability of the Dysfunctional Behavior Rating Instrument. *Acta Psychiatrica Scandinavica* 1991; 84: 103–106.

Global Assessment of Psychiatric Symptoms (GAPS)
Raskin, A., Crook, T. Global Assessment of Psychiatric Symptoms (GAPS). *Psychopharmacology Bulletin* 1988; 24: 721–725.

Gottfries-Bråne-Steen Scale
Gottfries, C.G., Bråne, G., Gullberg, B., Steen, G. A new rating scale for dementia syndrome. *Archives of Gerontology and Geriatrics* 1982; 1: 311–330.

Irritability/Apathy Scale
Burns, A., Folstein, S., Brandt, J., Folstein, M. Clinical assessment of irritability, aggression, and apathy in Huntington and Alzheimer's disease. *Journal of Nervous and Mental Disease* 1990; 178: 20–26.

Manchester and Oxford Universities Scale for the Psychopathological Assessment of Dementia (MOUSEPAD)
Allen, N.H.P., Gordon, S., Hope, T., Burns, A. Manchester and Oxford Universities Scale for the Psychopathological Assessment of Dementia (MOUSEPAD). *British Journal of Psychiatry* 1996; 169: 293–307.

Neurobehavioral Rating Scale
Levin, H.S., High, W.M., Goethe, K., et al. The Neurobehavioral Rating Scale: Assessment of the behavioral sequelae of head injury by the clinician. *Journal of Neurology Neurosurgery & Psychiatry* 1987; 50: 183–193.

Neuropsychiatric Inventory (NPI)
Cummings, J., Mega., M., Gray K, et al. The Neuropsychiatric Inventory: Comprehensive assessment of psychopathology in dementia. *Neurology*, 1994; 44: 2308–2314.

Neuropsychiatric Inventory—Nursing Home Version (NPI-NH)
Cummings, J.L. The Neuropsychiatric Inventory: assessing psychopathology in dementia patients. *Neurology*, 1997; 48 (Suppl 6): S10–S16.

Pittsburgh Agitation Scale
Rosen, J., Burgio, L., Killar, M., et al. The Pittsburgh Agitation Scale. *American Journal of Geriatric Psychiatry* 1994; 2: 52–59.

Revised Memory and Behavior Problems Checklist
Teri, L., Truaz, P., Logsdon, R., et al. Assessment of behavioral problems in dementia: The Revised Memory and Behavior Problems Checklist. *Psychology & Aging* 1992; 7: 622–631.

Sandoz Clinical Assessment—Geriatric (SCAG)
Shader, R.L., Harmatz, J.S., Salzman, C. A new scale for clinical assessment in geriatric populations: Sandoz Clinical Assessment—Geriatric (SCAG). *Journal of the American Geriatrics Society* 1974; 22: 107–113.

Self-Psychology Rating Scale
Lazarus, L.W., Cohler, B.L., Lesser, J. Dissolution of the self in Alzheimer's disease—clinical implications. In: Bergener, M., Finkel, S.I. (eds). *Treating Alzheimer's disease and other dementias*. New York: Springer Publishing Co, 1995; 496–509.

References and recommended reading

Alzheimer, A. About a peculiar serious illness percent of the cerebral cortex (1906). *Neurologisches Centralblatt* 1995; 23: 1129–1136.

Alzheimer's Disease International *Alzheimer's Disease International 2009 World Alzheimer Report*. Prince, M. and Jackson, J. (Eds). Accessed 23 December 2009 from http://www.alz.co.uk/research/worldreport/

Bachman, D.L., Charleston, S.C., Philip, A.W., et al. Sexual differences in incidence and prevalence for Alzheimer's disease: The Framingham Study. *Neurology 1990*; 40 (Suppl 1): 176.

Ballard, C., Brown, R., Fossey, J., et al. Brief psychosocial therapy for the treatment of agitation in Alzheimer disease (The CALM-AD Trial). *American Journal of Geriatric Psychiatry* 2009; 17: 726–733.

Bird, M., Llewellyn-Jones, R., Korten, A., et al. A controlled trial of a predominantly psychosocial approach to BPSD: treating causality. *International Psychogeriatrics* 2007; 19(5): 874–91.

Brayne, C. Incidence of dementia in England and Wales. The MRC cognitive function and ageing study. *Alzheimer's Disease and Associated Disorders* 2006; 20 (S47–S51).

Brodaty, H., Draper, B., Saab, D., et al. Psychosis, depression and behavioral disturbances in Sydney nursing home residents: Prevalence and predictors. *International Journal of Geriatric Psychiatry* 2001; 16: 504–512.

Brody, J.A. *An epidemiologist views senile dementia—facts and figures. American Journal of Epidemiology* 1982; 113: 155–162.

Burgio, L. Interventions for the behavioral complications of Alzheimer's disease: Behavioral approaches. *International Psychogeriatrics* 1996; 8 (Suppl 1): 45–52.

Cohen-Mansfield, J., Marx, M.S., Rosenthal, A.S. A description of agitation in a nursing home. *Journal of Gerontology: Medical Sciences* 1989; 44: M77–M84.

Cohen-Mansfield, J. Assessment of disruptive behavior/agitation in the elderly: Function, methods and difficulties. *Journal of Geriatric Psychiatry Neurology* 1995; 8 (Suppl 1): 52–60.

Cohen-Mansfield, J. Conceptualization of agitation: Results based on the Cohen-Mansfield Agitation Inventory and the Agitation Behavior Mapping Instrument. *International Psychogeriatrics* 1996; 8 (Suppl 3): 309–315.

Colerick E.J., George, L.K. Predictors of institutionalization among caregivers of patients with Alzheimer's disease. *Journal of the American Geriatrics Society* 1986, 34: 492–498.

Copeland, J.R., Davidson, I.A., Dewey, M.E., et al. Alzheimer's disease, other dementias and pseudodementia: prevalence, incidence and three-year outcome in Liverpool. *British Journal of Psychiatry* 1992; 161: 230–239.

Cummings, J.L., Mega, M., Gray, K., et al. The Neuropsychiatric Inventory: Comprehensive assessment of psychopathology in dementia. *Neurology* 1994; 44: 2308–2314.

Deimling, G.T., Bass, D.M. Symptoms of mental impairment among elderly adults and their effects on family caregivers. *Journal of Gerontology* 1986; 41: 778–784.

de Vugt, M.E., Stevens, F., Aalten, P., et al. A prospective study of the effects of behavioral symptoms on the institutionalization of patients with dementia. *International Psychogeriatrics* 2005; 17(4):577–589.

Draper, B., Snowdon, J., Meares, S., et al. Case-controlled study of nursing home residents referred for treatment of vocally disruptive behavior. *International Psychogeriatrics* 2000; 12: 333–334.

Esquirol, J.E.D. *Des Maladies Mentales* 1938.

Ferri, C.P., Ames, D., Prince, M. Behavioral and psychological symptoms of dementia in developing countries. *International Psychogeriatrics* 2004; 16(4):441–459.

Finkel, S.I., Burns, A. *BPSD Consensus Statement, International Psychogeriatric Association* 1999.

Finkel, S.I., Costa e Silva, J., Cohen, G., et al. Behavioral and psychological signs and symptoms of dementia: a consensus statement on current knowledge and implications for research and treatment. *International Psychogeriatrics* 1996; 8 (Suppl 3): 497–500.

Herrmann, N., Lanctôt, K.L., Sambrook, R., et al. The contribution of neuropsychiatric symptoms to the cost of dementia care. *International Journal of Geriatric Psychiatry* 2006; 21(10):972–976.

Hinton, L., Tomaszewski Farias, S., Wegelin, J. Neuropsychiatric symptoms are associated with disability in cognitively impaired Latino elderly with and without dementia: results from the Sacramento Area Latino study on Aging. *International Journal of Geriatric Psychiatry* 2008; 23(1):102–108.

Husebo, B.S., Ballard, C., Sandvik, R. et al. Efficacy of treating pain to reduce behavioral disturbances in residents of nursing homes with dementia: clustered randomized clinical trial. *British Medical Journal* 2011; doi: 10.1136/bmj.d4065.

Jeste, D.V., Blazer, D., Casey, D., et al. ACNP white paper: Update on use of antipsychotic drugs in elderly persons with dementia. *Neuropsychopharmacology* 2008; 33: 957–970.

McCarthy, J. F., Blow, F.C., et al. "Disruptive Behaviors in Veterans Affairs Nursing Home Residents: How Different Are Residents with Serious Mental Illness?" *Journal of the American Geriatrics Society* 2004; 52(12): 2031–2038.

Meares, S., Draper, B. Treatment of Vocally Disruptive Behavior of Multifactorial Aetiology *International Journal of Geriatric Psychiatry* 1999; 14: 285–290.

Morriss, R.K., Rovner, B.W., Folstein, M.F., German, P.S. Delusions in newly admitted residents of nursing homes. *American Journal of Psychiatry* 1990; 147: 299–302.

O'Connor, D.W., Ames, D., Gardner, B. et al. Psychosocial treatments of behavior symptoms in dementia: a systematic review of reports meeting quality standards. *International Psychogeriatrics* 2009a; 21(2): 225–240.

O'Connor, D.W., Ames, D., Gardner, B., et al. Psychosocial treatments of psychological symptoms in dementia: a systematic review of reports meeting quality standards. *International Psychogeriatrics* 2009b; 21(2): 241–251.

O'Donnell, B.F., Drachman, D.A., Barnes, H., et al. Incontinence and troublesome behaviors predict institutionalization in dementia. *Journal of Geriatrics Psychiatry Neurology* 1992; 5: 45–52.

Proitsi, P., Hamilton, G., Tsolaki, M., et al. A multiple indicators multiple causes (MIMIC) model of behavioral and psychological symptoms in dementia (BPSD), *Neurobiology of Aging* 2009; doi:10.1016/j.neurobiolaging.2009.03.005

Rabinowitz, J., Davidson, M., De Deyn, P.P., et al. Factor analysis of the Cohen-Mansfield Agitation Inventory in three large samples of nursing home patients with dementia and behavioral disturbance. *American Journal of Geriatric Psychiatry* 2005; 13: 991–998.

Rabins, P.V., Mace, N.L., Lucas, M.J. The impact of dementia on the family. *JAMA* 1982; 248: 333–335.

Reisberg, B., Auer, S.R., Monteiro, I.M. Behavioral pathology in Alzheimer's disease (BEHAVE-AD) rating scale. *International Psychogeriatrics* 1996; 8 (Suppl 3): 301–308.

Robert, P.H., Verhey, F.R., Byrne, E.J., et al. Grouping for behavioral and psychological symptoms in dementia: clinical and biological aspects. Consensus paper of the European Alzheimer disease consortium. *European Psychiatry: the Journal of the Association of European Psychiatrists* 2005; 20(7): 490–496.

Rodney, V. Nurse stress associated with aggression in people with dementia: its relationship to hardiness, cognitive appraisal and coping. *Journal of Advanced Nursing* 2000; 3(1): 172–180.

Rovner, B.W., German, P.S., Broadhead, J., et al. The prevalence and management of dementia and other psychiatric disorders in nursing homes. *International Psychogeriatrics* 1990; 2:13–24.

Savva, G.M., Zaccai, J., Matthews, F.E., et al. Prevalence, correlates and course of behavioral and psychological symptoms of dementia in the population. *British Journal of Psychiatry* 2009; 194: 212–219.

Selbaek, G., Kirkevold, O., Engedal, K. The prevalence of psychiatric symptoms and behavioral disturbances and the use of psychotropic drugs in Norwegian nursing homes. *International Journal of Geriatric Psychiatry* 2007; 22(9): 843–849.

Steele, C., Rovner, B., Chase, G.A., Folstein, M. Psychiatric symptoms and nursing home placement of patients with Alzheimer's disease. *American Journal of Psychiatry* 1990; 147: 8.

Steinberg, M., Shao, H., Zandi, P. et al. Point and 5-year prevalence of neuropsychiatric symptoms in dementia: the Cache County Study. *International Journal of Geriatric Psychiatry* 2008; 23: 170–177.

Steinberg, M., Tschanz, J.T., Corcoran, C., et al. The persistence of neuropsychiatric symptoms in dementia: the Cache County Study. *International Journal of Geriatric Psychiatry* 2004; 19(1):19–26.

Tariot, P.N., Mack, J.L., Patterson, M.B., et al. The behavior rating scale for dementia of the consortium to establish a registry for Alzheimer's disease. The behavioral pathology committee of the consortium to establish a registry for Alzheimer's disease. *American Journal of Psychiatry* 1995; 152(9): 1349–1357.

Tariot, P.N. CERAD behavior rating scale for dementia. *International Psychogeriatrics* 1996; 8 (Suppl 3): 317–320.

World Health Organisation. *The world is ageing fast—have we noticed?* 2009. Accessed 23 December 2009 from http://www.who.int/ageing/en/index.html

Zuidema, S.U., Derksen, E., Verhey, F.R., Koopmans, R.T. Prevalence of neuropsychiatric symptoms in a large sample of Dutch nursing home patients with dementia. *International Journal of Geriatric Psychiatry* 2007; 22(7): 632–638.

INTERNATIONAL PSYCHOGERIATRIC ASSOCIATION

www.ipa-online.org

MODULE 2

Clinical issues

The IPA Complete Guides to Behavioral and Psychological Symptoms of Dementia

BPSD

Specialists Guide

Specialists • Primary Care Physicians • Nurses

MODULE 2: Clinical issues

CONTENTS

Key messages	**2.2**
BPSD	**2.2**
Clinical presentation	2.2
Duration and course	2.3
Variation with type of dementia	2.3
Specific symptomatology: psychological	**2.5**
Psychotic symptoms	2.5
Delusions	2.5
Hallucinations	2.6
Misidentification	2.7
Diagnostic criteria for psychosis of Alzheimer's disease	2.8
Depression	2.10
Apathy	2.11
Anxiety	2.11
Specific symptomatology: behavioral	**2.12**
Wandering	2.12
Agitation/Aggression	2.12
Resistiveness to care	2.13
Inappropriate sexual behaviors	2.13
Catastrophic reaction	2.14
Sundowning	2.14
Assessment tools	**2.14**
Delirium: a differential diagnosis from BPSD	**2.14**
Causes of delirium	2.15
Appendix 1. Diagnostic classification of signs and symptoms in patients with dementia: a historical review	**2.16**
Appendix 2. Rating scales for BPSD in clinical settings	**2.17**
References and recommended reading	**2.19**

Key messages

- Behavioral and psychological symptoms of dementia (BPSD) are very common and are significant symptoms of the illness. Among the most intrusive and difficult BPSD to cope with are psychological symptoms of:
  - Delusions
  - Hallucinations
  - Misidentifications
  - Depression
  - Sleeplessness
  - Anxiety
- And behavioral symptoms of:
  - Physical aggression
  - Wandering
  - Restlessness
- Moderately common BPSD which can also be distressing include:
  - Agitation
  - Culturally inappropriate behavior
  - Sexual disinhibition
  - Pacing
  - Screaming
- BPSD that are common and upsetting, but that are more manageable and less likely to result in institutionalization include:
  - Crying
  - Cursing
  - Apathy
  - Repetitive questioning
  - Shadowing (stalking)

BPSD

Clinical presentation

Behavioral and psychological symptoms of dementia (BPSD) are very common and are significant symptoms of the illness, contributing most to caregiver burden and often resulting in premature institutionalization of the person with dementia (see Module 1).

Detailed studies of the occurrence of BPSD suggest that any symptom can occur during any stage in dementia, and at certain stages virtually all patients demonstrate some type of BPSD (Reisberg et al., 1989). One study of BPSD found that 64% of patients with Alzheimer's disease (AD) had one or more BPSD at initial evaluation (Devanand et al., 1997). The majority of these people were living at home. In a community-based population survey using the Neuropsychiatric Inventory (NPI), Lyketsos et al., (2000) reported that people with dementia had over 40 times the rate of behavioral disturbance than did the rest of the population, 61% of people with dementia had at least one behavioral disturbance and 31% had severe levels of BPSD (defined as an NPI score of ≥ 6). A more recent study from the UK compared 587 patients with dementia living in the community with 2,050 non-demented controls. The study found that "BPSD affect nearly all dementia patients." They also noted that all BPSD were more common in dementia patients versus controls except sleep problems, and that BPSD symptoms often co-occur, e.g. depression and anxiety. Psychosis occurred more frequently with declining

cognition and anxiety and depression were more common in younger dementia patients (Savva et al., 2009). The average prevalence of at least one BPSD symptom in residents with dementia living in long-term care facilities is 82%, with agitation and apathy being most prevalent of all BPSD symptoms (Selbaek et al., 2013). Large proportions of residents with dementia living in long-term care facilities were found to have exhibited one or more of four kinds of behavioral symptoms in the previous week (1) physically aggressive behaviors (e.g., hitting, kicking); (2) verbally aggressive behaviors (e.g., cursing); (3) physically non-aggressive behaviors (e.g., pacing); and (4) resistance to care (e.g., resistance with personal care) (IOM 2012). Depression and psychotic symptoms often accompany these behaviors. Resident-to-staff and resident-to-resident sexual aggression is also prevalent in long-term care facilities (Rosen et al., 2010).

Characteristics of BPSD are listed in Table 2.1. A historical review of the nosology or classification of BPSD is presented in this Module's Appendix 1. A variety of instruments have been developed to quantify BPSD, and theories behind existing rating scales are reviewed in this Module's Appendix 2.

Table 2.1: Characteristics of BPSD

• Psychotic symptoms	• Misidentification syndromes
• Apathy	• Aggressivity
• Delusions	• Depression
• Anxiety	• Wandering
• Hallucinations	• Sundowning
• Agitation	• Sexual
– Verbal	• Impulsive
– Physical	• Catastrophic reactions

Duration and course

As noted in Module 1, different BPSD occur during different phases of the illness. Affective symptoms are more likely to occur earlier in the course of the illness (Reisberg et al., 1989; Rubin et al., 1988). Agitated and psychotic behaviors are frequent in patients with moderately impaired cognitive function; however, these become less evident in the advanced stages of dementia, most likely because of the deteriorating physical and neurological condition of the patient (Tariot and Blazina, 1994). The prevalent neuropsychiatric symptoms in 123 hospice-eligible patients with advanced dementia residing in a nursing home were agitation or aggression (50%), depression (46%), and withdrawal/lethargy (43%) (Kverno et al., 2008). Some BPSD are more persistent than others. For example, one study has shown that agitation is the most enduring behavioral symptom in patients with mild to moderate AD over a five-year observation period (Devanand et al., 1997).

Variation with type of dementia

More than 70 conditions can cause dementia in the elderly (Cohen et al., 1993). By far the most common is Alzheimer's disease (AD) (greater than 50%), followed by vascular dementia (15–20%). Cases of combined AD and vascular dementia (VaD) account for about 20%. The prevalence of Lewy body dementia (DLB) has been estimated to be as high as 20% (Perry,

1990; Jellinger, 1996; Barker et al., 2002), and this figure may be even higher if AD with Parkinsonian features is included. Using the Revised Consensus Criteria for DLB, recent studies have found DLB to be the second most common cause of progressive dementia after AD (Aarsland et al. 2008).

Some studies have found few differences between the prevalence of BPSD in AD and VaD (Cohen et al., 1993; Tariot and Blazina, 1994; Thompson et al., 2010); others have reported a higher rate of delusions in AD and a higher rate of depression in VaD (Lyketsos et al., 2000). Overall, depression, emotional lability, and apathy seem to be more common in VaD versus AD and psychosis less common. Depression has an especially strong relationship with VaD (O'Brien et al., 2003). In the study by Cohen, et al. (1993), patients with mixed AD and VaD had the highest levels of psychiatric disturbance, all symptom levels were high (30% of all patients showed three or more psychiatric symptoms), symptoms increased with severity of the dementia, and the most frequent symptom was agitation, followed by symptoms of depression, apathy and aberrant behavior. More recently, a study by Staekenborg et al., (2010), found different rates of BPSD in small vessel disease VaD compared to large vessel disease VaD. Small vessel VaD showed more apathy, aberrant motor behavior and hallucinations. Large vessel VaD had higher rates of agitation/aggression and euphoria. This study found BPSD in 92% of the total VaD population with 65% having apathy, 45% depression, 42% irritability and 40% showing agitation/aggression.

Visual hallucinations are more commonly found in people with dementia with Lewy bodies than in those with Alzheimer's disease or Parkinson's disease (Ala et al., 1997; Beal and Vonsattel, 1998). These occur in approximately 80% of patients with dementia with Lewy bodies compared with about 20% of Alzheimer's disease patients (McKeith et al., 1992). A recent prospective, community-based, autopsy-confirmed study of 148 patients with dementia found 27 to have had visual hallucinations. Those with visual hallucinations were younger at intake and more likely to have agitation, delusions and apathy. Seventy-eight percent of those with visual hallucinations were found to have Lewy body pathology—of these, 59% also had DAT at autopsy (Tsuang et al., 2009).

Parkinson's disease dementia (PDD) is increasingly being recognized with recently proposed diagnostic guidelines (Goetz et al., 2008). PDD presents with prominent executive function disturbance in a patient with at least a two-year history of Parkinson's disease (PD). Most often the dementia in PD is seen eight or more years after PD onset. PDD has less prominent memory disturbance early on and a higher association with depression than AD (Robottom and Weiner, 2009).

Frontotemporal dementia (FTD) has been associated with higher incidences of many symptoms (Mendez et al., 2008) including impulsivity (Lindau et al., 1998), compulsive behaviors (Rosso et al., 2001), hypersexuality (Cummings and Duchen, 1981) and verbal outbursts (Mendez et al., 1998). FTD is significantly associated with increased caregiver distress (Mourik et al., 2004). Emergence of artist abilities has been associated with left temporal involvement in frontotemporal dementia (Miller et al., 1998). The anatomic distribution of asymmetric atrophy in frontotemporal dementia has been correlated with specific BPSD (Snowden et al., 1996). Troublesome and disruptive behaviors have been reported to occur earlier and to be more frequent in Huntington's chorea and Creutzfeldt-Jakob disease (Cummings and Duchen, 1981). A recent study has found that BPSD occur in all stages of Huntington's disease; often, behavioral

problems arise prior to onset of motor symptoms; apathy is related to disease severity, while depression and irritability are not (Kingma et al., 2008). A 25-year analysis of the literature on Creutzfeldt-Jakob disease relative to BPSD found that 80% demonstrated BPSD within the first 100 days of the illness with 26% having BPSD at the time of presentation. The most common symptoms were sleep disturbance, psychosis, and depression. Psychiatric symptoms often preceded formal diagnosis (Wall et al., 2005).

These distinctions are blurred in cases of mixed etiology, including those patients with combined vascular dementia and a degenerative dementia like Alzheimer's disease. In general, any BPSD can occur in any dementia.

Specific symptomatology: psychological

Psychotic symptoms

A review of 55 studies published from 1990-2003 found that psychosis has been reported in 41% of patients with AD, with 36% having delusions and 18% having hallucinations. African American or black ethnicity and more severe cognitive impairment were associated with higher rates of psychosis and the presence of psychotic symptoms was associated with a more rapid rate of cognitive decline in AD. The intensity of psychotic symptoms often diminished after one-year follow-up (Ropacki et al., 2005).

Delusions

The frequency of delusions in people with dementia is cited as being between 10% and 73% depending on the study population and the definition of dementia (Wragg and Jeste, 1989). The most common delusions in demented people are persecutory or paranoid (Morris et al., 1990). One study (Omar et al., 2009) looked at delusions in frontotemporal lobar degeneration. Delusions were seen in 14% of patients and were often seen early in the course of the disease, were prominent, and persistent. Paranoid and somatic delusions were most common.

Delusions occur in different guises in dementia. Five typical delusions seen in dementia (predominantly dementia of the Alzheimer's type) are documented in the Behavioral Pathologic Rating Scale for Alzheimer's disease (BEHAVE-AD; Reisberg et al., 1989):

1. *People are stealing things*
   The probable psychological explanation for this, the most common delusion in people with dementia, is that patients cannot remember the precise location of common household objects. If the delusion is severe the person with dementia will believe that others are coming into the home to hide or steal objects.
2. *House is not one's home*—which may also be classified as misidentification (Burns, 1996)
   The main contributory factor to this belief is that the patient no longer remembers or recognizes his/her home. And, those who reside in institutional settings often develop the belief, even after many years, that they need to go home. So fixed is the delusion in some older people with dementia, that they can attempt to leave the house to go 'home'. This results in wandering. Of course for many patients who are institutionalized this belief is reality and not delusional.

3. *Spouse (or other caregiver) is an impostor*—can also be classified as misidentification (Burns, 1996) or as Capgras phenomenon or delusion. This is a frequent delusion that, in some instances, can provoke anger or violence towards the perceived impostor. This is extremely upsetting to the spouse or caregiver who is already likely to be distressed by the failure to be recognized.
4. *Abandonment*
   Persons with dementia commonly believe they have been abandoned or institutionalized, or imagine that there is a conspiracy to institutionalize them. Although intellectual function declines as dementia progresses, patients retain some insight into their condition. The individual's awareness of having become a burden may be related to this delusion of abandonment. Importantly, for many residents of nursing homes, abandonment may be the reality and not a delusion.
5. *Infidelity*
   Occasionally, persons with dementia will become convinced that their spouse is unfaithful—sexually or otherwise. This conviction may also extend to other caregivers.

According to an analysis of several studies (Tariot and Blazina, 1994), the most frequent single delusion is that 'people are stealing things,' experienced by 18% to 43% of patients. The 'delusion of abandonment' is also relatively common with estimates of its frequency ranging from 3% to 18% of patients (Tariot and Blazina, 1994). As noted above, the 'delusion of infidelity' is occasional with frequency estimates ranging from 1% to 9% of patients (Tariot and Blazina, 1994).

At least two studies suggest that delusions are a risk factor for physical aggression. A study by Deutsch et al. (1991) found that 43.5% of patients with a diagnosis of probable AD had delusions. The presence of delusions was a significant predictor of physical aggression. Gilley et al., (1997) also reported that the presence of delusions predicts the occurrence and frequency of physical aggression with 80% of study participants who showed high rates of physical aggression (i.e. more than one episode per month) also having delusions. A recent study from Taiwan showed that a given dementia patient's personal history may determine the unique nature of her/his delusions and visual hallucinations (Pai, 2008).

Hallucinations

Estimates of the frequency of hallucinations in people with dementia range from 12% to 49% (Swearer, 1994). Visual hallucinations are the most common (occurring in up to 30% of patients with dementia) and these are more common in moderate than in mild or severe dementia (Swearer, 1994). In people with Lewy bodies, reports of frequency have been as high as 80% (McKeith et al., 1992). Patients with dementia may also have auditory hallucinations (present in up to 10%), but other types, such as those of an olfactory or tactile nature, are rare (Swearer, 1994).

One common visual hallucination involves seeing people in the home who are not really there, e.g. phantom boarders, also classed as misidentification syndromes. Sometimes these hallucinations are very upsetting to the person with dementia and require treatment. At other times they are not a source of stress (except possibly for the caregiver) and therefore intervention is not required.

In patients with moderately impaired cognitive function, an association may exist between visual misperceptions and hallucinations. A significant percentage of people with dementias have functional impairments related to visual agnosias (difficulty recognizing faces or objects) and many have problems with contrast sensitivity, especially at low frequencies. In such individuals, the boundaries between light and dark appear blurred, partially explaining the common occurrence of visual hallucinations and misidentifications. Thus, examination of auditory and visual function is an essential part of the assessment of any person with dementia with hallucinations (see box below).

To anticipate the presence of, or potential for, visual hallucinations in a person with dementia, it is important to:

- evaluate the visual perceptual functions of each patient
- optimize ambient illumination and enhance visual contrast
- educate caregivers about the visual perceptual impairment experienced by persons with dementia and how it affects activities of daily living.

Misidentifications

Misidentifications in dementia are examples of disorders of perception (Burns, 1996). Unlike hallucinations (which occur in the absence of an external stimulus), misidentifications are misperceptions of external stimuli and can be defined as misperceptions with an associated belief or elaboration that is held with delusional intensity.

Although misidentifications have been defined in several ways, there are four main types:

- Presence of persons in the patient's own house (the 'phantom boarder' syndrome)
- Misidentification of the patient's own self (often seen as not recognizing their own mirror reflection)
- Misidentification of other persons
- Misidentification of events on television (the patient imagines these events are occurring in real three-dimensional space)

The frequency of misidentifications varies from study to study, depending on the definition used and the population studied. In a prospective, longitudinal, clinical-pathologic study of 178 AD patients (Burns, 1996), it was found that:

- 17% of patients believed someone else was in their house
- 4% would talk to themselves in the mirror as if to another person
- 12% believed other people were not who they were
- 6% misidentified people on television and could not appreciate that they were not actually present in the room

A study of misidentifications in various dementias found them to be present in 16% of AD patients, 17% of those with DLB, and 0% in FTD and PDD (Harciarek and Kertesz, 2008).

Misidentification where a person with dementia does not recognize his or her partner can be especially distressing for a spouse caregiver. Subsequent potential for aggression in patients can make the symptoms particularly worrisome.

In 1990, Ellis and Young described three forms of delusional misidentification which are described here:

- **Capgras syndrome** is the most common of the delusional misidentification syndromes (Harciarek and Kertesz, 2008). Sometimes called the syndrome of imposters, Capgras syndrome involves the delusional belief that persons have been replaced by identical doubles. Capgras syndrome may be a form of hypoidentification and related to a type of reduplicative paramnesia. Some patients with Capgras syndrome reduplicate more than just other people (e.g., houses, pets and objects). Capgras syndrome is associated with loss of the autonomic signs that normally accompany the recognition of familiar faces (Ellis et al., 1997). They propose that Capgras patients interpret the loss of affective response for familiar people in a paranoid suspicious way, and this leads them to the conclusion that the person must be an impostor.
- **Fregoli syndrome** is a type of misidentification where patients become convinced that people are dressing up as others in order to affect or influence them. In many ways, Fregoli syndrome is similar to normal experience. If a non-demented person expects to meet someone, they may briefly misidentify a stranger as that person, although they quickly correct the mistake when inconsistent evidence is noted. A patient with Fregoli syndrome attributes the inconsistent evidence to the effects of the disguise.
- **Intermetamorphosis** describes a situation in which the physical appearance of a person is perceived to correspond with the appearance of someone else.

Many family members and caregivers find their own ways of dealing with misidentifications. It is important to realize that what works with one person may not be appropriate for another, and the chosen approach needs to be worked out carefully with reference to the individual's pre-morbid characteristics. In some cases, humor will be appropriate; in other cases, reassurance or diversionary tactics may be more successful (see Module 5).

Diagnostic criteria for psychosis of Alzheimer's disease

These diagnostic criteria (Jeste and Finkel, 2000) are an attempt to identify single aspects of BPSD to allow more specific therapeutic trials. It is hoped that the rigor in which psychosis in dementia is separated from psychosis in other conditions will allow regulatory agencies to approve indications for therapy specifically for Psychosis of Alzheimer's disease. Current efforts are also underway to define psychoses in other dementing illnesses more precisely.

Table 2.2: Proposed Diagnostic Criteria for Psychosis in Alzheimer's disease

Characteristic symptoms

Presence of visual or auditory hallucinations, or delusions, or both.

Primary diagnosis

All the criteria for dementia of the Alzheimer type are met.*

Chronology of the onset of symptoms of psychosis *vs* onset of symptoms of dementia

There is evidence from the history that the symptoms in Criterion A have not been present continuously since prior to the onset of dementia.

Duration and severity

The symptom(s) in Criterion A have been present, at least intermittently, for 1 month or longer. Symptoms are severe enough to cause some disruption in patients' and/or others' functioning.

Exclusion of schizophrenia and related psychotic disorders

Criteria for schizophrenia, schizoaffective disorder, delusional disorder or mood disorder with psychotic features have never been met.

Relationship to delirium

The disturbance does not occur exclusively during the course of delirium.

Exclusion of other causes of psychotic symptoms

The disturbance is not better accounted for by another general medical condition or direct physiological effects of a substance (e.g. a drug abuse, a medication).

*For other dementias, such as vascular dementia, Criterion B will need to be modified appropriately.

Adapted from Jeste and Finkel (2000)

Table 2.3: Psychosis of AD compared with Schizophrenia in the elderly

	Psychosis of AD	Schizophrenia
Bizarre or complex delusions	Rare	Frequent
Misidentifications of caregivers	Frequent	Rare
Common form of hallucinations	Visual	Auditory
Schneiderian first-rank symptoms	Rare	Frequent
Active suicidal ideation	Rare	Frequent
Past history of psychosis	Rare	Frequent
Eventual remission of psychosis	Frequent	Uncommon
Need for long-term treatment with antipsychotics	Uncommon	Very common
Mean optimal daily dose of antipsychotics	15–25% of that in a young adult with schizophrenia	40–60% of that in a young adult with schizophrenia

Adapted from Jeste and Finkel (2000).

Depression

Depressive symptoms affect a sizable minority of dementia patients at some time during the course of their dementia. Most studies have been of patients with AD and show depressed mood to occur most frequently in 40–50% of patients and a major depressive disorder being less common in 10–20% of patients than subsyndromal depression (Wragg and Jeste, 1989).

There is often discordance between self-reported symptoms of depression and the observations of collateral sources (Burke et al., 1998). A five-year longitudinal study of patients with AD showed recurrence rates of 85% for depressive symptoms over one year (Levy et al., 1996). A premorbid history of depression increases the chance of depression developing with AD (Harwood, et al., 1999).

Diagnosing depression can be difficult, particularly in patients with moderate and severe dementia. In early dementia, depressed mood and symptoms can usually be elicited according to DSM5 criteria during a patient interview. As the dementia progresses, diagnosis of depression becomes more difficult because of the increasing language and communication difficulties, and because apathy, weight loss, sleep disturbance and agitation can occur as part of the dementing illness. Families, who have intuitiveness about their loved-one with dementia, may suspect depression when the clinician may not. Depressive disorder should therefore be considered when one or more of the following conditions are noted:

- Acute, unexplained behavior changes
- A pervasive depressed mood and loss of pleasure
- Family suspicion of depression
- Self-deprecatory statements and expressed wishes to die
- A family or personal history of depression prior to the onset of dementia.
- Rapid decline in cognition (Starkstein et al., 2008)

Differential diagnosis of depression in dementia often involves discriminating depression from apathy and pathological affect-crying. Consensus diagnostic criteria for depression in Alzheimer's disease have been proposed (Olin et al., 2002).

Apathy

Apathy and related symptoms are among the most common of the BPSD (Lyketsos et al., 2000). Apathy is present in up to 50% of patients in the early and intermediate stages of AD and other dementias. Apathy may increase with severity of AD (Turro-Garriga et al., 2009) and persistent apathy may be a risk-factor functional decline in AD (Lechowski et al., 2009).

Patients who are apathetic show a lack of interest in daily activities and personal care and a decrease in different types of interaction:

- Social interaction
- Facial expression
- Vocal inflection
- Emotional responsiveness
- Initiative

The symptoms of apathy may be mistaken for those of major depression. Both apathy and depression can manifest as diminished interest, psychomotor retardation and lack of energy and insight. Although lack of motivation occurs in apathy and depression, the syndrome of apathy denotes lack of motivation without the dysphoria or vegetative symptoms of depression. The clinician must distinguish a patient who is apathetic from one who is depressed, since the management of each disorder differs. For example, on a pharmacological basis, a patient with depression may require antidepressant medication, while another with apathy may benefit from a cholinesterase inhibitor or a psycho-stimulant (Padala et al., 2010). Recently, diagnostic criteria for apathy in AD have been proposed (Robert et al., 2009).

Anxiety

Anxiety in dementia may be related to the manifestation of other BPSD or occur independently. Rates of anxiety may be higher in VaD than AD and anxiety decreases in severe dementia (Seignourel et al., 2008). A Canadian study found the prevalence of anxiety disorders in AD and other dementias to be 16% versus 4% in age-matched, non-demented controls (Nabalamba and Patten, 2010). Patients with anxiety and dementia may express previously non-manifest concerns about their finances, future and health (including their memory) and worries about previously non-stressful events and activities like being away from home (Reisberg et al., 1986).

A common manifestation of anxiety in dementia is 'Godot syndrome'. A person with Godot syndrome will repeatedly ask questions about an upcoming event—a behavior which appears to result from decreased cognitive (specifically memory) abilities and from the inability to channel remaining thinking capacities productively. This can become so incessant and persistent as to create a major burden for the patient's family and caregivers (Reisberg et al., 1986).

Another anxiety symptom characteristic of dementia patients is fear of being left alone (Reisberg et al., 1986). This fear can be considered a phobia since the anxiety is out of proportion to any real danger. This phobia may become apparent as soon as the spouse or other caregiver goes into another room or may be expressed as repeated requests not to be left alone. Patients with AD sometimes develop other phobias, such as fear of crowds, travel, the dark, or activities such as bathing.

Specific symptomatology: behavioral

Wandering

Wandering is one of the most troublesome of the BPSD, particularly in terms of the burden it places on caregivers. Wandering often results in persons having dementia being admitted to a long-term care facility. It is frequent cause of referral to psychiatric services. Wandering behaviors includes aimless walking and exit seeking/repeatedly attempting to leave the house. Faulty navigational ability, boredom, and anxiety may underlie some wandering behaviors.

Agitation/Aggression

Agitation is defined as inappropriate verbal, vocal or motor activity that is not judged by an outside observer to result directly from the needs or confusion of the person (Cohen-Mansfield, 2000). Its prevalence in persons having dementia increases with degree of cognitive impairment. Agitation in persons having dementia is a complex phenomenon. Neurobiological changes associated with dementia, comorbid medical factors, psychological, social and environmental factors interacting with premorbid personality influence development of agitation. Aberrant motor behavior may be more prevalent and severe in AD compared to VaD (Fernandez-Martinez et al., 2008). Among patients having vascular dementia, agitation may be more common in patients with large vessel disease compared to small vessel disease (Staekenborg et al., 2009). Cohen-Mansfield Agitation Inventory (CMAI) and Pittsburg Agitation Scale (PAS) are often used in clinical settings besides research settings to assess agitation (Cohen-Mansfield, 1986; Rosen et al., 1994). Four subtypes have been identified using CMAI (listed in Table 2.4)

Table 2.4: Subtypes of agitation

Physically non-aggressive behaviors	Physically aggressive behaviors
• General restlessness/purposeless hyperactivity/ repetitive physical movements • Wandering • Rummaging • Repetitive mannerisms • Pacing • Hiding things • Inappropriate dressing or undressing	• Hitting • Screaming • Pushing • Scratching • Kicking • Biting • Grabbing
Verbally non-aggressive behaviors	**Verbally aggressive behaviors**
• Constant requests for attention • Verbal bossiness • Complaining or whining • Expressions of what appears to be unrealistic fears • Repetitive sentences/questions/verbalizations • Repetitive health complaints • Repetitive anxious complaints or concerns	• Screaming • Cursing • Temper outbursts

Physically and verbally aggressive behaviors are more likely to occur in patients having dementia who have poor social relationships. Verbally aggressive behavior is associated with depression, pain and other health problems. Agitation correlates strongly with irritability, disinhibition and delusions. Agitation and aggression are among the most troublesome BPSD for caregivers and, along with depression and psychosis, are leading predictors of institutionalization (Gaugler et al., 2009).

Resistiveness to care

Resistiveness to care is another distinct behavioral syndrome and thus needs to be differentiated from agitation (Volicer et al., 2007). It involves resisting taking medications, activities of daily living (ADL) assistance or eating. It is related to the ability of person having dementia to understand, and thus, increases in prevalence with worsening of cognitive impairment. Resistiveness to care is associated with verbally and physically abusive behavior towards caregivers (Volicer et al., 2009).

Inappropriate sexual behaviors

Inappropriate verbal and physical sexual behaviors (also referred to as sexual disinhibition or hypersexuality) involve persistent, uninhibited sexual behaviors directed at oneself or at others. They are prevalent in patients who have dementia. They are profoundly disruptive to caregivers (family and professional) and other individuals in the immediate surroundings. Substantial mental and physical harm can occur, secondary to these behaviors (Guay, 2008). Inappropriate sexual behaviors also pose complex logistical and ethical problems for caregivers (Wallace and Safer, 2009).

Catastrophic reaction

Catastrophic reaction is an acute expression of overwhelming anxiety and frustration—often triggered in persons having dementia by adverse experiences such as frustration with getting dressed, or with paying bills, etc. They are also sometimes referred to as rage reactions. They are typically brief and self-limited, and can be avoided by assigning manageable tasks for the person having dementia. They manifest as sudden angry outbursts, verbal aggression (e.g., shouting and cursing), threats of physical aggression and physical aggression. Delirium, pain, infection and certain medications can also provoke catastrophic reactions.

Sundowning

Sundowning is the occurrence and exacerbation of BPSD in the afternoon or evening. Agitation and sleep disturbances commonly accompany sundowning. Sundowning increases burden of care on caregivers as it often occurs when the staffing in institutional setting is at the lowest levels. The circadian, hormonal, physiological, and environmental correlations with sundowning have been described (Sharer, 2008). AD and other dementias cause disturbances of circadian rhythms and sundowning may be related to a phase delay of body temperature caused by dementing illness (Volicer et al., 2001).

Assessment tools

The use of valid and standardized outcome measures for the assessment of BPSD is critical not only in research settings but also in some clinical settings (e.g., to measure response to antipsychotics or antidepressants). The Neuropsychiatric Inventory (NPI) and the Behavioral Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD) are two of the best measures recommended for measuring behavioral disturbances in individuals with dementia (Jeon et al., 2011). These global scales may not be adequate to measure depressive symptoms as they rely primarily on mood symptoms (mainly sadness). Depression specific scales are preferred over these global scales to measure depression. The Cornell Scale for Depression in Dementia (CSDD) is recommended for measuring depression in individuals with advanced dementia who cannot give valid self-report of depressive symptoms (Alexopoulos et al., 1988). The Geriatric Depression Scale (30- and 15-item versions) (GDS) can be used to measure depressive symptoms in individuals with mild dementia (Yesavage et al., 1983).

Delirium: a differential diagnosis from BPSD

Patients who have dementia are at higher risk for developing delirium. Patients who have delirium may experience the behavioral and psychological symptoms seen in dementia. Diagnosing delirium in a cognitively intact patient is fairly straightforward, with the sudden onset of global impairment that is easy to recognize. One simple method for detection of delirium is the Confusion Assessment Method or CAM (Inouye et al., 1990), which requires the clinician to assess the following four symptoms:

1. Acute onset and fluctuating course
2. Inattention
3. Disorganized thinking
4. Altered level of consciousness

To satisfy criteria for presumptive diagnosis of delirium, the patient must have symptoms 1 and 2; and either symptoms 3 or 4. Making this diagnosis in a person whose brain has already been damaged by dementia is often difficult since the delirium is superimposed on existing disordered thought and confusion. In both dementia and delirium, slowing of electroencephalographic activity is noted (except in delirium resulting from sedative withdrawal), as are altered sleep-wake cycles and diurnal variations. Despite their similarities, it is usually possible to differentiate between delirium and dementia because delirium usually presents with:

- Acute or subacute onset of symptoms
- Heightened or reduced attention in a patient with pre-existing dementia, or, prominent fluctuations in symptoms
- Visual hallucinations accompanied by agitation
- Altered psychomotor activity and occasionally asterixis

Causes of delirium

Once delirium is diagnosed, appropriate treatment depends on identifying the cause. There are many causes of delirium. The most common causes are noted here:

- Infection, especially urinary tract infection
- Medication
- Malnutrition/dehydration
- Metabolic illnesses (e.g., certain renal or hepatic diseases)
- Changes/stress in the patient's environment
- Surgery

The following are scenarios that illustrate the varied causes of delirium:

- Patients taking drugs metabolized by the P450 system, including common antihypertensive medications and many psychoactive drugs, may be at risk for delirium if they drink grapefruit juice, a potent inhibitor of the P450 3A4 isoenzyme.
- Alternative medications which often have psychoactive and anticholinergic properties can trigger delirium, as can eye drops with beta-blocker properties.
- Delirium may result if a person with dementia unknowingly takes medication prescribed for family members or friends.
- Sedative use as well as the consumption of alcohol by a person with dementia can produce delirium, both by itself and as a withdrawal syndrome.
- Among nursing home residents, hypoxia is a frequent cause of delirium. This condition can result from pneumonia, congestive heart failure, sleep apnea or, less commonly, pulmonary embolism.
- Urinary retention and fecal impaction also must be considered as possible causes of delirium in persons with dementia.

To summarize, delirium and dementia are often difficult to distinguish. This is due in large measure to overlapping symptom profiles and etiologies. In addition, dementia and delirium frequently coexist. Nonetheless, it is important to identify delirium because this will often lead to different therapeutic strategies. Treatment of the causes of delirium in demented patient will often lead to significant improvements in BPSD.

Appendix 1. Diagnostic classification of signs and symptoms in patients with dementia: a historical review

DSM-I, II and *III*

Both the *Diagnostic and Statistical Manual of Mental Disorders (DSM)-I* and *DSM-II* focused on the cognitive aspects of dementia, rather than the specific behavioral features. The *DSM-III* (American Psychiatric Association, 1980), viewed by many as a substantial advance in diagnostic clarity, was based on the greater detail with which it described different conditions and the use of specific diagnostic criteria. Few overall changes were made in the revision of the *DSM-III* (*DSM-III-R*; American Psychiatric Association, 1987), with scant attention paid to the types of symptoms or behaviors often so troubling in managing patients with dementia.

The NINCDS-ADRDA

In 1984, criteria for the clinical diagnosis of AD were published in a report from the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Association (NINCDS-ADRDA; McKhann et al., 1984). The NINCDS-ADRDA criteria for probable AD did mention depression, insomnia, delusions, illusions, hallucinations, catastrophic reactions (verbal, emotional and physical outbursts) and sexual disorders as associated symptoms of AD.

DSM-IV and *DSM-IV-TR*

The *DSM-IV* (American Psychiatric Association, 1994) and subsequently *DSM-IV*-Text Revision (*DSM-IV-TR*) (American Psychiatric Association, 2000) criteria for dementia incorporated the multiple cognitive deficits standard of the NINCDS-ADRDA criteria. In *DSM-IV-TR*, greater attention was given to describing associated clinical features, such as problems with perception, mood and emotion, behavior and motor function. When the *DSM-IV* and the *DSM-IV-TR* were being compiled, a number of U.S. experts strongly recommended including a variety of descriptive categories to denote BPSD of patients with dementia. Ultimately, the decision was made not to include these and instead, the phrase "with behavioral disturbance' was included as a "specifier" to identify patients requiring additional treatment to manage their challenging clinical problems.

The *DSM5* criteria

The *DSM5* uses the terms *major neurocognitive disorder* and *minor neurocognitive disorder* to replace the term *dementia* (American Psychiatric Association, 2013). Major neurocognitive disorder criteria are similar to dementia and minor neurocognitive disorder overlaps with mild cognitive impairment. *DSM5* also allows specifying if the cognitive disturbance is with or without behavioral disturbance and to specify severity of major neurocognitive disorder (mild, moderate, severe). Only two neurocognitive disorders in *DSM5* have specific behavioral or psychological symptoms as part of the criteria for their diagnosis. The *DSM5* criteria for major or mild neurocognitive disorder with Lewy bodies specifies recurrent visual hallucinations that are well formed and detailed as one of its three core diagnostic features and rapid eye movement sleep behavior disorder as one of its suggestive diagnostic features. The *DSM5* criteria for behavioral variant of major or mild frontotemporal neurocognitive disorder involves presence

of three or more of the following five behavioral symptoms: behavioral disinhibition, apathy/inertia, loss of sympathy or empathy, perseverative/stereotyped or compulsive/ritualistic behaviors, and hyperorality. One benefit of not using the term *dementia* is that the associated stigma and resulting emotional distress may be less with the use of *major neurocognitive disorder* as diagnosis.

The ICD-10 Classification of Mental and Behavioral Disorders: Clinical descriptions and diagnostic guidelines

These guidelines (World Health Organization [WHO], 1992) followed a somewhat different tradition from *DSM-IV* and continued to combine both clinical features and course in the concept of dementia. ICD-10 did not include a designation to characterize patients with BPSD, although subtypes of dementia (delusions, hallucinatory, depressive and mixed) were described.

Summary

Although the specifying phrase 'with behavioral disturbance' was added to *DSM-IV*, *DSM-IV-TR*, and now *DSM5*, it is unclear how this term has been used in everyday clinical practice. Neither *DSM5* nor any other diagnostic nomenclature provides a structured approach to identifying the degree or type of neuropsychiatric signs or symptoms present. As such, several questions remain:

- When BPSD are treated effectively, should the diagnosis change?
- Does a particular BPSD have prognostic significance?
- Are these symptoms or symptom clusters (i.e., possible syndromes) sufficiently stable to warrant specific subtype or a typology?

Despite the fact that the BPSD have been described in one form or another for over a century, a nosology that guides physicians regarding its measurement or classification is still awaited.

Appendix 2. Rating scales for BPSD in clinical settings

In research and clinical settings, several rating scales listed in Table 2.5 are recommended to improve assessment of BPSD and to assess response to treatment (Conn and Thorpe, 2007, Burns et al., 2003). This list is not exhaustive but meant to provide some familiarity with available tools that have been used and studied in mental health assessment in persons having dementia. Use of rating scales improves differentiation of BPSD. The differentiation of behaviors and their etiology are important to treatment planning. Many of these rating scales are especially useful in institutional settings. In order to improve consistency, all staff using screening tools must be trained in their use and facility inter-rater reliability established.

Table 2.5: Rating scales to assess BPSD

1. Comprehensive instruments: Neuropsychiatric inventory (NPI) (Cummings et al.,1994), The Behavior Rating Scale for Dementia of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD-BRSD) (Tariot et al., 1995), and Behavioral Pathology in Alzheimer's disease (BEHAVE-AD) is used to assess the spectrum of BPSD (Reisbert et al., 1987).
2. Depression: Cornell Scale for Depression in Dementia (CSDD) (Alexopoulos et al., 1988).
3. Agitation: Cohen-Mansfield Agitation Inventory (CMAI) (Cohen-Mansfield et al., 1989) and Pittsburg Agitation Scale (PAS) (Rosen et al., 1994) are used to assess agitation.
4. Caregiver distress due to BPSD: Neuropsychiatric inventory—Distress subscale (NPI-D) is used to assess distress that caregivers experience in response to each symptom in NPI (Cummings et al., 1994).

Sources of information

Rating scales have been based on four sources of information:

- Family caregivers
- Professional caregivers
- Physician's observations of persons with dementia
- Self-report by person with dementia

Family caregivers are intimately familiar with BPSD and are well-positioned to report such data. Scales based on family reports are appropriate for assessing outpatients living at home. However, the results may be biased by caregiver mood, the sophistication of the caregiver as an observer and the education level of the caregiver. BEHAVE-AD and NPI are examples of caregiver-based instruments.

Professional caregivers' reports, and rating scales based on these (e.g., the Nurses' Observation Scale for Inpatient Evaluation [NOSIE] (Honigfeld and Klett, 1965), and the CMAI), are appropriate for assessing institutionalized patients. These are used primarily with nursing staff and have the advantage of being based on information from persons more experienced in the observation of BPSD. To overcome some of the methodological difficulties, researchers have begun using videotapes of institutionalized patients and scoring randomly selected observation periods. Many research studies use the Minimum Data Set (MDS) behavioral symptoms data to assess presence of BPSD. Validity of such data has been called into question recently and in its place, twice-daily completion of a behavioral symptoms checklist containing the MDS items during the week of the assessment has been suggested to significantly improve the accuracy of the recorded data (Bharucha et al., 2008).

Physicians' direct observations of patients have the advantage of using highly skilled observes, which tends to increase the reliability of the results. A disadvantage of scales based on physicians' observations is that they capture only the symptoms observed during a limited observation period. The Neurobehavior Rating Scale (NRS) is an example of a tool of this type (Sultzer et al., 1992).

Self-reports by patients are reliable and valid only in the early stages of a dementing illness. Nevertheless, self-reports of mood changes have been used in some studies applying the Geriatric Depression Scale (GDS), a self-rated depression assessment scale (Yesavage et al., 1983).

Content of rating scales for BPSD

BEHAVE-AD assesses BPSD considered to be characteristic of AD. NPI has scales for BPSD common to AD, but also includes scales for symptoms characteristic of frontotemporal degeneration and other dementias.

Outcome of assessment

Most rating instruments for BPSD were designed for cross-sectional use to identify specific symptoms. Longitudinal studies are necessary, however, to determine whether BPSD are trait phenomena that characterize a subgroup of patients in whom they occur continuously, tend to recur, or are state phenomena that are transient and occur more or less randomly in different patients during the course of dementing illness.

References and recommended reading

Aalten, P., Verhey, F.R., Boziki, M., et al. Neuropsychiatric syndromes in dementia. Results from the European Alzheimer Disease Consortium: Part I. *Dementia & Geriatric Cognitive Disorders* 2007; 24(6): 457–463.

Aalten, P., Verhey, F.R., Boziki, M., et al. Consistency of neuropsychiatric syndromes across dementias: results from the European Alzheimer Disease Consortium. Part II. *Dementia & Geriatric Cognitive Disorders* 2008; 25(1): 1–8.

Aarsland, D., Rongve, E., Nore, S.P., et al. Frequency and case identification of dementia with Lewy bodies using the revised consensus criteria. *Dementia & Geriatric Cognitive Disorders* 2008; 26(5): 445–452.

Ala, T., Yang, K., Sung, J., Frey, W. Hallucinations and signs of Parkinsonism help distinguish patients with dementia and cortical Lewy bodies from patients with Alzheimer's disease at presentation: A clinicopathological study. *Journal of Neurology Neurosurgery Psychiatry* 1997; 62:16–21.

Alexopoulos, G.S., Abrams, R.C., Young, R.C., Shamoian, C.A. Cornell Scale for Depression in Dementia. *Biological Psychiatry* 1988; 23(3): 271–284.

American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*. Arlington, VA, 2013; pg. 591–644.

Bharucha, A.J., Vasiliescu, M., Dew, M.A., et al. Prevalence of behavioral symptoms: comparison of the minimum data set assessments with research instruments. *Journal of the American Medical Directors Association* 2008; 9(4): 244–250.

Cohen-Mansfield, J. Theoretical frameworks for behavioral problems in dementia. *Alzheimer's Care Quarterly* 2000; 1:8–12.

Devanand, D., Jacobs, D., Tang, M., et al. The course of psychopathologic features in mild to moderate Alzheimer disease. *Archives of General Psychiatry* 1997; 54: 257–263

Fernandez-Martinez, M., Castro, J., Molano, A., et al. Prevalence of neuropsychiatric symptoms in Alzheimer's disease and vascular dementia. *Current Alzheimer Research* 2008; 5(1): 61–69.

Gaugler, J.E., Yu, F., Krichbaum, K., Wyman, J.F. Predictors of nursing home admission for persons with dementia. *Medical Care* 2009; 47: 191–198.

Gauthier, S., Cummings, J., Ballard, C., et al. Management of behavioral problems in Alzheimer's disease. *International Psychogeriatrics* 2010; 22(3): 346–372.

Goetz, G.C., Emre, M., Dubois, B. Parkinson's disease dementia: definitions, guidelines, and research perspectives in diagnosis. *Annals of Neurology* 2008; 64 Suppl 2: S81–S92.

Grossberg, G.T. The ABC of Alzheimer's disease: behavioral symptoms and their treatment. *International Psychogeriatrics* 2002; 14: S27–S49.

Guay, D.R. Inappropriate sexual behaviors in cognitively impaired older individuals. *American Journal of Geriatric Pharmacotherapy* 2008; 6(5): 269–288.

Harciarek, M., Kertesz, A. The prevalence of misidentification syndromes in neurodegenerative diseases. *Alzheimer Disease & Associated Disorders* 2008; 22(3); 163–169.

Inouye, S., van Dyck, C., Alessi, C., et al. Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Annals of Internal Medicine* 1990; 113: 941–948.

IOM (Institute of Medicine). *The Mental Health and Substance Use Workforce for Older Adults: In Whose Hands?* Washington, DC, United States. The National Academies Press 2012.

Jeon, Y., Sansoni, J., Low, L., et al. Recommended measures for the assessment of behavioral disturbances associated with dementia. *American Journal of Geriatric Psychiatry* 2011; 19: 403–415.

Jeste, D., Finkel, S. Psychosis of Alzheimer's disease and related dementias. Diagnostic criteria for a distinct syndrome. *American Journal of Geriatric Psychiatry* 2000; 8:29–34

Kingma, G.M., van Duijn, E., Timman, R., et al. Behavioural problems in Huntington's disease using the Problem Behaviors Assessment. *General Hospital Psychiatry* 2008; 30(2): 155–161.

Kverno, K.S., Rabins, P.V., Blass, D.M., et al. Prevalence and treatment of neuropsychiatric symptoms in advanced dementia. *Journal of Gerontological Nursing* 2008; 34(12): 8–15.

Lechowski, L., Benoit, M., Chassagne, P., et al. Persistent apathy in Alzheimer's disease as an independent factor of rapid functional decline: the REAL longitudinal cohort study. *International Journal of Geriatric Psychiatry* 2009; 24(4): 341–346.

Lobo, A., Launer, L.J., Fratiglioni, L., et al. Prevalence of dementia and major subtypes in Europe: A collaborative study of population-based cohorts: Neurological Diseases in the Elderly Research Group. *Neurology* 2000; 54 (Suppl 5): S4–S9.

Locca, J.F., Bula, C.J., Zumbach, S., Bugnon, O. Pharmacological treatment of behavioral and psychological symptoms of dementia (BPSD) in nursing homes: development of practice recommendations in a Swiss canton. *Journal of the American Medical Directors Association* 2008; 9(6): 439–448.

Lyketsos, C.G., et al. Mental and behavioral disturbances in dementia: findings from the Cache County study on memory and aging. *American Journal of Psychiatry* 2000; 157:708–714

Lyketsos, C.G., Lopez, O., Jones, B., et al. Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: results from the cardiovascular health study. *JAMA* 2002; 288(12): 1475–1483.

Marin, D., Green, C., Schmeidler, J., et al. Noncognitive disturbances in Alzheimer's disease: frequency, longitudinal course, and relationship to cognitive symptoms. *Journal of the American Geriatrics Society* 1997; 45: 1331–1338.

McKeith, I., Fairbairn, A., Perry, R., et al. Neuroleptic sensitivity in patients with senile dementia of the Lewy body type. *British Medical Journal* 1992; 305: 673–78.

Mendez, M.F., Lauterbach, E.C., Sampson, S.M., and ANPA Committee on Research. An evidence-based review of the psychopathology of Frontotemporal Dementia: A report of the ANPA Committee on Research. *Journal of Neuropsychiatry Clinical Neurosciences* 2008; 20: 130–149.

Mourik, J.C., Rosso, S.M., Duivenvoorden, H.J., et al. Frontotemporal dementia: behavioral symptoms and caregiver distress. *Dementia & Geriatric Cognitive Disorders* 2004; 18(3–4): 299–306.

Nabalamba, A., Patten, S.B. Prevalence of mental disorders in a Canadian household population with dementia. *Canadian Journal of Neurological Sciences* 2010; 37(2): 186–194.

O'Brien, J. Behavioral symptoms in vascular cognitive impairment and vascular dementia. *International Psychogeriatrics* 2003; 15(Suppl 1): 133–138.

Okura, T., Plassman, B.L., Steffens, D.C., et al. Prevalence of neuropsychiatric symptoms and their association with functional limitations in older adults in the United States: the aging, demographics, and memory study. *Journal of the American Geriatrics Society* 2010; 58(2): 330–337.

Olin, J., Schneider, L., Katz, I., et al. Provisional diagnostic criteria for depression of Alzheimer disease. *American Journal of Geriatric Psychiatry* 2002; 10: 125–128.

Omar, R., Sampson, E.L., Loy, C.T., et al. Delusions in frontotemporal lobar degeneration. *Journal of Neurology* 2009; 256(4): 600–607.

Padala, P.R., Burke, W.J., Shostrom, V.K., et al. Methylphenidate for apathy and functional status in dementia of the Alzheimer's type. *American Journal of Geriatric Psychiatry* 2010; 18(4): 371–374.

Pai, M.C., Delusions and hallucinations in dementia patients: focus on personal history of the patients. *Tohoku Journal of Experimental Medicine* 2008; 216(1): 1–5.

Perry, R., Irving, D., Blessed, G., et al.,. Senile dementia of the Lewy body type. A clinically and neuropathologically distinct form of Lewy body dementia in the elderly. *Journal of Neurological Sciences* 1990; 95: 119–139.

Reisberg, B., Borenstein, J., Salob, S.P., et al. Behavioral symptoms in Alzheimer's disease: phenomenology and treatment. *Journal of Clinical Psychiatry* 1987; 48: 9–15.

Reisberg, B., Franssen, E., Sclan, S., et al. Stage specific incidence of potentially remediable behavioral symptoms in aging and Alzheimer's disease: a study of 120 patients using the BEHAVE-AD. *Bulletin of Clinical Neurosciences* 1989; 54: 95–112.

Robert, P., Onyike, C.U., Leentjens, A.F., et al. Proposed diagnostic criteria for apathy in Alzheimer's disease and other neuropsychiatric disorders. *European Psychiatry* 2009; 24(2): 98–104.

Robottom, B.J., Weiner, W.J. Dementia in Parkinson's disease. *International Review Neurobiology* 2009; 84: 229–244.

Ropacki, S.A., Jeste, D.V. Epidemiology of and risk factors for Psychosis of Alzheimer's disease: a review of 55 studies from 1990–2003. *American Journal of Psychiatry* 2005; 162(11): 2022–2030.

Rosen, T., Lachs, M.S., Pillemer, K. Sexual aggression between residents in nursing homes: Literature synthesis of an underrecognized problem. *Journal of the American Geriatrics Society* 2010; 58: 1070–1079.

Rubin, E., Morris, J., Berg, L. The progression of personality changes in senile dementia of the Alzheimer's type. *Journal of the American Geriatrics Society* 1988; 35: 721–725.

Savva, G.M., Zaccai, J., Matthews, F.E., et al. Prevalence, correlates and course of behavioural and psychological symptoms of dementia in the population. *British Journal of Psychiatry* 2009; 194(3): 212–219.

Seignourel, P.J., Kunik, M.E., Snow, L., et al. Anxiety in Dementia: a critical review. *Clinical Psychology Reviews* 2008; 28(7): 1071–1082.

Selbaek, G., Engedal, K., Bergh, S. The prevalence and course of neuropsychiatric symptoms in nursing home patients with dementia: A systematic review. *Journal of the American Medical Directors Association* 2013; 14(3): 161–169.

Sharer, J. Tackling sundowning in a patient with Alzheimer's disease. *Medsurg Nursing* 2008; 17(1): 27–29.

Staekenborg, S.S., Su, T., van Straaten, E.C., et al. Behavioral and psychological symptoms in vascular dementia: differences between small and large-vessel disease. *Journal of Neurology Neurosurgery Psychiatry* 2010; 81(5): 547–551.

Starkstein, S.E., Mizrahi, R., Power, B.D. Depression in Alzheimer's disease: phenomenology, clinical correlates, and treatment. *International Reviews Psychiatry* 2008; 20(4): 382–388.

Sultzer, D., Levin, J., Mahler, M., et al. Assessment of cognitive, psychiatric, and behavioral disturbances in patients with dementia: the Neurobehavioral Rating Scale. *Journal of the American Geriatrics Society* 1992; 40: 549–555.

Swearer, J. Behavioral disturbances in dementia. In: *Handbook of dementing illnesses*. Morris, J.C. (ed). New York: Marcel Dekker Inc., 1994.

Tariot, P., Blazina, L. The psychopathology of dementia. In: *Handbook of dementing illnesses*. Morris, J.C. (ed). New York: Marcel Dekker Inc., 1994.

Tariot, P., Mack, J., Patterson, M., et al. The Behavior Rating Scale for Dementia of the Consortium to Establish a Registry for Alzheimer's Disease. The Behavioral Pathology Committee of the Consortium to Establish a Registry for Alzheimer's Disease. *American Journal of Psychiatry* 1995; 152:1349–1357.

Thompson, C., Brodaty, H., Trollor, J., Sachdev, P. Behavioral and psychological symptoms associated with dementia subtypes. *International Psychogeriatrics* 2010; 22: 300–305.

Tsuang, D., Larson, E.B., Bolen, E., et al. Visual hallucinations in dementia: a prospective community based study with autopsy. *American Journal of Geriatric Psychiatry* 2009; 17(4): 317–323.

Turro-Garriga, O., Lopez-Pousa, S., Vilalta-Franch, J., et al. A longitudinal study of apathy in patients with Alzheimer's disease. *Journal of Neurology* 2009; 48(1): 7–13.

Volicer, L., Bass, E.A., Luther, S.L. Agitation and resistiveness to care are two separate behavioral syndromes of dementia. *Journal of the American Medical Directors Association* 2007; 8(8):527–532.

Volicer, L., Harper, D.G., Manning, B.C., et al. Sundowning and circadian rhythms in Alzheimer's disease. *American Journal of Psychiatry* 2001; 158(5): 704–711.

Volicer, L., Van der Steen, J.T., Frijters, D.H. Modifiable factors related to abusive behaviors in nursing home residents with dementia. *Journal of the American Medical Directors Association* 2009; 10(9): 617–622.

Wallace, M., Safer, M. Hypersexuality among cognitively impaired older adults. *Geriatric Nursing* 2009; 30(4): 230–237.

Wall, C.A., Rummans, T.A., Aksamit, A.J., et al. Psychiatric manifestations of Creutzfeldt-Jakob disease: a 25 year analysis. *Journal of Neuropsychiatry Clinical Neurosciences* 2005; 17(4): 489–495.

Webster, J., Grossberg, G. Disinhibition, apathy, indifference, fatigability, complaining and negativism. *International Psychogeriatrics* 1996; 8 (Suppl 3): 403–408.

Yesavage, J.A., Brink, T.L., Rose, T.L., et al. Development and validation of a geriatric depression scale: A preliminary report. *Journal of Psychiatric Research* 1983; 17: 37–49.

Zubenko, G., Rosen, J., Sweet, R., et al. Impact of hospitalization on behavioral complications of Alzheimer's disease. *American Journal of Psychiatry* 1992; 8: 1484–1491.

Zuidema, S., Koopmans, R., Verhey, F. Prevalence and predictors of neuropsychiatric symptoms in cognitively impaired nursing home patients. *Journal of Geriatrics Psychiatry Neurology* 2007; 20(1): 41–9.

Books

Psychiatric consultation in long-term care. A guide to health care providers. Desai, A.K., Grossberg, G.T. The Johns Hopkins Press, Baltimore, Maryland 2010.

Psychiatry in long-term care. Reichman, W.E. and Katz, P.R., editors. Oxford University Press.

Geropsychology and Long Term Care. Rosowsky, E., Casciani, J.M., Arnold, M., editors. Springer 2009.

Assessment Scales in Old Age Psychiatry, 2nd Ed. Burns, A., Lawlor, B., Craig, S. Taylor and Francis. London, United Kingdom 2003.

Delirium: A differential diagnosis from BPSD

Inouye, S., vanDyck, C., Alessi, C., et al. Clarifying confusion: the confusion assessment method—A new method for detection of delirium. *Annals of Internal Medicine* 1990; 113: 941–948.

Inouye, S., Carpentier, P. Precipitating factors for delirium in hospitalized elderly persons: predictive model and interrelationship with baseline vulnerability. *JAMA* 1996; 275: 852–857.

Luxenberg, J., Delirium. *Geriatrics: A LANGE clinical manual.* Lonergan, T. editor. Appleton and Lange, Stamford, Connecticut, United States 1996.

Steward, R., Hale, W. Acute confusional states in older adults and the role of polypharmacy. *Annual Reviews Public Health* 1992; 13: 415–430.

Appendix 1. Diagnostic classification of signs and symptoms in patients with dementia: a historic review

American Psychiatric Association. *Diagnostic and statistical manual of mental disorders. Third edition.* American Psychiatric Association, Washington, DC, United States 1980.

American Psychiatric Association. *Diagnostic and statistical manual of mental disorders. Third edition (Revised).* American Psychiatric Association, Washington, DC, United States 1987.

American Psychiatric Association. *Diagnostic and statistical manual of mental disorders. Fourth edition.* American Psychiatric Association, Washington, DC, United States 1994.

American Psychiatric Association. *Diagnostic and statistical manual of mental disorders. Fourth edition (text revision).* American Psychiatric Association, Washington, DC, United States 2000.

McKhann, G., Drachman, D., Folstein, M., et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of the Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984; 34: 939–944.

World Health Organization. *The ICD-10 classification of mental and behavioral disorders: Clinical descriptors and diagnostic guidelines.* Geneva 1992.

Appendix 2. Rating scales for BPSD in clinical settings

Alexopoulos, G.S., Abrams, R.C., Young, R.C., Shamoian, C.A. Cornell scale for depression in dementia. *Biological Psychiatry* 1988; 23: 271–284.

Cohen-Mansfield, J., Marx, M., Tosenthal, A. A description of agitation in a nursing home. *Journal of Gerontology* 1989; 44: M77–M84.

Cohen-Mansfield, L. Agitated behaviors in the elderly II. Preliminary results in the cognitively deteriorated. *Journal of the American Geriatrics Society* 1986; 34: 722–727.

Conn, D., Thorpe, L. Assessment of behavioral and psychological symptoms associated with dementia. *Canadian Journal of Neurological Sciences* 2007; Suppl 1: S67–S71.

Cummings, J.L., Mega, M.S., Gray, K., Rosenberg-Thompson, S., Gornbein, T. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology* 1994; 44: 2380–2384.

Rosen, J., Burgio, L., Kollar, M., et al. The Pittsburgh Agitation Scale: a user friendly instrument for rating agitation in dementia patients. *American Journal of Geriatric Psychiatry* 1994; 2: 52–59.

Reisberg, B., Ferris, S., de Leon, M., Crook, T. The Global Deterioration Scale for assessment of primary degenerative dementia. *American Journal of Psychiatry* 1982; 139: 1136–1139.

Rosen, J., Burgio, L., Kollar, M., et al. The Pittsburgh Agitation Scale: a user friendly instrument for rating agitation in dementia patients. *American Journal of Geriatric Psychiatry* 1994; 2: 52–59.

Tariot, P., Mack, J., Patterson, M., et al. The Behavior Rating Scale for Dementia of the Consortium to Establish a Registry for Alzheimer's Disease. The Behavioral Pathology Committee of the Consortium to Establish a Registry for Alzheimer's Disease. *American Journal of Psychiatry* 1995; 152: 1349–1357.

INTERNATIONAL PSYCHOGERIATRIC ASSOCIATION

www.ipa-online.org

MODULE 3

Etiology

The IPA Complete Guides to Behavioral and Psychological Symptoms of Dementia

BPSD

Specialists Guide

Specialists • Primary Care Physicians • Nurses

MODULE 3: Etiology

CONTENTS

Key messages	**3.2**
Introduction	**3.2**
Genetic abnormalities in dementia—relationship to BPSD	**3.3**
Alzheimer's disease	3.3
Psychosis	3.3
Aggression and agitation	3.3
Depression	3.4
Other BPSD	3.4
Other types of dementia	3.4
Neurotransmitter changes in dementia—relationship to BPSD	**3.4**
Dementia-related changes in the cholinergic system	3.5
Dementia-related changes in the dopamine system	3.5
Dementia-related changes in the norepinephrine system	3.6
Dementia-related changes in the serotonin system	3.6
Dementia-related changes in glutamate concentrations	3.7
Dementia-related changes in the gamma-aminobutyric-acid (GABA) system	3.7
Neuroendocrine dysfunction in dementia	3.7
Neuropathologic changes in dementia—relationship to BPSD	**3.8**
Psychotic symptoms	3.8
Structural neuroimaging	**3.8**
Functional neuroimaging	**3.9**
Circadian rhythms—relationship to BPSD	**3.10**
Biologic correlates of circadian rhythm disturbances	3.10
Other clinical contributors to BPSD	**3.10**
Personality/psychological contributors to BPSD	3.11
Environmental, physical, and social contributors to BPSD	3.12
Caregiver factors	3.13
Conclusion	**3.14**
References and recommended reading	**3.14**

Key messages

- There are multiple etiologies for the behavioral and psychological symptoms of dementia (BPSD).
- Currently, the best model is one that incorporates genetic (receptor polymorphism), neurobiological (neurochemical, neuropathology), psychological (e.g., premorbid personality, response to stress), and social aspects (e.g., environmental change and caregiver factors) of etiology.
- There has been much research observing neurochemical and neuropathological changes in the brains of people with dementia, but only broad correlations of changes to BPSD can be made. Further research is required before definite conclusions linking neurochemical and neuropathological changes to specific symptoms can be drawn.
- Functional neuroimaging studies suggest that BPSD are not random consequences of diffuse brain illness, but are fundamental expressions of regional cerebral pathology. The different changes in neuroimaging and neurochemistry found in various types of dementia suggest that there are different patterns according to the disease type.
- Disruptions of circadian rhythms can result in BPSD and lead to agitation during the day and restlessness at night. Furthermore, abnormalities in circadian rhythm may be responsible for 'sundown' syndrome.
- The emergence of BPSD and the need for hospitalization are often associated with antecedent life events characterized by change in social routine and environment or the development of physical discomforts and disorders.

Introduction

We are in the early stages of understanding the etiologies for the behavioral and psychological symptoms of dementia (BPSD). Currently, the best model incorporates four aspects of BPSD:

- Genetic (mainly receptor polymorphism)
- Neurobiological (neurochemical, neuropathology)
- Psychological (e.g., premorbid personality, response to stress or discomfort)
- Social aspects (e.g., environmental change and caregiver factors)

For a particular symptom (or group of symptoms), the relative input from each causal source can vary. The importance of an interactive causal model is that it has implications for the development of treatment strategies (see Modules 5 and 6).

This module reviews what is known about likely genetic and neurobiological causes of BPSD and discusses the role of psychological and environmental contributors to these symptoms.

Genetic abnormalities in dementia—relationship to BPSD

Studies have indicated different genetic factors to be associated with various BPSD symptoms as well as types of dementia, although some findings are contradictory and others lack independent replication. Most research has focused on Alzheimer's disease (AD). Many studies have focused on Apolipoprotein E (APOE) genotypes and although there are contradictory findings, the cumulative evidence from longitudinal studies suggests that there is no association between APOE genotypes and BPSD as a whole in AD (Panza et al., 2012).

Alzheimer's disease

Psychosis. A genome screen for AD involving the combination of samples from the United States and the United Kingdom found that there was a significant association between proband psychosis status and the occurrence of psychosis in AD in siblings with linkage peaks occurring on chromosomes 7 and 15 (Hollingworth et al., 2007). These results suggest an increased familial risk of psychosis in AD. A meta-analysis of serotonergic system genes found that there was a robust, strong, positive association between the C allele of HTR2A and symptoms of psychosis, suggesting that the HTR2A T102C polymorphism is a significant risk factor for psychosis in AD (Ramanathan et al., 2009). These receptors may also modulate antipsychotic response (Engelborghs et al., 2006), and there is an association with psychosis onset and severity of depressive symptoms (Wilkosz et al., 2007). There are contradictory findings about the association of the serotonin transporter gene (SERT) polymorphisms with psychosis (Quaranta et al., 2009; Pritchard et al., 2007; Ueki et al., 2007), although the largest cohort of 1,008 probable AD cases in the UK observed a significant association between SERT polymorphism STin2 and psychosis (Proitsi et al., 2012).

Polymorphisms in dopamine receptors have also been associated with psychosis in most, but not all, studies (Aarsland et al., 2005; Sato et al., 2009), particularly D3 genes, where two studies found homozygous carriers of the 1 allele to be at increased risk (Holmes et al., 2001; Sweet et al., 1998). Some cathecol-O-methyltransferase (COMT) haplotypes may increase risk for schizophrenia and other psychoses, including psychosis in AD (Sweet et al., 2005). One group demonstrated a synergic effect of COMT and the serotonin gene-linked promoter region (Borroni et al., 2006). A number of other associations with psychosis have not been independently replicated, including the interleukin-1β gene promoter (the CC genotype and C allele) (Craig et al., 2004a), neuregulin-1 polymorphism (Go et al., 2005), and oligodendrocyte lineage transcription factor 2 gene (Sims et al., 2009).

Aggression and agitation. Aggression in AD has been linked with polymorphic variation at the tryptophan gene (Craig et al., 2004) and polymorphic variation of the serotonin transporter gene (Ueki et al., 2007; Pritchard et al., 2007a). There are contradictory findings about APOE e4 allele and aggression in AD (Craig et al., 2004; Engelborghs et al., 2006; Pritchard et al., 2007b). Agitation in AD has been associated with polymorphisms of the D1 dopamine receptor gene (Holmes et al., 2001) and the dopamine transporter gene 3' variable number tandem repeats (VNTR) (Proitsi et al., 2012), and there are contradictory findings regarding links with the serotonin transporter gene (Sukonick et al., 2001; Assal et al., 2004). There are also possible associations between variations on the dopamine transporter gene and aberrant motor behavior (Pritchard et al., 2008; Proitsi et al., 2012) and irritability (Pritchard et al., 2008).

Depression. Depression in AD is linked to 5-HT2A & 5-HT2C polymorphisms in some (Holmes et al., 2003), but not all, studies (Pritchard et al., 2008b), although the latter study did find a link with anxiety. Depression has also been linked with polymorphisms of the interleukin-1β gene promoter with an association with the T-variant (McCulley et al., 2004), but there is no association with APOE e4 allele (Craig et al., 2005; Pritchard et al., 2007b). More recently a direct association was found between the dopamine receptor 3 Ball polymorphism and depression (Proitsi et al., 2012). There is also some evidence of an association between a positive family history of depression and an increase in the frequency of BPSD occurring for the first time within Alzheimer's disease (Holmes, 2000).

Other BPSD. In their large cohort of 1,008 probable AD cases, Proitsi et al., (2012) found associations between sleep disturbances and the dopamine receptor 4 VNTR and with apathy and the SERT gene VNTR 5HTTLPR.

Other types of dementia

Few studies have examined genetic influences on BPSD in other types of dementia. In dementia with Lewy bodies (DLB) and Parkinson's dementia, delusions were associated with the APOE e2 allele (Engelborghs et al., 2006). One study found an association of the APOE e4 allele with aggression in frontotemporal dementia (FTD) but not mixed dementia or AD (Engelborghs et al., 2006).

Further investigations are needed to enhance our knowledge about correlations of genetic abnormalities and specific BPSD symptomatology but the overall picture emphasizes the importance of the serotonergic system (Aarsland et al., 2005).

Neurotransmitter changes in dementia—relationship to BPSD

Significant and multiple neurotransmitter changes have been identified in the brains of people afflicted by dementia—whether dementia of the Alzheimer's type (AD), dementia with Lewy bodies (DLB), frontotemporal dementia (FTD), or vascular dementia (VaD). Such neurotransmitter changes may have a direct effect on brain function and might also cause neuroendocrine dysfunction in dementia, mainly in the form of overactivity in the hypothalamic-pituitary-adrenal (HPA) axis. Neurotransmitters affected in dementia are the following:

- Acetylcholine
- Dopamine
- Norepinephrine
- Serotonin
- Glutamate
- Gamma-aminobutyric acid

Neurotransmitter changes in the brains of people with the most common cause of dementia, Alzheimer's disease (AD), have been most extensively documented, and thus, much of the following text refers to AD-specific changes.

Dementia-related changes in the cholinergic system

A person with AD has several deficits:

- Severe disturbances of the cholinergic system
- Decreased cholineacetyltransferase activity
- Decreased number of cell bodies in the nucleus basalis of Meynart

Disturbed functioning of the cholinergic system can cause memory impairment, confusion, and delirium. Thus, cholinergic drugs, such as acetylcholinesterase inhibitors, may benefit cognitive function in patients with AD (Pinto et al., 2011). Less well-studied are the effects of cholinergic drugs on BPSD and reduced levels of awareness or alertness. The cholinergic deficit in dementia with Lewy-bodies (DLB) is reported to be three times as severe as in Alzheimer's disease. Therefore, acetylcholinesterase inhibitors may be even more effective in patients with this form of dementia.

Drugs with anticholinergic effects, such as scopolamine and tricyclic antidepressants, may cause delirium in elderly patients, particularly in those with dementia. Delirium is associated with many BPSD including hallucinations and delusions, sleep fragmentation, and psychomotor agitation (see Module 2). In DLB, visual hallucinations and delirium are frequently present throughout the disease course, and in DLB but not AD, there is a reported link between cholinergic deficits in the temporal cortex and visual hallucinations (Minger et al., 2000; Ballard et al., 2000).

In AD there is a reported link between choline acyltransferase (ChAT) activity in the frontal and temporal cortices and aggression and ratios of ChAT activity to dopamine D1 receptor binding, and DA concentration in temporal cortex were also reduced (Minger et al., 2000). There is also a reported link between reduced ChAT activity in the frontal and temporal cortices and aimless and excessive walking in AD (Minger et al., 2000). A review of the cholinergic hypothesis of BPSD concluded that behaviors such as agitation, apathy and psychosis may represent a specific central cholinergic deficiency syndrome (Pinto et al., 2011).

Dementia-related changes in the dopamine system

Levels of the catecholamines dopamine and norepinephrine are decreased in discrete areas of the brains of AD patients. Approximately 25% of patients with AD have Parkinsonian symptoms, which are associated with dopamine deficiencies. Dopamine also plays a role in cognitive function, such as working memory. In addition, aggressive behavior may, like psychosis, be related to the dopaminergic system. As noted earlier, in AD patients with aggression, ratios of ChAT activity to dopamine D1 receptor binding and DA concentration in the temporal cortex are reported to be reduced (Minger et al., 2000). Further, dementia patients with aggression improve in behavior when treated with dopamine-blocking agents (Jeste et al., 2008). Another study reported that apathy in AD was associated with a blunted dopaminergic brain-reward system (Lanctôt et al., 2008). In FTD, the dopamine system has been reported to be associated with aggression and agitation with increased activity and altered serotonergic modulation of dopamine neurotransmission (Engelborghs et al., 2008).

Dementia-related changes in the norepinephrine system

Dementia-related changes in the norepinephrine system are complex. Patients with AD show structural defects such as a decreased number of norepinephrine neurons in the locus coeruleus, which leads to reduced norepinephrine levels in brain areas such as the neocortex. Reduced norepinephrine levels are associated with higher rates of depressive symptoms or major depressive disorder in patients with AD. Aggressive behavior in AD has been linked with the combination of locus coeruleus neuronal loss and upregulated expression levels of tyrosine hydroxylase mRNA. This leads to increased postsynaptic sensitivity to norepinephrine, suggesting that a lower concentration of norepinephrine produces an amplified effect possibly due to an increase in norepinephrine synthetic capacity in residual cells (Peskind et al., 1995; Matthews et al., 2002; Herrmann et al., 2004). Upregulation of alpha-1 adrenoreceptors is associated with aggressive behavior and chronic treatment with neuroleptic medication in patients with Alzheimer's disease (Sharp et al., 2007).

In contrast, levels of 3-methoxy-4-hydroxy-phenylglycol (MHPG), the metabolite of norepinephrine, are significantly increased in the caudate nucleus, hippocampus, and cingulate gyrus in patients with AD, possibly as a compensatory mechanism. The high levels of MHPG in the caudate nucleus and hippocampus indicate abnormally high activity in the turnover of norepinephrine. The finding that MHPG levels in the cerebrospinal fluid are not decreased in AD also supports this possibility.

Higher levels of norepinephrine have been found in the substantia nigra of patients with AD and psychotic symptoms than in patients without these symptoms (Zubenko et al., 1991).

Dementia-related changes in the serotonin system

Concentrations of serotonin are significantly reduced in several brain areas in patients with AD, although the end metabolite (5-hydroxyindoleacetic acid) is found in normal concentrations. Reduced concentrations of serotonin in the presubiculum have been found in AD patients with psychotic symptoms (Zubenko et al., 1991). There is a complex relationship between aggression in AD and central serotonin activity as measured by prolactin response to fenfluramine challenge with interactions involving gender and cognitive impairment (Lanctôt et al., 2002). Aggressive behavior in AD has been linked with 5-HT1A receptor changes (Lai et al., 2003).

Abnormal functioning of the serotonergic system is implicated in several pathologic disorders. Thus, some of the BPSD may be due to abnormalities in the serotonergic system, which may result in the following:

- Depressed mood
- Anxiety
- Agitation
- Restlessness

Studies involving serotonergic agents for the treatment of BPSD have yielded mixed results (Jeste et al., 2008). One study of 15 patients with frontotemporal dementia and severe BPSD found that a blunted response to a citalopram challenge, implying a dysfunctional serotonergic system, predicted a more positive treatment outcome (Herrmann et al., 2012).

Dementia-related changes in glutamate concentrations

Glutamate is the dominant excitatory neurotransmitter in the brain. It is difficult to say to what extent glutamate concentrations in brain tissue are a marker for metabolism of the glutamate neurotransmitter, but data indicate that patients with AD have fairly severe glutamate loss. The imbalance between the glutamate and dopaminergic systems may lead to dysfunction in the cortical neostriatal-thalamic circuit, which may result in psychotic symptoms. There is some limited evidence that memantine, a low-affinity antagonist to glutamate NMDA receptors, might be effective in the treatment of BPSD (Maidment et al., 2008).

Dementia-related changes in the gamma-aminobutyric acid (GABA) system

GABA is a major inhibitory neurotransmitter that has been a target for anxiolytics, anticonvulsants, and hypnotics. Research on the role of disruption of GABA pathways in AD has yielded contradictory findings that might reflect subtypes of the disease (Lanctôt et al., 2004). Changes in GABA may be related to BPSD—for example, plasma GABA levels are correlated with depression and apathy scores on the NPI in severe AD (Lanctôt et al., 2007).

Neuroendocrine dysfunction in dementia

In patients with AD, levels of somatostatin, vasopressin, corticotropin-releasing hormone, substance P, and neuropeptide Y are significantly reduced in the cortical and subcortical areas of the brain, whereas levels of the peptide galanin are increased. However, changes in the hypothalamus differ from those in the cortical areas and other subcortical nuclei. According to some investigators, levels of somatostatin, vasopressin, and neuropeptide Y, as well as those of galanin, are significantly increased in the hypothalamus. The increased concentrations of some neuropeptides might be due to lost inhibitory control over the hypothalamus resulting from failing feedback mechanisms from stress systems. This may lead to more agitation, restlessness, sleep disturbance, and other stress-related symptoms.

Results of the dexamethasone suppression test in patients with dementia have shown over-activity in the HPA axis. Between 40% and 60% of patients with dementia have pathologic dexamethasone depression test results; that is, they cannot suppress their cortisol levels when given dexamethasone. Increased release of cortisol in these patients may underlie their disturbed diurnal rhythms and sleep disturbances. Stress-intolerant high cortisol levels also can precipitate confusion.

Some types of aggressive behavior in AD are associated with a blunted growth hormone response to clonidine challenge, a marker of central norepinephrine responsiveness (Herrmann et al., 2004).

Neuropathologic changes in dementia—relationship to BPSD

Despite the clinical importance of BPSD, the neuropathological basis for their expression is not yet well understood; however, with improvements in investigative techniques, advances have been made.

Psychotic symptoms

There is a limited body of literature on the relationship between psychotic symptoms in AD and pathology. In general, psychosis is more common in declining cognition and increasing severity of neuropathology in AD (Aarsland et al., 2005; Savva et al., 2009). A review of the clinicopathological correlates of BPSD concluded that psychotic symptoms in people with dementia usually demonstrate preferential involvement of the frontal lobe and/or limbic regions, although visual hallucinations tend to involve the occipital lobes (Casanova et al., 2011).

Delusions are common in extrapyramidal disorders (Sachdev and Keshaven, 2010). It also appears that they are associated with calcification of the basal ganglia. They are commonly seen in patients with temporal lobe disorders and more commonly occur in patients with disorders involving the left, rather than the right, side of the brain. In addition, delusional misidentification has been found to be related to an increased number of dystrophic neurites in the frontal, parietal, and occipital cortices (Mkaetova-Ladinska et al., 1995).

Patients with DLB also experience psychotic symptoms, and in such patients, levels of acetyltransferase are reported to be reduced in the parietal, temporal, and occipital cortices. Neuronal counts are decreased in the nucleus basalis (Perry et al., 1990). In DLB, visual hallucinations, but not delusions, are associated with less tangle burden but more cortical Lewy body pathology (Ballard et al., 2004). In DLB, hallucinations and delusions are related to different underlying brain changes with delusions, but not hallucinations, having similar substrates in DLB and AD.

Aggressive behavior was reported to be associated with neuropathologic lesions in the basal nucleus of Meynert and the locus coeruleus, and with a preservation of neurons in the substantia nigra pars compacta. Apathy and communication failure are related to more severe changes in the hippocampus and the basal nucleus of Meynert (Forstl, 2000) and the anterior cingulate gyrus (Casanova et al., 2011). More severe neuropathologic changes in the aminergic brain stem nuclei and loss of dorsal raphe serotonergic nuclei are associated with depressive symptoms in AD patients (Forstl et al., 1992).

Structural neuroimaging

There is limited evidence from structural neuroimaging studies for relationships between ventricular size (or atrophy) and clinical symptoms, including:

- Depression
- Pathologic affect
- Hallucinations
- Delusional misidentifications

Historically, Jacoby and Levy (1980) found less severe atrophy in AD patients with delusions than in those without; and Bondareff et al., (1994; 1996) found smaller ventricle-brain ratios associated with delusions of theft. However, not all studies have supported these findings.

More recent structural imaging studies have focused on FTD. There have been inconsistent findings regarding specific abnormalities associated with apathy in FTD but in general there is disruption of cortical-basal ganglia circuits. One study found that apathy was associated with atrophy in the dorsal anterior cingulate cortex and dorsolateral prefrontal cortex (Massimo et al., 2009); a second study reported that severity of apathy correlated with atrophy in the right dorsolateral prefrontal cortex (Zamboni et al., 2008); while a third study of behavioral variant FTD found apathy to be associated with atrophy of the right caudate (including the ventral striatum), the right temporoparietal junction, right posterior inferior and middle temporal gyri, and left frontal operculumanterior insula region (Eslinger et al., 2012). Disinhibition in FTD was associated with atrophy in the medial orbital frontal cortex in one study (Massimo et al., 2009), while severity of disinhibition correlated with atrophy in the nucleus accumbens, right superior temporal sulcus, and right mediotemporal limbic structures in another study (Zamboni et al., 2008). A third study reported atrophy in orbitofrontal/subgenual, medial prefrontal cortex and anterior temporal lobe areas (Hornberger et al., 2011). A recent meta-analysis concluded that there was evidence of gray matter changes in the frontal-striatal-limbic brain areas in patients with behavioral variant FTD (Pan et al., 2012).

Functional neuroimaging

In recent years there has been a marked increase in functional imaging studies of BPSD, particularly in AD, and these studies suggest that BPSD (in AD at least) are associated with dysfunction in specific brain regions. Table 3.1 summarizes some of the functional neuroimaging findings in AD.

Table 3.1: Functional neuroimaging and BPSD in Alzheimer's disease

BPSD	Neuroimaging finding
Psychosis	Hypoperfusion in frontal and temporal lobes (Robert et al., 2005)
Depression	Hypoperfusion in frontal, temporal, and parietal lobes (Robert et al., 2005)
Aggression	Hypoperfusion in temporal cortex (Hirono et al., 2000; Lanctôt et al., 2004)
Apathy	Hypoperfusion in frontosubcortical structures, especially anterior cingulate (Migneco et al., 2001; Benoit et al., 2002; Lanctôt et al., 2007; Marshall et al., 2007)
Sleep loss	Hyperperfusion in right middle frontal gyrus (Ismail et al., 2009)
Appetite loss	Hypoperfusion in left ant. cingulate and left orbitofrontal cortices (Ismail et al., 2008)

In DLB, hypometabolism in visual association areas rather than the primary visual cortex are reported to be involved in visual hallucinations (Perneczky et al., 2008). In a study of the behavioral variant of FTD, the "disinhibited" phenotype correlated with SPECT scan hypoperfusion in the region of the anterior cingulate and anterior temporal cortex bilaterally, and for apathetic phenotype, in the left dorsolateral frontal cortex (Borroni et al., 2012).

Circadian rhythms—relationship to BPSD

Changes in circadian rhythm (e.g., fragmented sleep-wake patterns) may be age-related and occur in many older persons, but these changes are particularly pronounced in patients with AD, DLB, and other synucleinopathies. Changes in sleep architecture (i.e., reduced rapid eye movement and slow-wave sleep) mean that patients are more likely to nap during the day and to be awake at night (Winograd and Jarvik, 1986; Prinz and Viliello, 1993). Patients whose nocturnal restlessness disrupts the sleep of the caregiver are more likely to be institutionalized than those who have cognitive impairment alone.

Disruptions of circadian rhythms can result in BPSD—agitation during the day and restlessness at night. Furthermore, abnormalities in circadian rhythm may be responsible for 'sundown syndrome' (i.e., the appearance or exacerbation of symptoms of confusion associated with the late afternoon or early evening hours) (Evans, 1987), but a minority of dementia patients show a clear increase of agitation in the later hours peaking at around 4:00 p.m. (Cohen-Mansfield, 2007). Cohen-Mansfield hypothesized that day-shift staff fatigue might be a contributing explanation for the phenomena.

Investigations have shown that Alzheimer's patients reveal increased nocturnal activity and a significant phase-delay in their rhythms of core-body temperature and of activity compared with patients with FTD. The rhythms of FTD patients are highly fragmented and phase-advanced in comparison with controls, and they are apparently uncoupled from the rhythm of core-body temperature (Harper et al., 2001). Differences have also been reported between AD and DLB in the type of sleep/wake cycle disturbances (Robert et al., 2005).

Biologic correlates of circadian rhythm disturbances

The degenerative changes in the retina and optic nerve associated with dementia decrease patients' exposure to light, affecting the synchronization of the brain's biologic clock to 24-hour environmental cues. This biologic reduction to light exposure is exacerbated by the environmental reduction in light exposure experienced by patients with dementia. Dementia patients (especially those in nursing homes) are more likely to remain inside and thus have less exposure to sunlight.

The suprachiasmatic nucleus, a small structure located on top of the optic chiasm, also known as the biologic clock, is involved in regulating circadian and circannual rhythms. The suprachiasmatic nucleus works by generating biologic rhythms corresponding to an approximately 24-hour period. Normally, in a process called entraining, this endogenous suprachiasmatic nucleus rhythm is synchronized to the 24-hour environmental light-dark cycle. There are now data to show that disturbances of circadian rhythms in dementia are related to changes in the suprachiasmatic nucleus, such as a substantial decrease in the number of vasopressin-expressing neurons.

Other clinical contributors to BPSD

In general, BPSD increase with declining cognition (Cohen-Mansfield and Libin, 2005; Starr and Lonie, 2007; Pagonabarraga et al., 2008; Proitsi et al., 2009), although there is some evidence that premorbid intelligence might be a factor (Starr and Lonie, 2007). BPSD are also associated with

increasing functional disability (Hinton et al., 2008), and impaired communication is associated with aggression and depression (Talerico et al., 2002). There are gender differences with psychosis (Steinberg et al., 2006; Proitsi et al., 2009; Murayama et al., 2009; Kitamura et al., 2012), verbal agitation (Draper et al., 2000; Cohen-Mansfield and Libin, 2005), anxiety (Steinberg et al., 2006; Kitamura et al., 2012) being more common in females, and aggression more common in males (Whall et al., 2008; Lovheim et al., 2009; Kitamura et al., 2012). Anxiety and depression are more common in younger individuals (Savva et al., 2009; Proitsi et al., 2009) and irritability in higher-functioning groups (Savva et al., 2009).

Executive impairment early in the course of dementia was found to be associated with BPSD and carer stress 3-6 years later (Tsoi et al., 2008). Frontal symptoms are associated with increased severity and frequency of agitation and aggression, as well as increased severity of psychosis and depression (Senanarong et al., 2004; Engelborghs et al., 2006).

Some BPSD are more common in different types of dementia, although there are contradictory findings. Disinhibition, apathy, and aberrant motor behavior distinguish FTD from other types of dementia in most, but not all, studies (Senanarong et al., 2004; Engelborghs et al., 2005; Srikanth et al., 2005; De Vugt et al., 2006), while high rates of hallucinations and disinhibition have been reported in DLB (Engelborghs et al., 2005; Chiu et al., 2006). There have been few differences in BPSD or discrepant findings reported between VaD and AD (Senanarong et al., 2004; Srikanth et al., 2005; Steinberg et al., 2006; de Vugt et al., 2006) and between FTD and progressive supranuclear palsy (Yatabe et al., 2011).

Personality/psychological contributors to BPSD

Self-psychology adds another dimension to understanding the psychological reactions that occur in patients with dementia and can impact on BPSD. Little attention has been paid to regression in the self-sector of personality experienced by patients with dementia, yet the essence of the patient's identity—or self-esteem—is eroded and devastated by this illness. Regression in the self-sector may be caused by a combination of neurological deterioration and concomitant psychological reactions to the dissolution of the self, and may result in depressive or psychotic symptoms. Patients who have shown suspicious, aggressive, or controlling behaviors prior to the onset of dementia are more likely to subsequently develop BPSD.

A high level of neuroticism in Alzheimer's patients might be associated with a higher risk of BPSD. A low level of premorbid neuroticism was linked to depressive signs and symptoms, and troublesome behavior was associated with a higher level of premorbid neuroticism in one study (Meins et al., 1998), while another found that delusions of theft were related to premorbid neurotic personality (Murayama et al., 2009). A third study found a relationship between neuroticism and anxiety/total NPI score and not affective disturbance (Archer et al., 2007). This latter study also found that lower premorbid agreeableness was associated with agitation and irritability symptoms in Alzheimer's disease and predicted an "agitation/apathy" syndrome. A study of wandering behavior reported an association with premorbid extroversion and negative verbalization stress response (Song and Algase, 2008). However, results are mixed about whether an individual's premorbid personality has a role in the development of BPSD—for example, one group found no meaningful relationship between premorbid personality and subsequent BPSD, and concluded that biological and environmental factors appear more important (Low et al., 2002).

Stressful life events trigger depression and excess psychiatric morbidity in both the cognitively intact and people with dementia. Cognitively impaired people are often more susceptible to the effects of stressful life events. Therefore, clinical strategies that minimize or buffer the effects of social or environmental change might prevent deterioration in, or development of, BPSD. However, a well-weighted balance of daily activity is an important component of therapeutic interventions to avoid under- and overstimulation.

Most patients with dementia are advanced in age. They do not only suffer from the dementing illness; they also present with other somatic diseases or are susceptible to develop somatic disturbances. Somatic diseases are a crucial factor for BPSD (Steinberg et al., 2006). They may trigger these symptoms, and this may include through the development of comorbid delirium (Holtta et al., 2011), or they may contribute to their presence over time. One study found that 36% of community residing people with dementia and behavioral symptoms had undiagnosed acute illnesses with bacteriuria (15%), hyperglycemia (6%) and anemia (5%) being most prevalent. The behavior most often associated with detected illness was resisting or refusing care (Hodgson et al., 2011). The following disturbances play a major role: cardiovascular disease, urinary tract and other infections, and pain syndromes or somatic symptoms due to pharmacologically mediated adverse events. Discomforts have been found to be associated with verbal agitation and non-aggressive physical agitation (Pelletier and Landreville, 2007). Such discomforts might also relate to the physical environment such as high climate temperature (Cornali et al., 2004).

Investigations into the psychology of the self have led to new ways of understanding a dementing patient's attempts to maintain some semblance of self-esteem and identity following progressive cognitive decline and have also led to an appreciation of these aids in the understanding of behaviors that may manifest as BPSD (see Module 5).

Environmental, physical, and social contributors to BPSD

There is evidence that certain environmental features in residential care are associated with lower levels of BPSD and better well-being of residents (Fleming et al., 2009). In their review of the empirical literature on the design of physical environments for people with dementia, Fleming et al., (2009) found:

- Unobtrusive safety features improve resident well-being and reduce depression, though there is some evidence that an overemphasis on safety might have a detrimental effect. One study reported that increased security measures were associated with risk-taking behavior and passive self-harm (Low et al., 2004).
- Provision of a variety of spaces in environments reduces anxiety and depression, improves social interaction, and might assist residents in finding their way around.
- Availability of single rooms is beneficial.
- Optimization of levels of stimulation by reducing unhelpful stimulation while increasing helpful stimuli is effective—for example, there is good evidence that illumination beyond that which is considered to be normal can improve sleep patterns and reduce BPSD.
- Small facility size is associated with lower levels of aggression.

Patients with dementia are sensitive to change in their social environment. The emergence of BPSD and the need for hospitalization are often associated with previous life-events characterized by change in social routine and environment (Eriksson, 2000). Relocation can increase depressive behavior, mortality and agitation in patients with dementia, with many patients showing significant disturbed behavior and disorientation for three months after a move (Anthony et al., 1987). The greatest effects of relocation on mortality are observed among patients with moderate cognitive impairment.

Environmental change and stressful events may increase HPA axis activity, thereby causing depression and further exacerbating cognitive deterioration through hippocampal neuron fallout. Alternatively, abnormalities in the HPA axis that occur as part of the degenerative process in AD may actually cause the increased agitation and depression seen in patients with this disease.

Environmental improvement with increased stimulation can also change the neurotransmitter milieu, with increases in cerebrospinal fluid levels of somatostatin and homovanillic acid paralleling an improvement in BPSD. Thus, environmental and behavioral changes appear to be related, and this association is reflected by changes in the underlying neurobiology (Lawlor, 1996).

Caregiver factors

Caregiver distress and poor interpersonal interactions between the patient and caregiver can exacerbate BPSD. Caregiver avoidance and care-receiver insecure attachment styles are associated with increased BPSD (Perren et al., 2007). When the patient and caregiver have had a poor premorbid relationship, the caregiver may misinterpret agitated behavior as purposefully provocative and worsen the situation with an angry retort. Inappropriate caregiver strategies have been reported to be associated with delusions (Riello et al., 2002), aggression (Hamel et al., 1990), and hyperactive behavior (de Vugt et al., 2004).

Similarly, patients with dementia and agitation have diverse reactions to caregiver intrusion into their personal space. In a study of 24 nursing home residents with agitation and severe cognitive impairment, touch was related to an increase in aggression but to a decrease in physically non-aggressive behaviors (Marx and Werner, 1989). The positive relationship between aggression and touching suggests that touching may be interpreted as a violation of personal space by some patients with dementia. Conversely, for others, touching may act as a quieting and comforting form of communication, as shown by the decrease in strange movements seen in this study. These findings highlight the need to educate caregivers (especially professional caregivers working in residential units) about the likely diverse reactions of different individuals to such simple interventions as touch (see Module 5).

Studies focusing on psychotherapeutic intervention for caregivers have convincingly demonstrated that a modification of problematic behavior among caregivers may alleviate, or even obviate, the occurrence of BPSD in dementia patients (Ballard et al., 2000; Haupt et al., 2000). For instance, in a 3-month, expert-based group intervention with caregiving relatives of dementing patients, agitation and anxiety occurring in familiar surroundings were significantly improved in these patients (Haupt et al., 2000).

Conclusion

Etiological factors of BPSD are multifaceted. Biological and non-biological factors contribute to the development of BPSD. The coming years will hopefully integrate these aspects into a model of diagnosis and therapeutic management which combines pharmacological and nonpharmacological strategies as well as involving the caregiver in the therapeutic process. Development of knowledge of etiological factors of BPSD will strengthen the establishment of such an integrative model.

References and recommended reading

Genetic abnormalities in demented patients—relationship to BPSD

Aarsland, D., Sharp, S., Ballard, C. Psychiatric and behavioral symptoms in Alzheimer's disease and other dementias: etiology and management. *Current Neurology and Neuroscience Reports* 2005; 5(5): 3354.

Assal, F., Alarcon, M., Solomon, E.C., et al. Association of the serotonin transporter and receptor gene polymorphisms in neuropsychiatric symptoms in Alzheimer's disease. *Archives of Neurology* 2004; 61: 124953.

Borroni, B., Grassi, M., Agosti, C., et al. Cumulative effect of COMT and 5-HTTLPR polymorphisms and their interaction with disease severity and comorbidities on the risk of psychosis in Alzheimer disease. *American Journal of Geriatric Psychiatry* 2006; 14: 343351.

Craig, D., Hart, D.J., McCool, K., et al. The interleukin 1beta gene promoter polymorphism (-511) acts as a risk factor for psychosis in Alzheimer's dementia; *Annals of Neurology* 2004a, 56: 121124.

Craig, D., Hart, D.J., McCool, K., et al. Apolipoprotein E ε4 allele influences aggressive behavior in Alzheimer's disease. *Journal of Neurology, Neurosurgery and Psychiatry* 2004b; 75: 1327–1330.

Craig, D., Hart, D.J., McIlroy, S.P., et al. Association analysis of apolipoprotein E genotype and risk of depressive symptoms in Alzheimer's disease. *Dementia & Geriatric Cognitive Disorders* 2005; 19: 154–157.

Engelborghs, S., Dermaut, B., Marien, P., et al. Dose dependent effect of APOE epsilon4 on behavioral symptoms in frontal lobe dementia. *Neurobiology of Aging* 2006; 27(2): 285–292.

Go, R.C., Perr, R.T., Wiener, H., et al. Neuregulin-1 polymorphism in late onset Alzheimer's disease families with psychoses. *American Journal of Medical Genetics. Part B, Neuropsychiatric Genetics* 2005; 139B: 28–32.

Hollingworth, P., Hamshere, M.L., Holmans, P.A., et al. Increased familial risk and genomewide significant linkage for Alzheimer's disease with psychosis. *American Journal of Medical Genetics. Part B, Neuropsychiatric Genetics* 2007; 144B: 841–848.

Holmes, C. Contribution of genetics to the understanding of behavioral and psychological symptoms of dementia. *International Psychogeriatrics* 2000; 12 (suppl): 83–89.

Holmes, C., Smith, H., Ganderton, R., et al. Psychosis and aggression in Alzheimer's disease: the effect of dopamine receptor gene variation. *Journal of Neurology, Neurosurgery and Psychiatry* 2001; 71: 777–779.

Holmes, C., Arranz, M., Collier, D., et al. Depression in Alzheimer's disease: the effect of serotonin receptor gene variation. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics* 2003; 119: 40–43.

McCulley, M.C., Day, I.N., Homes, C. (2004). Association between interleukin 1-beta promoter (-511) polymorphism and depressive symptoms in Alzheimer's disease. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics* 2003; 124: 50–53.

Panza, F., Frisardi, V., Seripa, D., et al. Apolipoprotein E genotypes and neuropsychiatric symptoms and syndromes in late-onset Alzheimer's disease. *Ageing Research Reviews* 2012; 11: 87–103.

Pritchard, A.L., Pritchard, C.W., Bentham, P., et al. Role of serotonin transporter polymorphisms in the behavioral and psychological symptoms in probable Alzheimer's disease. *Dementia & Geriatric Cognitive Disorders* 2007a; 24: 201–206.

Pritchard, A.L., Harris, J., Pritchard, C.W., et al. The effect of the apolipoprotein E gene polymorphisms and haplotypes on behavioral and psychological symptoms of patients with probable Alzheimer's disease. *Journal of Neurology, Neurosurgery and Psychiatry* 2007b; 78(2): 123–126.

Pritchard, A.L., Pritchard, C.W., Bentham, P., et al. Investigation of the role of the dopamine transporter in susceptibility to behavioral and psychological symptoms in probable Alzheimer's disease. *Dementia & Geriatric Cognitive Disorders* 2008a; 26: 257–260.

Pritchard, A.L., Harris, J., Pritchard, C.W., et al. Role of 5HT 2A and 5HT 2C polymorphisms in behavioral and psychological symptoms of Alzheimer's disease. *Neurobiology of Aging* 2008b; 29(3): 341–347.

Proitsi, P., Lupton, M.K., Reeves, S.J. et al. Association of serotonin and dopamine gene pathways with behavioral subphenotypes in dementia. *Neurobiology of Aging* 2012; 33(4): 791–803.

Quaranta, D., Bizzarro, A., Marra, C., et al. Psychotic symptoms in Alzheimer's disease and 5-HTTLPR polymorphism of the serotonin transporter gene: evidence for an association. *Journal of Alzheimer's Disease* 2009; 16: 173–180.

Ramanathan, S., Glatt, S.J. Serotonergic system genes in psychosis of Alzheimer dementia: meta-analysis. *American Journal of Geriatric Psychiatry* 2009; 17: 839–846.

Sato, N., Ueki, A., Ueno, H., et al. Dopamine D3 receptor gene polymorphism influences on behavioral and psychological symptoms of dementia (BPSD) in mild dementia of Alzheimer's type. *Journal of Alzheimer's Disease* 2009; 17: 441–448.

Sims, R., Hollingworth, P., Moskvina, V., et al. Evidence that variation in the oligodendrocyte lineage transcription factor 2 (OLIG2) gene is associated with psychosis in Alzheimer's disease. *Neuroscience Letters* 2009; 461: 54–59.

Sukonick, D.L., Pollock, B.G., Sweet, R.A., et al. The 5-HTTPR*S/*L polymorphism and aggressive behavior in Alzheimer's disease. *Archives of Neurology* 2001; 58: 1425–1428.

Sweet, R.A., Devlin, B., Pollock, B.G., et al. Catechol-O-methyltransferase haplotypes are associated with psychosis in Alzheimer disease. *Molecular Psychiatry* 2005; 10: 1026–1036.

Sweet, R.A., Nimgaonkar, V.L., Kamboh, M.I., et al. Dopamine receptor genetic variation, psychosis, and aggression in Alzheimer disease. *Archives of Neurology* 1998; 55: 1335–1340.

Ueki, A., Ueno, H., Sato, N., et al. Serotonin transporter gene polymorphism and BPSD in mild Alzheimer's disease. *Journal of Alzheimer's Disease* 2007; 12(3): 245–253.

Wilkosz, P.A., Kodavali, C., Weamer, E.A., et al. Prediction of psychosis onset in Alzheimer disease: the role of depression symptom severity and the HTR2A T102C polymorphism. *American Journal of Medical Genetics. Part B, Neuropsychiatric Genetics* 2007; 144B: 1054–1062.

Neurotransmitter changes in dementia—relationship to BPSD

Engelborghs, S., Vloeberghs, E., Le Bastard, N., et al. The dopaminergic neurotransmitter system is associated with aggression and agitation on frontotemporal dementia. *Neurochemistry international* 2008; 52(6): 1052–1060.

Herrmann, N., Black, S.E., Chow, T., et al. Serotonergic function and treatment of behavioral and psychological symptoms of frontotemporal dementia. *American Journal of Geriatric Psychiatry* 2012; 20: 789–797.

Herrmann, N., Lanctôt, K.L., Eryavec, G., et al. Growth hormone response to clonidine predicts aggression in Alzheimer's disease. *Psychoneuroendocrinology* 2004; 29(9): 1192–1197.

Herrmann, N., Lanctôt, K.L., Khan, L.R. The role of norepinephrine in the behavioral and psychological symptoms of dementia. *Journal of Neuropsychiatry & Clinical Neurosciences* 2004; 16(3): 261–276.

Jeste, D.V., Blazer, D., Casey, D., et al. ACNP White Paper: Update on use of antipsychotic drugs in elderly persons with dementia. *Neuropsychopharmacology* 2008; 33: 957–970.

Lanctôt, K.L., Herrmann, N., Mazzotta, P., et al. GABAergic function in Alzheimer's disease: evidence for dysfunction and potential as a therapeutic target for the treatment of behavioral and psychological symptoms of dementia. *Canadian Journal of Psychiatry* 2004; 49(7): 439–453.

Lanctôt, K.L., Herrmann, N., Rothenburg, L., et al. (Behavioral correlates of GABAergic disruption in Alzheimer's disease. *International Psychogeriatrics* 2007; 19(1): 151–158.

Lanctôt, K. L., Herrmann, N., Black, S.E., et al. Apathy associated with Alzheimer disease: use of dextroamphetamine challenge. *American Journal of Geriatric Psychiatry* 2008; 16: 551–557.

Maidment, I.D., Fox, C.G., Boustani, M., et al. Efficacy of memantine on behavioral and psychological symptoms related to dementia: a systematic meta-analysis. *Annals of Pharmacotherapy* 2008; 42(1): 32–38.

Matthews, K.I., Chen, C.P., Esiri, M.M., et al. Noradrenergic changes, aggressive behavior, and cognition in patients with dementia. *Biological Psychiatry* 2002; 51: 407–416.

Minger, S.L., Esiri, M.M., McDonald, B., et al. Cholinergic deficits contribute to behavioral disturbances in patients with dementia. *Neurology* 2000; 55: 1460–1467.

Peskind, E.R., Wingerson, D., Murray, S., et al. Effects of Alzheimer's disease and normal aging on cerebrospinal fluid norepinephrine responses to yohimbine and clonidine. *Archives of General Psychiatry* 1995; 52: 774–782.

Pinto, T., Lanctôt, K.L., Herrmann, N. Revisiting the cholinergic hypothesis of behavioral and psychological symptoms of dementia of the Alzheimer's type. *Ageing Research Reviews* 2011; 10(4): 404–412.

Sharp, S.I., Ballard, C.G., Chen, C.P., et al. Aggressive behavior and neuroleptic medication are associated with increased number of alpha1-adrenoreceptors in patients with Alzheimer's disease. *American Journal of Geriatric Psychiatry* 2007; 15: 435–437.

Zubenko, G.S., Moosy, J., Martinez, J., et al. Neuropathologic and neurochemical correlates of psychoses in primary dementia. *Archives of Neurology* 1991; 48: 619–624.

Neuropathology changes in dementia—relationship to BPSD

Ballard, C.G., Jacoby, R., Del Ser, T., et al. Neuropathological substrates of psychiatric symptoms in prospectively studied patients with autopsy-confirmed dementia with Lewy bodies. *American Journal of Psychiatry* 2004; 161: 843–849.

Bondareff, W. Neuropathology of psychotic symptoms in Alzheimer's disease. *International Psychogeriatrics* 1996; 8 (Suppl 3): 233–237.

Casanova, M.F., Starkstein, S.E., Jellinger, K.A. Clinicopathological correlates of behavioral and psychological symptoms of dementia. *Acta Neuropathologica* 2011; 122(2): 117–135.

Forstl, H. Neuropathology of behavioral and psychological symptoms of dementia. *International Psychogeriatrics* 2000; 12 (suppl): 77–83.

Forstl, H., Burns, A., Luthert, P., et al. Clinical and neuropathological correlates of depression in Alzheimer's disease. *Psychological Medicine* 1992; 22: 877–884.

Mkaetova-Ladinska, E.B., Harrington, C.R., Xuereb, J., et al. In: *Treating Alzheimer's and other dementias*. Bergener, M., Finkel, S.I. (eds). New York: Springer Publishing Co, 1995; 57–80.

Perry, R.H., Irving, D., Blessed, G., et al. Senile dementia of Lewy body type, a clinically and neuropathologically distinct form of dementia. *Journal of the Neurological Science* 1990; 95: 119–139.

Sachdev, P., Keshavan, M.S. (eds.) *Secondary Schizophrenia.* Cambridge; Cambridge University Press 2010.

Savva, G.M., Zaccai, J., Matthews, F.E., et al. Prevalence, correlates and course of behavioral and psychological symptoms of dementia in the population. *British Journal of Psychiatry* 2009; 194(3): 212–219.

Neuroimaging (structural and functional)

Benoit, M., Koulihaly, P.M., Migneco, O., et al. Brain perfusion in Alzheimer's disease with and without apathy: a SPECT study with statistical parametric mapping analysis. *Psychiatry Research Neuroimaging* 2002; 114: 103–111.

Bondareff, W., Harrington, C., Wischik, C.M., Hauser, D.L., Kopp, U. Immunohistochemical staging of neurofibrillary degeneration in Alzheimer's disease. *Journal of Neuropathology & Experimental Neurology* 1994; 53: 158–164.

Bondareff, W. Neuropathology of psychotic symptoms in Alzheimer's disease. *International Psychogeriatrics* 1996; 8 (Suppl 3): 233–237.

Borroni, B., Grassi, M., Premi, E., et al. Neuroanatomical correlates of behavioural phenotypes in behavioural variant of frontotemporal dementia. *Behavioural Brain Research* 2012; 235(2): 124–129.

Eslinger, P.J., Moore, P., Antani, S., et al. Apathy in frontotemporal dementia: behavioral and neuroimaging correlates. *Behavioral Neurology* 2012; 25(2): 127–136.

Hirono, N., Mega, M.S., Dinov, I.D., et al. Left frontotemporal hypoperfusion is associated with aggression in patients with dementia. *Archives of Neurology* 2000; 57: 861–866.

Hornberger, M., Geng, J., Hodges, J.R. Convergent grey and white matter evidence of orbitofrontal cortex changes related to disinhibition in behavioural variant frontotemporal dementia. *Brain* 2011; 134 (Pt9): 2502–2512.

Ismail, Z., Herrmann, N., Rothenburg, S., et al. A functional neuroimaging study of appetite loss in Alzheimer's disease. *Journal of Neurological Sciences* 2008; 271(1–20): 97–103.

Ismail, Z., Herrmann, N., Francis, P.L., et al. A SPECT study of sleep disturbance and Alzheimer's disease. *Dementia & Geriatric Cognitive Disorders* 2009; 27(3): 254–259.

Jacoby, R., Levy, R. Computed tomography in the elderly-2. Senile dementia. *British Journal of Psychiatry* 1980; 136: 256–269.

Lanctôt, K.L., Herrmann, N., Nadkarni, N.K., et al. Medial temporal hypoperfusion and aggression in Alzheimer disease. *Archives of Neurology* 2004; 61(11): 1731–1737.

Lanctôt, K.L., Moosa, S., Herrmann, N., et al. (A SPECT study of apathy in Alzheimer's disease. *Dementia & Geriatric Cognitive Disorders* 2007; 24(1): 65–72.

Marshall, G.A., Monserratt, L., Harwood, D., et al. Positron Emission Tomography metabolic correlates of apathy in Alzheimer's disease. *Archives of Neurology* 2007; 64: 1015–1020.

Massimo, L., Powers, C., Moore, P., et al. Neuroanatomy of apathy and disinhibition in frontotemporal lobar degeneration. *Dementia & Geriatric Cognitive Disorders* 2009; 27(1): 96–104.

Migneco, O., Benoit, M., Koulibaly, P.M., et al. Perfusion brain SPECT and statistical parametric mapping analysis indicate that apathy is a cingulated syndrome: a study in Alzheimer's disease and non-demented patients. *NeuroImage* 2001; 13: 896–902.

Pan, P.L., Song, W., Yang, J., et al. Gray matter atrophy in behavioral variant frontotemporal dementia: a meta-analysis of voxel-based morphometry studies. *Dementia & Geriatric Cognitive Disorders* 2012; 33(2–3): 141–148.

Perneczky, R., Drzezga, A., Boecker, H., et al. Cerebral metabolic dysfunction in patients with dementia with Lewy bodies and visual hallucinations. *Dementia & Geriatric Cognitive Disorders* 2008; 25: 531–538.

Robert, P.H., Verhey, F.R., Byrne, E.J., et al. Grouping for behavioral and psychological symptoms in dementia: clinical and biological aspects. Consensus paper of the European Alzheimer disease consortium. *European Psychiatry* 2005; 20(7): 490–496.

Zamboni, G., Huey, E.D., Krueger, F., et al. Apathy and disinhibition in frontotemporal dementia: insights into their neural correlates. *Neurology* 2008; 71(10): 736–742.

Circadian Rhythms—relationship to BPSD

Bliwise, D.L. Sleep in normal aging and dementia. *Sleep* 1993; 16: 440–481.

Evans, L.K. Sundown syndrome in institutionalized elderly. *Journal of the American Geriatrics Society* 1987; 35: 101–108.

Cohen-Mansfield, J. Temporal patterns of agitation in dementia. *American Journal of Geriatric Psychiatry* 2007; 15(5): 395–405.

Harper, D.G., Stopa, E.G., McKee, A.C., et al. Differential circadian rhythm disturbances in men with Alzheimer disease and frontotemporal degeneration. *Archives of General Psychiatry* 2001; 58: 353–360.

Prinz, P.N., Vitiello, M.V. Sleep in Alzheimer's disease. In: *Sleep disorders and insomnia in the elderly: Facts and research in gerontology.* Alberrede, J.L., Marley, J.E., Roth, T., Vellas, B.J. (eds). Paris: Serdi 1993.

Winograd, C.H., Jarvik, L.F. Physician management of the demented patient. *Journal of the American Geriatrics Society* 1986; 34: 295–308.

Other clinical contributors to BPSD

Chiu, M.J., Chen, T.F., Yip, P.K., et al. Behavioral and psychologic symptoms in different types of dementia. *Journal of the Formosan Medical Association* 2006; 105(70): 556–562.

Cohen-Mansfield, J., Libin, A. Verbal and physical non-aggressive agitated behaviors in elderly persons with dementia: robustness of syndromes. *Journal of Psychiatric Research* 2005; 39(3): 325–332.

de Vugt, M.E., Riedijk, S.R., Aalten, P., et al. Impact of behavioral problems on spousal caregivers: a comparison between Alzheimer's disease and frontotemporal dementia. *Dementia & Geriatric Cognitive Disorders* 2006; 22(1): 35–41.

Draper, B., Snowdon, J., Meares, S., et al. Case-controlled study of nursing home residents referred for treatment of vocally disruptive behavior. *International Psychogeriatrics* 2000; 12: 333–344.

Engelborghs, S., Maertens, K., Nagels, G., et al. Neuropsychiatric symptoms of dementia: cross-sectional analysis from a prospective, longitudinal Belgian study. *International Journal of Geriatric Psychiatry* 2005; 20(11): 1028–1037.

Engelborghs, S., Maertens, K., Marien, P., et al. Behavioral and psychological correlates of frontal lobe features in dementia. *Psychological Medicine* 2006; 36(8): 1173–1182.

Hinton, L., Tomaszewski, F.S., Wegelin, J. Neuropsychiatric symptoms are associated with disability in cognitively impaired Latino elderly with and without dementia: results from the Sacramento Area Latino study on Aging. *International Journal of Geriatric Psychiatry* 2008; 23(1): 102–108.

Hodgson, N.A., Gitlin, L.N., Winter, L., Czekanski, K. Undiagnosed illness and neuropsychiatric behaviors in community residing older adults with dementia. *Alzheimer's Disease and Associated Disorders* 2011; 25: 109–115.

Holtta, E., Laakkonen, M.L., Laurila, J.V. et al. The overlap of delirium with neuropsychiatric symptoms among patients with dementia. *American Journal of Geriatric Psychiatry* 2011; 19(12): 1034–1041.

Kitamura, T., Kitamura, M., Hino, S., et al. Gender differences in clinical manifestations and outcomes among hospitalized patients with behavioural and psychological symptoms of dementia. *Journal of Clinical Psychiatry* 2012; 73(12): 1548–1554.

Lovheim, H., Sandman, P.O., Karlsson, S., et al. Sex differences in the prevalence of behavioral and psychological symptoms of dementia. *International Psychogeriatrics* 2009; 21(3): 469–475.

Muryama, N., Iseki, E., Endo, T., et al. Risk factors for delusion of theft in patients with Alzheimer's disease showing mild dementia in Japan. *Aging & Mental Health* 2009; 13(4): 563–568.

Pagonabarraga, J., Llebaria, G., Garcia-Sanchez, C., et al. A prospective study of delusional misidentification syndrome in Parkinson's disease with dementia. *Movement Disorders* 2008; 23(3): 443–448.

Proitsi, P., Hamilton, G., Tsolaki, M., et al. A Multiple Indicators Multiple Causes (MIMIC) model of Behavioral and Psychological Symptoms in Dementia (BPSD). *Neurobiology of Aging* 2009; doi:10.1016/j.neurobiolaging.2009.03.005

Senanarong, V., Cummings, J.L., Fairbanks, L., et al. Agitation in Alzheimer's disease is a manifestation of frontal lobe dysfunction. *Dementia & Geriatric Cognitive Disorders* 2004; 17(1–2): 14–20.

Srikanth, S., Nagaraja, A.V., Ratnavalli, E. Neuropsychiatric symptoms in dementia—frequency, relationship to dementia severity and comparison in Alzheimer's disease, vascular dementia and frontotemporal dementia. *Journal of the Neurological Sciences* 2005; 236(1–2): 43–48.

Starr, J.M., Lonie, J. Relationship between behavioral and psychological symptoms of dementia and cognition in Alzheimer's disease. *Dementia & Geriatric Cognitive Disorders* 2007; 24(5): 343–347.

Steinberg, M., Corcoran, C., Tschanz, J.T., et al. Risk factors for neuropsychiatric symptoms in dementia: the Cache County study. *International Journal of Geriatric Psychiatry* 2006; 21: 824–830.

Talerico, K.A., Evans, L.K., Strumpf, N.E. Mental health correlates of aggression in nursing home residents with dementia. *The Gerontologist* 2002; 42: 169–177.

Tsoi, T., Baillon, S., Lindesay, J. Early frontal executive impairment as a predictor of subsequent behavior disturbance in dementia. *American Journal of Geriatric Psychiatry* 2008; 16(2): 102–108.

Whall, A.L., Colling, K.B., Kolanowski, A., et al. Factors associated with aggressive behavior among nursing home residents with dementia. *Gerontologist* 2008; 48(6): 721–731.

Yatabe, Y., Hashimoto, M., Kaneda, K., et al., Neuropsychiatric symptoms of progressive supranuclear palsy in a dementia clinic. *Psychogeriatrics* 2011; 11(1): 54–59.

Personality/psychological contributors to BPSD

Archer, N., Brown, R.G., Reeves, S.J., et al. Premorbid personality and behavioral and psychological symptoms in probable Alzheimer disease. *American Journal of Geriatric Psychiatry* 2007; 15: 202–213.

Cornali, C., Franzoni, S., Riello, R., et al. Effect of high climate temperature on the behavioral and psychological symptoms of dementia. *Journal of the American Medical Directors Association* 2004; 5(3): 161–166.

Low, L.F., Brodaty, H., Draper, B. The relation of premorbid personality to behavioral and psychological symptoms of dementia in nursing home residents. *International Journal of Geriatric Psychiatry* 2002; 17: 779–783.

Meins, W. Impact of personality on behavioral and psychological symptoms of dementia. *International Psychogeriatrics* 2000; 12 (Suppl): 107–111.

Pelletier, I.C., Landreville, P. Discomfort and agitation in older adults with dementia. BMC *Geriatrics* 2007; 7: 27.

Song, J.A., Algase, D. Premorbid characteristics and wandering behavior in persons with dementia. *Archives of Psychiatric nursing* 2008; 22(6): 318–327.

Environmental, physical, and social contributors to BPSD

Anthony, K., Proctor, A.W., Silverman, A.M., Murphy, E. Mood and behavior problems following the relocation of elderly patients with mental illness. *Age and Ageing* 1987; 16: 355–365.

Ballard, C., Lowery, K., Powell, I., O'Brien, J., James, I. Impact of behavioral and psychological symptoms of dementia on caregivers. *International Psychogeriatrics* 2000; 12 (Suppl): 93–107.

de Vugt, M.E., Stevens, F., Aalten, P., et al. Do caregiver management strategies influence patient behavior in dementia? *International Journal of Geriatric Psychiatry* 2004; 19: 85–92.

Eriksson, S. Impact of environment on behavioral and psychological symptoms of dementia. *International Psychogeriatrics* 2000; 12 (Suppl): 89–93.

Fleming, R., Crookes, P., Sum, S. A review of the empirical literature on the design of physical environments for people with dementia. http://www.dementia.unsw.edu.au/DCRCweb.nsf/page/TechDesign 2009; accessed January 4, 2010.

Hamel, M., Gold, D.P., Andres, D., et al. Predictors and consequences of aggressive behavior by community-based dementia patients. *Gerontologist* 1990; 30: 206–211.

Haupt, M., Karger, A., Jonner, M. Improvement of agitation and anxiety in demented patients after psychoeducative group intervention with their caregivers. *International Journal of Geriatric Psychiatry* 2000; 15: 1125–1129.

Lawlor, B.A. Environmental and social aspects of behavioral disturbances in dementia. *International Psychogeriatrics* 1996; 8 (Suppl 3): 259–261.

Marx, M.S., Werner, P. Agitation and touch in the nursing home. *Psychological Reports* 1989; 64: 1019–1026.

Perren, S., Schmid, R., Herrmann S., et al. The impact of attachment on dementia-related problem behavior and spousal caregivers' well-being. *Attachment & Human Development* 2007; 9(2): 163–178.

Riello, R., Geroldi, C., Zanetti, O., et al. Caregiver's distress is associated with delusions in Alzheimer's disease. *Journal of Behavioral Medicine* 2002; 28(Fall): 92–98.

INTERNATIONAL PSYCHOGERIATRIC ASSOCIATION

www.ipa-online.org

MODULE 4

Role of family caregivers

The IPA Complete Guides to Behavioral and Psychological Symptoms of Dementia

BPSD

Specialists Guide

Specialists • Primary Care Physicians • Nurses

MODULE 4: Role of family caregivers

Contents

Key messages	**4.2**
Introduction	**4.2**
What is caregiver burden?	**4.3**
Measuring caregiver burden	**4.3**
Factors associated with caregiver burden	**4.4**
Cultural, racial and ethnic factors	4.6
The impact of BPSD on family caregivers	**4.8**
Psychological health	4.8
Physical health	4.8
The impact of family caregivers on BPSD	**4.9**
Caregiver interventions for BPSD	**4.10**
Other interventions	**4.11**
Barriers to caregivers seeking assistance	**4.12**
Elements of success	**4.12**
Recommendations for caregivers	**4.13**
Conclusion	**4.14**
References and recommended reading	**4.14**

Key messages

- Support by caring relatives is a key factor in community care of people with dementia.
- The emotional relationship between the caregiver and the person with dementia significantly determines whether family care can be maintained.
- An effective care system enables caregivers to continue caring for their family members with dementia at home and, at the same time, minimizes the negative consequences to them.
- The demands of caregiving may not precipitate an illness event per se in the caregiver, but rather, may aggravate existing vulnerabilities to illness.
- Enhancing the skill of the caregiver to interact with the person with dementia may prolong the caregiver's ability to provide in-home care and improve the quality of life of both.
- Behavioral and psychological symptoms of dementia (BPSD) are a potent cause of caregiver distress. Less well appreciated is that caregiver distress and poor interpersonal relations between the person with dementia and the caregiver can exacerbate BPSD.
- Caregivers can provide useful information about antecedents of, and possible reasons for, behavioral problems. This information usually requires more than a single, brief interview.
- Caregivers who have had a poor premorbid relationship with the person with dementia are more likely to misinterpret agitated behavior as purposefully provocative and worsen the situation with an angry retort.
- Caregiver interventions have proved to be effective in increasing caregiver knowledge and reducing caregiver distress and BPSD.

Introduction

Support by caring relatives is the key to continuing community care of people with dementia. Community care recognizes the right of people with dementia to live as independently as possible in familiar surroundings, such as at home. Family care may not be possible or sustainable for a number of reasons. Many factors affect the well being of caregivers, for example, the emotional relationship between the responsible relative and the person with dementia significantly determines whether family care can be maintained. Troublesome BPSD, and the burden that they create for the family caregiver, are key factors in precipitating a move from family care to nursing home or other residential care (Merritt, 2011; Moore et al., 2013; Nobili et al., 2004; Yaffe et al., 2002).

Strategies have been demonstrated clinically and empirically to reduce the burden that caregivers experience in looking after a person with dementia. This module reviews the impact of BPSD on the psychological and physical health of family caregivers (i.e., their contribution to caregiver burden) as well as interventions to reduce that burden related to BPSD.

What is caregiver burden?

Schulz and Martire (2004) describe caregiving as:

"...the provision of extraordinary care, exceeding the bounds of what is normative or usual in family relationships. Caregiving typically involves a significant expenditure of time, energy, and money over potentially long periods of time; it involves tasks that may be unpleasant and uncomfortable and are psychologically stressful and physically exhausting."

Three different types of burden have been associated with a caregiving role (Montgomery et al., 1985; Savundranayagam et al., 2011; Savundranayagam and Montgomery, 2010):

- **Objective burden** refers to the perceived disruption to tangible aspects of a caregiver's life such as personal privacy and time for recreational activities.
- **Subjective demand burden** refers to the extent that the caregiver perceives their care responsibilities to be overly demanding. This includes reports of unreasonable requests and demands made by the care recipient.
- **Subjective stress burden** is the emotional impact of their role on the caregiver such as relationship stress, tension, anxiety, and depression.

Emotional, physical, and social burden as well as depression and psychological comorbidity have also been reported in caregivers of those with mild cognitive impairment (MCI; Bruce et al., 2008; Kim and Choi, 2012; Okura and Langa, 2011; Seeher, Brodaty et al., 2012; Seeher, Low et al., 2012) with greater burden being associated with neuropsychiatric symptoms (Ryan et al., 2012; Van Der Mussele et al., 2011; Werner, 2012).

Measuring caregiver burden

Although a recognized gold standard for measuring caregiver burden is lacking (Levy et al., 2012), the most widely referenced scale is the Zarit Caregiver Burden Interview (ZBI; Bachner and O'Rourke, 2007; Prince et al., 2012; Van Durme et al., 2012; Zarit et al., 1980). The instrument encompasses 22 items relevant to the wide range of interacting issues that can impact on caregiver burden and provides a global rating of burden. Higher scores indicate greater distress. Several short (Bedard et al., 2001; Gort et al., 2010; O'Rourke and Tuokko, 2003a, 2003b) and non-English language versions of the ZBI have been developed (Arai et al., 2003; Braun et al., 2010; Hirono et al., 1998; Van Durme et al., 2012).

Other measures of caregiver burden include:

- Caregiver Burden Inventory (Novak and Guest, 1989)
- Caregiver Perceived Burden Questionnaire (Erder et al., 2012)
- Caregiver Strain Index (Robinson, 1983; Sullivan, 2002; Thornton and Travis, 2003)
- Montgomery Borgatta Caregiver Burden Scale (Montgomery et al., 1985)
- Neuropsychiatric Inventory Caregiver Distress scale (Cummings, 1997; Cummings et al., 1994; Fuh et al., 2006; Kaufer et al., 1998)
- Neuropsychiatric Inventory—Nursing Home Distress Scale (Boada et al., 2005; Wood et al., 1999; Wood et al., 2000)
- Neuropsychiatric Inventory Questionnaire Caregiver Distress Scale (Kaufer et al., 2000)
- Relatives' Stress Scale (Greene et al., 1982; Ulstein, Wyller et al., 2007)

- Revised Memory and Behavior Problems Checklist—Caregiver Reaction Ratings (Teri et al., 1992)
- Screen for Caregiver Burden (Vitaliano et al., 1991)

See Van Durme et al., (2012) for a comprehensive review of instruments that assess the impact of caregiver burden, including those relevant to dementia. Note that subjective burden is sometimes conceptualized as strain (Montgomery et al., 1985; Morycz, 1985; Van Durme et al., 2012).

> A detailed assessment of the caregiver is a necessary step in reducing caregiver burden because a symptom or behavior that is stressful for one caregiver may not be stressful for another.

Factors associated with caregiver burden

BPSD, rather than cognitive dysfunction per se or physical dependence/functional impairment, impose the greatest burden on caregivers (Gitlin, 2012a; Levy et al., 2012; Machnicki et al., 2009; Pinquart and Sörensen, 2003; Savundranayagam et al., 2011; Savundranayagam and Montgomery, 2010).

BPSD include:

- Aggression
- Agitation
- Anxiety
- Apathy
- Depression
- Disinhibited behaviors
- Nocturnal disruption
- Psychotic symptoms
- Vocally disruptive behaviors
- Wandering

The above symptoms are recognized as the most burdensome and the most common reasons for psychiatric referral and premature institutionalization (Desai et al., 2012). However, the degree of burden associated with individual BPSD varies (Allegri et al., 2006; Barth et al., 2011; Bowen et al., 2012; Garavello et al., 2010; Lee and Thomas, 2011; Matsumoto et al., 2007; Okura and Langa, 2011; Ornstein and Gaugler, 2012; Ornstein, 2012; Rocca et al., 2010; Zweig et al., 2012).

While BPSD themselves are clearly the major contributor to caregiver burden, the reaction of the caregiver to BPSD is also important. Caregivers differ in their responses to BPSD and vary in their skills to manage them—not all caregivers find the same symptoms to be troublesome. Caregiver characteristics that are either predictive of, or alleviate, burden are shown in the boxes below and Figure 1 (Bakker et al., 2010; Brodaty and Green, 2002; Brodaty and Hadzi-Pavlovic, 1990; Chemali et al., 2012; Cohen, 2004; Contador et al., 2012; Cooper et al., 2007; Cooper et al., 2006; Cooper et al., 2008; Etters et al., 2008; Fearon et al., 1998; Gallagher et al., 2011; Garcia-Alberca et al., 2012a; 2012b; Gilleen et al., 2012; Gronning et al., 2012; Kunik et al., 2010; Livingston et al., 2005; Melo et al., 2011; Papastavrou et al., 2011; Pekkarinen et al., 2004; Prince et al., 2012; Romero-Moreno et al., 2011; Savundranayagam et al., 2005; Savundranayagam and Montgomery, 2010; Silvestre and Guarda, 2011; Vitaliano et al., 1991; Zarit et al., 2010; Zawadzki et al., 2011; Zucchella et al., 2012).

Table 4.1: Predictors of burden

Predictors of burden: Characteristics of the person with dementia

Very important in predicting caregiver burden

- Delusions, hallucinations and depression
- Disruptive behaviors (e.g., physical aggression, calling out, disinhibition)

Somewhat important in predicting caregiver burden

- Male gender (though not independently of BPSD, which occur in a higher proportion of men than women)
- Younger age of person with dementia
- Communication problems

Doubtful or not important in predicting caregiver burden (*when above variables are controlled for*)

- Type of dementia, particularly those with greater frontal involvement
- Severity of dementia (i.e., level of cognitive impairment, need for supervision and assistance)
- Cognitive status
- Functional status (i.e., ability to work and live independently, manage simple chores and care for self)
- Duration of dementia

Predictors of burden: Caregiver characteristics

- Care providers experience greater burden than care managers
- Spouses > relatives
- Women > men
- Older > younger
- Propinquity (caregivers in closest contact; cohabiting caregivers are under most stress)
- Immature coping mechanisms
- Less support from family and friends
- Less knowledge of dementia, its effects and management
- Poor premorbid relationship with person with dementia
- High levels of negative attitude and negative expressed emotions, notably hostility and criticism
- Personality influences
- Spouse versus caregiver role discrepancies

Protective factors: Caregiver characteristics

- Informal supports (e.g., caring family, friends, neighbors)
- Knowledge about dementia, its effects, and management
- Mature coping skills (e.g., problem solving)
- Support groups (e.g., Alzheimer's Association)
- Care providers belief in their personal abilities and internal locus of control

Cultural, racial and/or ethnic factors

Cultural, racial and/or ethnic differences can mediate factors associated with caregiver burden (Zekry et al., 2012) and contribute to BPSD (see Module 7). The following are relevant to specific countries and/or cultural groups:

Table 4.2: Cultural, racial and/or ethnic differences

Authors	Country/cultural group	Subject area
Abdollahpour et al., (2011)	Iran	Characteristics of person with dementia and caregiver burden
Akpinar et al. (2011)	Turkey	Gender effects on caregiving
Bergvall et al. (2011)	Sweden, UK, USA	Predictors of perceived caregiver burden
Cheah et al. (2012)	Multiethnic Asian in Singapore	Caregiver characteristics
Cipriani et al. (2011)	Japan	Aggressive behavior and caregiver stress
Chiu et al. (2012)	Taiwan	Caregiver's perspectives of care problems
Chun et al. (2007)	Korea	Differences in caregiver stress and coping
Conde-Sala et al. (2010)	Spain	Burden in caregiver spouses and adult children
Dhikav and Singh Anand (2012)	India	BPSD and caregiver burden
Duhig et al. (2012)	France, Germany, Italy, Spain, UK, USA	Cross-national comparison of caregiver burden
Etters et al. (2008)	USA	Caregiver burden
Frank-Garcia et al. (2012)	Spain	Disease progression and caregiver burden
Haley et al. (2004)	African-American and Caucasian, USA	Caregiver well-being, appraisal, and coping
Harris et al. (2011)	Latino/Hispanic, African-American and Caucasian in USA	Emotional impact of caregiving
Huang et al. (2012)	Taiwan	Caregiver burden associated with BPSD
Kim et al. (2012)	Korea	Risk factors for abusive behaviors
Kochhann et al. (2011)	Developing countries (Brazil)	BPSD and caregiver burden
Kurasawa et al. (2012)	Japan	BPSD, caregiver burden and institutionalization
Lim et al. (2012)	Singapore	Service utilization in dementia caregivers
Lin et al. (2012)	Chinese in Taiwan	BPSD and burden in family and foreign paid caregivers

Authors	Country/cultural group	Subject area
Liu (2010)	China	Impact of family caregiving
Moreno et al. (2010)	Colombia	Predictors of caregiver burden and satisfaction
Mori and Ueno (2011)	Japan	BPSD and caregiver burden
Oh (2012)	Korea	BPSD and family burden
Prince et al. (2012); Prince et al. (2004)	India, Taiwan, Hong Kong, China, Nigeria, Latin America, Caribbean	Dementia care and caregiver burden
Saldanha et al. (2010)	India	Correlates of caregiver burden
Shin et al. (2012)	Korea	Predictors of caregiver burden in Parkinson's disease dementia and Alzheimer's disease
Sumit et al. (2012)	India	Caregiver burden and dementia severity
Tan et al. (2005)	Chinese in Singapore	BPSD and caregiver distress
Uett and Linnamagi (2011)	Estonia	BPSD and caregiver burden
Yan and Kwok (2011)	Chinese in Hong Kong	Risk factors for abusive caregiver behaviors
Zhao et al. (2012)	Chinese	Apathy and caregiver burden

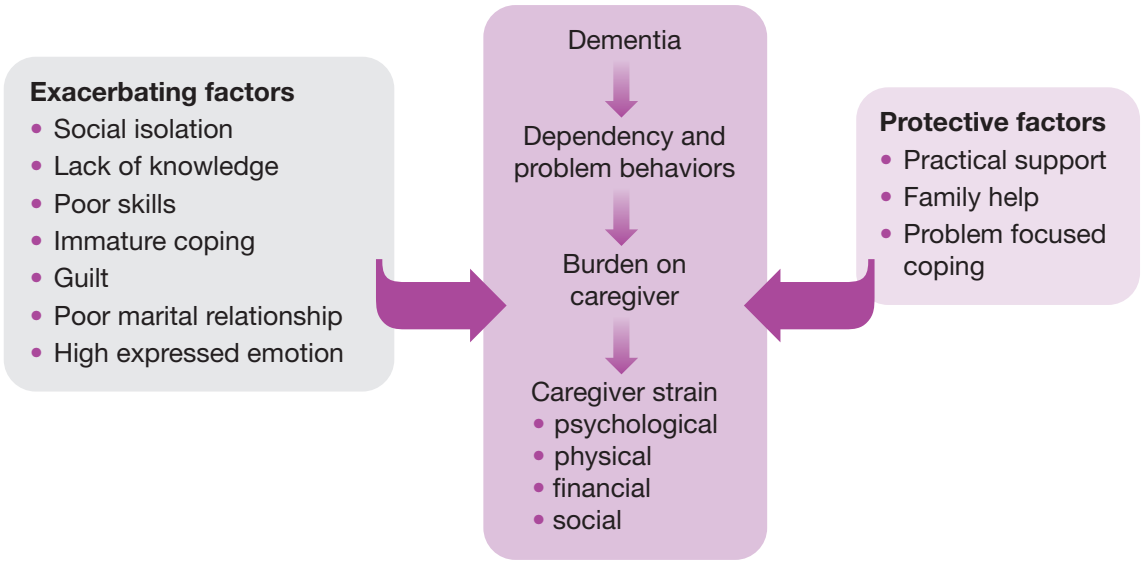


Figure 4.1: Model of effects of dementia on caregivers. Reprinted with permission from Brodaty (1997) and based on Poulshock and Deimling (1984).

The impact of BPSD on family caregivers

Psychological health

BPSD are the most consistent and important predictors of psychological distress in family caregivers, accounting for approximately 25% of the variance in psychological morbidity (Ballard et al., 2000; Black and Almeida, 2004; Brodaty, 1997). This relationship has been shown in studies from England, Scotland, Wales, Australia, Germany, Sweden, South America and the United States. It also has been shown for caregivers of people with Alzheimer's disease, vascular dementia, Huntington's chorea, Parkinson's disease, and stroke. The relationship holds whether psychological morbidity or stress is used to measure the effects on caregivers.

Caregivers are at high risk for developing psychological distress (Garcia-Alberca et al., 2012a; 2012b; George and Gwyther, 1986; Whitlatch et al., 1991) and rates of depression and anxiety are increased compared with the general population. The prevalence of depression in adult caregivers of those with dementia has ranged from 23–85% in developed countries (Adkins, 1999; Clare et al., 2002; Cuijpers, 2005) and rates of anxiety between 16–45% (Cooper et al., 2006; 2007; Schulz et al., 1995). Suicidal thoughts in caregivers have been associated with poorer mental health, lower community service use and dysfunctional coping strategies (O'Dwyer et al., 2013). In developing countries, rates of psychiatric morbidity range from 40–75% (The 10/66 Dementia Research Group, 2004). Furthermore, 7–31% of dementia caregivers take psychotropic drugs, which are slightly, but significantly, higher rates than expected in the general population (Camargos et al., 2012; Clipp and George, 1990; Schulz et al., 1995; Sleath et al., 2005).

Anger and resentment are emotions commonly felt by caregivers, sometimes bringing the caregiver to the point of violence (Cooper et al., 2008; Croog et al., 2006). Characteristics associated with caregivers being physically and psychologically abusive are more time spent caring, more aggressive behavior from care recipients, higher caregiver burden, poorer spousal relationship, and greater caregiver cognitive impairment, anxiety, depression and/or physical symptoms (Beach et al., 2005; Cooper et al., 2010). Specific BPSD such as aggression, nocturnal disruption and emotional lability are commonly identified determinants of caregivers' abusive behavior (Cooney et al., 2006; Cooper et al., 2010; Croog et al., 2006; Hansberry et al., 2005; Kim et al., 2012; Yan and Kwok, 2011).

Levels of interpersonal and family stress are high in families caring for a person with dementia. Among variables most strongly associated with caregivers' perceptions of interpersonal and family stress are behavioral and emotional changes experienced by the person with dementia, changes in the person with dementia's sleep pattern (Schulz et al., 1995) and demanding behaviors (Arango-Lasprilla et al., 2009; Brodaty and Hadzi-Pavlovic, 1990; Kramer et al., 1993; Peisah, 2006). Aneshensel and colleagues (1995) examined caregivers' responses as BPSD increase or decrease over time. BPSD were associated with greater caregiver depression when they resulted in an increase in subjective burden and a feeling of being trapped in the caregiving role.

Physical health

Caregiving can impact on physical health (Hooker et al., 2002; Vitaliano, 2003) through compromised immune function (Schulz and Martire, 2004; Segerstrom et al., 2008; Vedhara et al., 1999) and greater prevalence of heart disease among men caring for a spouse with

Alzheimer's disease (Vitaliano et al., 2002). Evidence also links caregiving to detrimental health-related behaviors when caregivers are less likely to engage in preventative health behaviors such as exercise, and more likely to smoke, drink alcohol and/or experience poor sleep patterns (Schulz and Williamson, 1997).

An important area of research evaluating health outcomes in caregivers focuses on changes in subclinical disease as indicators of health effects (Vitaliano et al., 2003):

- Hypertension
- Changes in stress hormones and neurotransmitters
- Antibody levels
- Insulin glucose levels
- progression of cardiovascular disease

> Although demands of caregiving may not precipitate an illness event per se, they may aggravate existing vulnerabilities.

It is likely that the prolonged stress and distress, inherent in caring for a spouse with dementia, may combine with genetic vulnerabilities and current disease status leading to more serious pathophysiology, particularly when both the disease condition and the stressor have been present for several years. Caring for a person with dementia can reduce the caregiver's life expectancy. Compared to non-caregivers, caregivers who report strain and burden associated with caregiving have had an increased rate of mortality (Schulz and Beach, 1999).

The impact of family caregivers on BPSD

While the negative effects of BPSD on the caregiver are well documented, there is little appreciation of the caregiver's ability to influence the occurrence and severity of BPSD. Documented significant correlations between caregiver distress and BPSD levels in people with dementia typically do not include the direction of causality (Cerveira et al., 2011; Dunkin and Anderson-Hanley, 1998; Fischer et al., 2012; Guerrero, 2012; Holst and Edberg, 2011; Kunik et al., 2010; Leggett et al., 2011; Mohamed et al., 2010; Ng et al., 2012; Okura and Langa, 2011; Tschanz et al., 2012; Van Der Linde et al., 2012). It is generally assumed that BPSD cause caregiver distress but the reverse may also be true (Kunik et al., 2010) (see Module 3).

The caregiver's approach to the person with BPSD can have a direct and significant impact on the person with dementia (see Table 4.3 below). For example, caregivers may believe that the BPSD are under the person with dementia's control and so represent antagonistic feelings toward the caregiver. Caregivers may experience the person with dementia's forgetfulness as irresponsibility, irascibility as a lack of appreciation, and repetitive questioning as a deliberate attempt to annoy. Caregivers may then express criticism or hostility toward the person with dementia, which can increase distress and exacerbate the behavior. Caregiver fatigue can likewise contribute to BPSD (Khachiyants et al., 2011) and higher caregiver burden. Caregiver depression has also been associated with reduced quality of life in the person with dementia (Black et al., 2012; Mohamed et al., 2010; Mougias et al., 2011).

Table 4.3: Caregiver behaviors that can exacerbate BPSD

- Creating sudden and unexpected changes in a person with dementia's routine or environment
- Instigating "power struggles" with the person with dementia: for example, insisting that the person with dementia do something a certain way or wear a particular article of clothing
- Placing demands on the person with dementia that exceed his or her capabilities
- Being excessively critical of the person with dementia
- Ignoring the person with dementia's needs
- Being excessively rigid or controlling
- Repeatedly prompting or questioning in an attempt to induce the person with dementia remember something
- Expressing anger or aggression toward the person with dementia
- Becoming exasperated
- "Talking down" to the person with dementia as if to a child

› Adverse caregiver behaviors have the potential to incite a catastrophic reaction when the person with dementia exhibiting the behavior is unable to deal with the additional stress.

Caregiver interventions for BPSD

A range of caregiver interventions can relieve caregiver burden, decrease caregiver psychological morbidity and delay institutionalization (Brodaty et al., 2003; Pinquart and Sörensen, 2006). An additional benefit is that these caregiver interventions, though not specifically focusing on BPSD, can decrease caregivers' appraisal and negative reactions to BPSD which may contribute to reducing BPSD in care recipients (Ayalon et al., 2006; Farran et al., 2007; Gallagher-Thompson et al., 2007; Glueckauf et al., 2003; Hebert et al., 2003; Hepburn et al., 2005; Mahoney et al., 2003; Marriott et al., 2000; Mittelman et al., 2006; Teri et al., 2002). Caregiver skills training or education interventions can include systematic, structured and individualized approaches (Gitlin et al., 2010b; Teri et al., 2005), as well as caregiver programs which target coping strategies, knowledge of dementia and/or BPSD management (Bourgeois et al., 2002; Brodaty and Gresham, 1989; Gavrilova et al., 2009; Guerra et al., 2011; Liddle et al., 2012; Monti et al., 2012; Teri et al., 2003; Teri et al., 1997; Ulstein, Sandvik et al., 2007). Caregiver training has also been compared with drug treatments (Teri et al., 2000).

Multicomponent interventions have also been shown to be of benefit. These include programs which may provide a combination of information, role playing, problem solving, BPSD skills training, stress management, telephone support, multidisciplinary collaboration, care management, cognitive rehabilitation, counseling, motor stimulation and/or light therapy (Belle et al., 2006; Brodaty et al., 2003; Burgio et al., 2009; Burns et al., 2003; Callahan et al., 2006; Dias et al, 2008; Gitlin et al., 2008; 2003; 2010a; Johnson et al., 2013; McCurry et al., 2005; Mittelman et al., 2004; Moniz-Cook et al., 2008; Nobili et al., 2004; Senanarong et al., 2004).

Enhancing the skills of the caregiver to interact with the person with dementia and better manage BPSD may prolong the caregiver's ability to provide in-home care and enhance the quality of life of both parties. In a meta-analysis of 23 studies meeting criteria for level II or III-1 evidence (NHMRC, 2000, 2009) Brodaty and Arasaratnam (2012) found that nonpharmacological interventions delivered by family caregivers have the potential to reduce the frequency and severity of BPSD, with effect sizes at least equaling those of pharmacotherapy, as well as to reduce caregivers' adverse reactions. Successful interventions typically provided nine to 12 individual sessions in the home of the person with dementia and the caregiver, tailored to their specific needs using multiple components over 3–6 months with periodic follow-up.

Individualized, multidimensional, flexible caregiver interventions that involve follow-up and an ongoing relationship between helper and caregiver demonstrate positive outcomes for caregivers as well as BPSD in care recipients (Lavoie et al., 2005) and can delay nursing home placement (Brodaty et al., 2003). Caregiver education or support in isolation appear to be less beneficial (Brodaty, 1994; Brodaty et al., 1994; Charlesworth et al., 2008; Devor et al., 2008; Gormley et al., 2001; Kurz et al., 2009; Marriott et al., 2000).

Those with dementia in the developing world rely primarily on families for support as health services are often ill-equipped to meet their needs (Dias et al., 2008; Prince et al., 2004; Shahly et al., 2013). Family caregivers with limited resources face additional challenges in developing countries as awareness and understanding of dementia are lacking; symptoms may be perceived to be part of normal aging, or denied because of the stigma attached to the illness (Dias et al., 2008; Patel and Prince, 2001; Senanarong et al., 2004). Caregiver interventions may be of benefit in developing countries where availability of formal supports is limited (Dias et al., 2008; Gavrilova et al., 2009; Guerra et al., 2011; Prince et al., 2012; Senanarong et al., 2004). Their impact may be greater in these settings than in high income countries (Brodaty et al., 2003; Gavrilova et al., 2009; Wortmann, 2011).

› Reducing BPSD can improve caregiver well-being and conversely the relief of caregiver burden can considerably decrease BPSD.

Other interventions

Research to assess the feasibility and/or acceptability of utilizing assistive technology in the management of BPSD is limited (Daniel et al., 2009; Westphal et al., 2010). Examples include telecare monitoring (Dunk and Doughty, 2006), automated telephone caregiver support (Mahoney et al., 2003), a computer-telephone integrated support system (Eisdorfer et al., 2003) and internet-based caregiver education (Lewis et al., 2010). The Aladdin Project is a pilot study of a technology platform installed in the home that detects BPSD and caregiver burden (Haritou et al., 2011; Haritou et al., 2012; Saez et al., 2011; Saeza et al., 2012). The system integrates monitoring safety and health aspects of the person with dementia with the workload, quality of life and mental health of the caregiver (Cuno et al., 2011; Haritou et al., 2012). Assistive technologies may help to delay institutionalization however, they typically require significant caregiver input and caregivers' lack of awareness of the technology may be a barrier to their use (Daniel et al., 2009; Van Den Heuvel et al., 2012).

Alzheimer Associations are another important form of intervention. Alzheimer's Disease International (ADI) is a global umbrella organization with associations in more than 80 countries of the developed and developing world (http://www.alz.co.uk/). Alzheimer's Associations are non-profit organizations which support those with dementia and their caregivers. Many of the associations provide Help Notes to assist in the management of BPSD, for example:

- http://www.fightdementia.org.au/about-dementia-and-memory-loss/help-sheets
- http://www.alzheimers.org.uk/site/scripts/documents_info.php?categoryID=200306&documentID=1211&pageNumber=7
- http://www.alz.org/alzheimers_disease_publications.asp

Referral of people with dementia and their families to Alzheimer Associations is part of the clinician's therapeutic collection of resources. Respite care and community services also offer support to caregivers. The effects of Alzheimer's Associations or respite care on BPSD or caregivers' reactions have not been adequately assessed.

Pharmacological interventions targeting BPSD have proven advantageous in reducing caregiver burden. A systematic review of eight randomized placebo-controlled double-blind studies of psychotropic medication for BPSD found that drugs targeting behavioral disturbances in the person with dementia reduced caregiver burden as well as time spent in caregiving and supervision (Schoenmakers et al., 2009).

Barriers to caregivers seeking assistance

Access to interventions aimed at reducing BPSD and caregiver burden may be limited by many factors, both logistical and perceived. These can include transportation costs, loss of wages, community privacy issues, stigma associated with dementia, mistrust of "outsiders" (Daunt, 2003; Glueckauf et al., 2005), distance, lack of awareness of available resources (Brodaty et al., 2005; Lim et al., 2012; Moore et al., 2013), reluctance to define themselves as caregivers (Liu 2009), financial strain (Gitlin, 2012b), lack of respite for the person with dementia to enable attendance (Winterton and Warburton, 2011), lack of cultural, social and/or religious concordance (Glueckauf et al., 2012; Napoles et al., 2010) and perceived lack of need (Brodaty et al., 2005; Lim et al., 2012). Creative solutions, flexibility and additional resources may be necessary to help overcome such barriers (Brodaty et al., 2005; Burgio et al., 2009; Glueckauf et al., 2012; 2005; Hepburn et al., 2003; Winterton and Warburton, 2011).

Elements of success

Interventions targeting caregiver burden and BPSD are most successful when they:

- Focus on the person with dementia as well as the caregiver
- Focus on training and skill building in addition to education and support; e.g., role plays, use of video feedback
- Are multidimensional, flexible and tailored to the needs of the caregiver and care recipient
- Are of sufficient duration and intensity and followed up with booster sessions
- When possible, are delivered to individual dyads or families in their own homes

There is also some evidence that the following are important:

- Combining pharmacotherapy where indicated (see Module 6)
- Including provision of information to family caregivers, which is insufficient alone unless combined with:
  - Techniques for dealing with specific BPSD (see Module 5)
  - Techniques for ensuring the person with dementia's physical safety and well-being
  - Techniques for coping with difficult activities of daily living (such as bathing and dressing)
  - Methods for obtaining additional personal assistance, entitlements and respite services (e.g., day care, home care)
- Collaborative care with a professional care manager; e.g., nurse working with caregiver
- Focusing on the medium to long-term

Recommendations for caregivers

Table 4.4: Caregiver characteristics that alleviate the occurrence and impact of BPSD

- An empathic, patient, kind, caring, warm attitude toward the person with dementia
- Efforts to understand the cause(s) of and meaning behind the behavior
- Flexible personality, enabling the caregiver to avoid rigid insistence on compliance
- Adaptability and ability to accept change
- Maintenance of realistic expectations of the person with dementia's abilities
- Reasonable degree of tolerance for "problem" behaviors such as repetitive actions
- Commitment to keep the person with dementia involved in day-to-day activities
- Fostering a sense of individualism and usefulness in the person with dementia
- Allowing the person with dementia to maintain a perception of control over his or her life and environment
- Sense of genuine concern for the person with dementia's well-being and best interests
- Respect for the person with dementia as an individual with valid emotions and feelings
- Absence of a feeling of shame over a loved one's illness
- Lack of desire to hide the disease from others
- Maintenance of a sense of humor
- Absence of thoughts which dwell on the person with dementia's limitations
- Development and maintenance of an emotional support structure

Conclusion

Family caregivers are critical to the well being of the person with dementia. Behavioral and psychological symptoms, which are ubiquitous in dementia and are a major source of distress to caregivers as well to the affected people themselves, can be alleviated. Diagnosis of the cause of behavioral disturbance is always the first step, after which there are many strategies to assist caregivers to handle distressing behaviors. These include behavior management, judicious use of medications and changes to the environment. Most importantly, the caregiver is uniquely placed to understand the context in which the behavior is occurring, its meaning; i.e., for the person behind the behavior, and the world of the person with dementia.

- Caregivers are crucial to the management of BPSD and the management of BPSD is crucial to caregiver

References and recommended reading

Abdollahpour, I., Noroozian, M., Nedjat, S., et al. Assessing the psychiatric symptoms in patients with dementia and their correlation with caregiver burden. *Iranian Journal of Epidemiology* 2011; 7(2): 51–59.

Adkins, V.K. Treatment of depressive disorders of spousal caregivers of persons with Alzheimer's disease: A review. *American Journal of Alzheimer's Disease and Other Dementias* 1999; 14: 289–293.

Akpinar, B., Kucukguclu, O., Yener, G. Effects of Gender on Burden Among Caregivers of Alzheimer's Patients. *Journal of Nursing Scholarship* 2011; 43(3): 248–254.

Allegri, R.F., Sarasola, D., Serrano, C.M., et al. Neuropsychiatric symptoms as a predictor of caregiver burden in Alzheimer's disease. *Neuropsychiatric Disease and Treatment* 2006; 2(1): 105–110.

Aneshensel, C.S., Pearlin, L.I., Mullan, J.T., et al. *Profiles in caregiving: The unexpected career.* San Diego, CA: Academic Press 1995.

Arai, Y., Tamiya, N., Yano, E. The short version of the Japanese version of the Zarit Caregiver Burden Interview (J-ZBI_8): its reliability and validity. *Nippon Ronen Igakkai zasshi; Japanese Journal of Geriatrics* 2003; 40(5): 497–503.

Arango-Lasprilla, J.C., Moreno, A., Rogers, H., et al. The effect of dementia patient's physical, cognitive, and emotional/behavioral problems on caregiver well-being: findings from a Spanish-speaking sample from Colombia, South America. *American Journal of Alzheimer's Disease and Other Dementias* 2009; 24(5): 384–395.

Ayalon, L., Gum, A.M., Feliciano, L., et al. Effectiveness of nonpharmacological interventions for the management of neuropsychiatric symptoms in patients with dementia: a systematic review. *Archives of Internal Medicine* 2006; 166(20): 2182–2188.

Bachner, Y.G., O'Rourke, N. Reliability generalization of responses by care providers to the Zarit Burden Interview. *Aging and Mental Health* 2007; 11(6): 678–685.

Bakker, C., de Vugt, M.E., Vernooij-Dassen, M., et al. Needs in early onset dementia: A qualitative case from the NeedYD study. *American Journal of Alzheimer's Disease and Other Dementias* 2010; 25(8): 634–640.

Ballard, C., Lowery, K., Powell, I., et al. Impact of Behavioral and Psychological Symptoms of Dementia on Caregivers. *International Psychogeriatrics* 2000; 12 (SupplementS1): 93–105.

Barth, A., Riedel, O., Wittchen, H.U. The psychopathological burden of outpatients with Alzheimer's Dementia and their caregivers—The idea-study (improving Alzheimer's Dementia treatment: Epidemiological assessment of patients', caregivers' and doctors' unmet needs and barriers). *Neurodegenerative Diseases* 2011; 8.

Beach, S.R., Schulz, R., Williamson, G.M., et al. Risk factors for potentially harmful informal caregiver behavior. *Journal of the American Geriatrics Society* 2005; 53(2): 255–261.

Bedard, M., Molloy, D.W., Squire, L., et al. The Zarit Burden Interview: a new short version and screening version. *The Gerontologist* 2001; 41(5): 652–657.

Belle, S.H., Burgio, L., Burns, R., et al. Enhancing the quality of life of dementia caregivers from different ethnic or racial groups. *Annals of Internal Medicine* 2006; 145: 727–738.

Bergvall, N., Brinck, P., Eek, D., et al. Relative importance of patient disease indicators on informal care and caregiver burden in Alzheimer's disease. *International Psychogeriatrics* 2011; 23(1): 73–85.

Black, B.S., Johnston, D., Morrison, A., et al. Quality of life of community-residing persons with dementia based on self-rated and caregiver-rated measures. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation* 2012; 21(8): 1379–1389.

Black, W., Almeida, O.P. A systematic review of the association between the Behavioral and Psychological Symptoms of Dementia and burden of care. *International Psychogeriatrics* 2004; 16(03): 295–315.

Boada, M., Tarraga, L., Modinos, G., et al. Neuropsychiatric Inventory-Nursing Home version (NPI-NH): Spanish validation. *Neurologia* 2005; 20(10): 665–673.

Bourgeois, M.S., Schulz, R., Burgio, L.D., et al. Skills training for spouses of patients with Alzheimer's disease: Outcomes of an intervention study. *Journal of Clinical Geropsychology* 2002; 8(1): 53–73.

Bowen, M., Rowe, M., D'Aoust, R., et al. For caregiver sleep: Not all stressors are created equal. *Alzheimer's and Dementia* 2012; (1): P380.

Braun, M., Scholz, U., Hornung, R., et al. The burden of spousal caregiving: a preliminary psychometric evaluation of the German version of the Zarit burden interview. *Aging and Mental Health* 2010; 14(2): 159–167.

Brodaty, H. Dementia and the family. In Bloch, S., Hafner, J., Harari, E., Szmukler, G. I. (Eds.), *The Family in Clinical Psychiatry* (pp. 224–246). Oxford: Oxford University Press 1994.

Brodaty, H. Caregivers and behavioral disturbances: Effects and interventions. *International Psychogeriatrics* 1997; 8(Supplement S3): 455–458.

Brodaty, H., Arasaratnam, C. Meta-analysis of nonpharmacological interventions for neuropsychiatric symptoms of dementia. *American Journal of Psychiatry* 2012; 169(9): 946–953.

Brodaty, H., Donkin, M. Family caregivers of people with dementia. *Dialogues in clinical neuroscience.* 2009; 11(2): 217–228.

Brodaty, H., Green, A. Who cares for the carer? The often forgotten patient. *Australian Family Physician* 2002; 31(9): 833–836.

Brodaty, H., Green, A., Koschera, A. Meta-analysis of psychosocial interventions for caregivers of people with dementia. *Journal of the American Geriatric Society* 2003; 51: 657–664.

Brodaty, H., Gresham, M. Effects of a training programme to reduce stress in carers of patients with dementia. *British Medical Journal* 1989; 299: 1375–1379.

Brodaty, H., Hadzi-Pavlovic, D. Psychosocial effects on carers of living with persons with dementia. *Australian and New Zealand Journal of Psychiatry* 1990; 24: 351–361.

Brodaty, H., Roberts, K., Peters, K. Quasi-experimental evaluation of an educational model for dementia caregivers. *International Journal of Geriatric Psychiatry* 1994; 9: 195–204.

Brodaty, H., Thomson, C., Thompson, C., et al. Why caregivers of people with dementia and memory loss don't use services. *International Journal of Geriatric Psychiatry* 2005; 20(6): 537–546.

Bruce, J.M., McQuiggan, M., Williams, V., et al. Burden among spousal and child caregivers of patients with mild cognitive impairment. *Dementia and Geriatric Cognitive Disorders* 2008; 25(4): 385–390.

Burgio, L.D., Collins, I.B., Schmid, B., et al. Translating the REACH caregiver intervention for use by area agency on aging personnel: the REACH OUT program. *The Gerontologist* 2009; 49(1): 103–116.

Burns, R., Nichols, L.O., Martindale-Adams, J., et al. Primary care interventions for dementia caregivers: 2-year outcomes from the REACH study. *The Gerontologist* 2003; 43(4): 547–555.

Callahan, C.M., Boustani, M.A., Unverzagt, F.W., et al. Effectiveness of collaborative care for older adults with Alzheimer disease in primary care: a randomized controlled trial. *Journal of the American Medical Association* 2006; 295(18): 2148–2157.

Camargos, E.F., Souza, A.B., Nascimento, A.S., et al. Use of psychotropic medications by caregivers of elderly patients with dementia: is this a sign of caregiver burden? *Arquivos de Neuro-Psiquiatria* 2012; 70(3): 169–174.

Cerveira, M.O., Kochhann, R., Godinho, C., et al. Neuropsychiatric symptoms as the main determinant of caregiver burden in alzheimer's disease. *Alzheimer's and Dementia* 2011; (1): S429.

Charlesworth, G., Shepstone, L., Wilson, E., et al. Befriending carers of people with dementia: randomised controlled trial. *British Medical Journal* 2008; 336(7656): 1295–1297.

Cheah, W.K., Han, H.C., Chong, M.S., et al. Multidimensionality of the Zarit Burden Interview across the severity spectrum of cognitive impairment: An Asian perspective. *International Psychogeriatrics* 2012; 24(11): 1846–1854.

Chemali, Z., Schamber, S., Tarbi, E.C., et al. Diagnosing early onset dementia and then what? A frustrating system of aftercare resources. *International Journal of General Medicine* 2012; 5(5): 81–86.

Chiu, Y.N., Chang, L.H., Wang, J. Caregivers' perspectives of care problems: An exploratory study in Taiwan. *Alzheimer's and Dementia* 2012; (1): P383.

Chun, M., Knight, B.G., Youn, G. Differences in stress and coping models of emotional distress among Korean, Korean-American and White-American caregivers. *Aging and Mental Health* 2007; 11(1): 20–29.

Cipriani, G., Vedovello, M., Nuti, A., et al. Aggressive behavior in patients with dementia: Correlates and management. *Geriatrics and Gerontology International* 2011; 11(4): 408–413.

Clare, L., Wilson, B. A., Carter, G., et al. Depression and anxiety in memory clinic attenders and their carers: implications for evaluating the effectiveness of cognitive rehabilitation interventions. *International Journal of Geriatric Psychiatry* 2002; 17: 962–967.

Clipp, E.C., George, L.K. Psychotropic drug use among caregivers of patients with dementia. *Journal of the American Geriatric Society* 1990; 38(3): 227–235.

Cohen, S. Social relationships and health. *American Psychologist*, 2004; 59: 676–684.

Conde-Sala, J. L., Garre-Olmo, J., Turro-Garriga, O., et al. Differential features of burden between spouse and adult-child caregivers of patients with Alzheimer's disease: An exploratory comparative design. *International Journal of Nursing Studies* 2010; 47(10): 1262–1273.

Contador, I., Fernandez-Calvo, B., Palenzuela, D.L., et al. Prediction of burden in family caregivers of patients with dementia: a perspective of optimism based on generalized expectancies of control. *Aging and Mental Health* 2012; 16(6): 675–682.

Cooney, C., Howard, R., Lawlor, B. Abuse of vulnerable people with dementia by their carers: can we identify those most at risk? *International Journal of Geriatric Psychiatry* 2006; 21(6): 564–571.

Cooper, C., Balamurali, T.B., Selwood, A., et al. A systematic review of intervention studies about anxiety in caregivers of people with dementia. *International Journal of Geriatric Psychiatry* 2007; 22(3): 181–188.

Cooper, C., Katona, C., Orrell, M., et al. Coping strategies and anxiety in caregivers of people with Alzheimer's disease: the LASER-AD study. *Journal of Affective Disorders* 2006; 90(1): 15–20.

Cooper, C., Owens, C., Katona, C., et al. Attachment style and anxiety in carers of people with Alzheimer's disease: results from the LASER-AD study. *International Psychogeriatrics* 2008; 20(3): 494–507.

Cooper, C., Selwood, A., Blanchard, M., et al. The determinants of family carers' abusive behaviour to people with dementia: Results of the CARD study. *Journal of Affective Disorders* 2010; 121(1–2): 136–142.

Cooper, C., Balamurali, T.B., Livingston, G. A systematic review of the prevalence and covariates of anxiety in caregivers of people with dementia. *International Psychogeriatrics* 2007; 19(2): 175–195.

Cooper, C., Manela, M., Katona, C., et al. Screening for elder abuse in dementia in the LASER-AD study: prevalence, correlates and validation of instruments. *International Journal of Geriatric Psychiatry* 2008; 23(3): 283–288.

Croog, S.H., Burleson, J.A., Sudilovsky, A., et al. Spouse caregivers of Alzheimer patients: problem responses to caregiver burden. *Aging and Mental Health* 2006; 10(2): 87–100.

Cuijpers, P. Depressive disorders in caregivers of dementia patients: A systematic review. *Aging and Mental Health* 2005; 9(4): 325–330.

Cummings, J.L. The Neuropsychiatric Inventory: assessing psychopathology in dementia patients. *Neurology* 1997; 48(5 Suppl 6): S10–S16.

Cummings, J.L., Mega, M., Gray, K., et al. The Neuropsychiatric inventory: Comprehensive assessment of psychopathology in dementia. *Neurology* 1994; 44(12): 2308–2314.

Cuno, S., Glickman, Y., Baboshin, A., et al. *Management, monitoring and supporting dementia patients at home by ALADDIN* Paper presented at the eChallenges e-2011 Conference, Florence, Italy 2011.

Daniel, K.M., Cason, C.L. Ferrell, S. Emerging technologies to enhance the safety of older people in their homes. *Geriatric Nursing* 2009; 30(6): 384–389.

Daunt, D.J. Ethnicity and recruitment rates in clinical research studies. *Applied Nursing Research* 2003; 16(3): 189–195.

de Paula Eduardo Garavello, A., Magaldi, R.M., Paschoal, S.M., et al. Impact of depressive symptoms on outcome of Alzheimer's disease. *Dementia and Neuropsychologia* 2010; 4(4): 346–352.

Desai, A.K., Schwartz, L. Grossberg, G.T. Behavioral disturbance in dementia. *Current Psychiatry Reports* 2012; 14(4): 298–309.

Devor, M., Renvall, M., Devor, M., et al. An educational intervention to support caregivers of elders with dementia. *American Journal of Alzheimer's Disease and Other Dementias* 2008; 23(3): 233–241.

Dhikav, V., Singh, A.K. Caregiver burden of behavioral and psychological symptoms of dementia among Indian patients with Alzheimer's disease. *International Psychogeriatrics* 2012; 24(9): 1531–1532.

Dias, A., Dewey, M.E., D'Souza, J., et al. The effectiveness of a home care program for supporting caregivers of persons with dementia in developing countries: a randomised controlled trial from Goa, India. *Public Library of Science One* 2008; 3(6): 1–7.

Duhig, A., Banerjee, S., Hass, S., et al. A cross-national study of carer burden in dementia. *Alzheimer's and Dementia* 2012; (1): P378.

Dunk, B., Doughty, K. *The Aztec Project—Providing assistive technology for people with dementia and their carers in Croydon.* Paper presented at the Laing and Bulsson Telecare and Assistive Technology Conference, London 2006.

Dunkin, J.J., Anderson-Hanley, C. Dementia caregiver burden: A review of the literature and guidelines for assessment and intervention. *Neurology* 1998; 51(1_Suppl_1): S53–S60.

Eisdorfer, C., Czaja, S.J., Loewenstein, D.A., et al. The effect of a family therapy and technology-based intervention on caregiver depression. *The Gerontologist* 2003; 43(4): 521–531.

Erder, M.H., Wilcox, T.K., Chen, W.H., et al. A new measure of caregiver burden in Alzheimer's disease: The caregiver-perceived burden questionnaire. *American Journal of Alzheimer's Disease and other Dementias* 2012; 27(7): 474–482.

Etters, L., Goodall, D., Harrison, B.E. Caregiver burden among dementia patient caregivers: a review of the literature. *Journal of the American Academy of Nurse Practitioners* 2008; 20(8): 423–428.

Farran, C.J., Gilley, D.W., McCann, J.J., et al. Efficacy of behavioral interventions for dementia caregivers. *Western Journal of Nursing Research* 2007; 29(8): 944–960.

Fearon, M., Donaldson, C., Burns, A., et al. Intimacy as a determinant of expressed emotion in carers of people with Alzheimer's disease. *Psychological Medicine* 1998; 28: 1085–1090.

Fischer, C.E., Ismail, Z., Schweizer, T.A. Impact of neuropsychiatric symptoms on caregiver burden in patients with Alzheimer's disease. *Neurodegenerative Disease Management* 2012; 2(3): 269–277.

Frank-Garcia, A., Salva, A., Lereun, C., et al. 12-month clinical evolution of moderate Alzheimer's disease patients in spain: the evocost study. *Value in Health* 2012; 15(7): A545.

Fuh, J-L., Lam, L., Hirono, N., et al. Neuropsychiatric Inventory Workshop: Behavioral and Psychologic Symptoms of Dementia in Asia. *Alzheimer Disease and Associated Disorders October/December* 2006; 20(4): 314–317.

Gallagher-Thompson, D., Gray, H.L., Tang, P.C., et al. Impact of in-home behavioral management versus telephone support to reduce depressive symptoms and perceived stress in Chinese caregivers: results of a pilot study. *American Journal of Geriatric Psychiatry* 2007; 15(5): 425–434.

Gallagher, D., Ni Mhaolain, A., Crosby, L., et al. Self-efficacy for managing dementia may protect against burden and depression in Alzheimer's caregivers. *Aging and mental health* 2011; 15(6): 663–670.

Garcia-Alberca, J.M., Cruz, B., Lara, J.P., et al. Disengagement coping partially mediates the relationship between caregiver burden and anxiety and depression in caregivers of people with Alzheimer's disease. Results from the MALAGA-AD study. *Journal of Affective Disorders* 2012a; 136(3): 848–856.

Garcia-Alberca, J.M., Cruz, B., Lara, J.P., et al. Anxiety and depression are associated with coping strategies in caregivers of Alzheimer's disease patients: results from the MALAGA-AD study. *International Psychogeriatrics* 2012b; 24(8): 1325–1334.

Gavrilova, S.I., Ferri, C.P., Mikhaylova, N., et al. Helping carers to care: The 10/66 Dementia Research Group's randomized control trial of a caregiver intervention in Russia. *International Journal of Geriatric Psychiatry* 2009; 24(4): 347–354.

George, L.K., Gwyther, L.P. Caregiver well-being: a multidimensional examination of family caregivers of demented adults. *The Gerontologist* 1986; 26(3): 253–259.

Gilleen, J., Greenwood, K., Archer, N., et al. The role of premorbid personality and cognitive factors in awareness of illness, memory, and behavioural functioning in Alzheimer's disease. *Cognitive Neuropsychiatry* 2012; 17(3): 227–245.

Gitlin, L.N. Good news for dementia care: Caregiver interventions reduce behavioral symptoms in people with dementia and family distress. *American Journal of Psychiatry* 2012a; 169(9): 894–897.

Gitlin, L.N. Interventions to promote well-being for people with dementia and their family caregivers. *Alzheimer's and Dementia* 2012b; (1): P229–P230.

Gitlin, L.N., Winter, L., Burke, J., et al. Tailored activities to manage neuropsychiatric behaviors in persons with dementia and reduce caregiver burden: a randomized pilot study. *The American Journal of Geriatric Psychiatry* 2008; 16(3): 229–239.

Gitlin, L.N., Winter, L., Corcoran, M., et al. Effects of the home environmental skill-building program on the caregiver-care recipient dyad: 6-month outcomes from the Philadelphia REACH Initiative. *The Gerontologist* 2003; 43(4): 532–546.

Gitlin, L.N., Winter, L., Dennis, M.P., et al. A biobehavioral home-based intervention and the well-being of patients with dementia and their caregivers: the COPE randomized trial. *Journal of the American Medical Association* 2010a; 304(9): 983–991.

Gitlin, L.N., Winter, L., Dennis, M. P., et al. Targeting and managing behavioral symptoms in individuals with dementia: A randomized trial of a nonpharmacological intervention. *Journal of the American Geriatrics Society* 2010b; 58(8): 1465–1474.

Glueckauf, R.L., Davis, W.S., Willis, F., et al. Telephone-based, cognitive-behavioral therapy for African American dementia caregivers with depression: initial findings. *Rehabilitation psychology* 2012; 57(2): 124–139.

Glueckauf, R.L., Loomis, J.S., Glueckauf, R.L., et al. Alzheimer's Caregiver Support Online: lessons learned, initial findings and future directions. *Neurorehabilitation* 2003; 18(2): 135–146.

Glueckauf, R.L., Stine, C., Bourgeois, M., et al. Alzheimer's Rural Care Healthline: Linking Rural Caregivers to Cognitive-Behavioral Intervention for Depression. *Rehabilitation Psychology* 2005; 50(4): 346–354.

Gormley, N., Lyons, D., Howard, R. Behavioural management of aggression in dementia: A randomized controlled trial. *Age and Ageing* 2001; 30(2): 141–145.

Gort, A.M., Mingot, M., March, J., et al. Short Zarit scale in dementias. *Clinical Medicine* 2010; 135(10): 447–449.

Greene, J.G., Smith, R., Gardiner, M., et al. Measuring behavioural disturbance of elderly demented patients in the community and its effects on relatives: a factor analytic study. *Age and Ageing* 1982; 11(2): 121–126.

Gronning, H., Kristiansen, S., Dyre, D., et al. Caregiver burden and consumption of social services among patients with early onset Alzheimer's disease compared to late onset Alzheimer's disease. *European Journal of Neurology* 2012; 19: 115.

Guerra, M., Ferri, C.P., Fonseca, M., et al. Helping carers to care: The 10/66 Dementia Research Group's randomized control trial of a caregiver intervention in Peru. *Brazilian Journal of Psychiatry* 2011; 33(1): 47–54.

Guerrero, S. Grief in spousal caregivers of persons with frontotemporal lobar degeneration: Exploring the relationship between challenging behaviors and caregiver grief. *Dissertation Abstracts International: Section B: The Sciences and Engineering* 2012; 72(9-B).

Haley, W.E., Gitlin, L.N., Wisniewski, S.R., et al. Well-being, appraisal, and coping in African-American and Caucasian dementia caregivers: findings from the REACH study. *Aging and Mental Health* 2004; 8(4): 316–329.

Hansberry, M.R., Chen, E., Gorbien, M.J. Dementia and elder abuse. *Clinics in Geriatric Medicine* 2005; 21(2): 315–332.

Haritou, M., Cuno, S., Glickman, Y., et al. *ALADDIN: a home care system for the efficient monitoring of elderly people with dementia.* Paper presented at the Ambient Assisted Living Forum, Lecce, Italy 2011.

Haritou, M., Glickman, Y., Androulidakis, A., et al. A Technology Platform for a Novel Home Care Delivery Service to Patients with Dementia. *Journal of Medical Imaging and Health Informatics* 2012; 2: 1–7.

Harris, G.M., Durkin, D.W., Allen, R.S., et al. Exemplary care as a mediator of the effects of caregiver subjective appraisal and emotional outcomes. *The Gerontologist* 2011; 51(3): 332–342.

Hebert, R., Levesque, L., Vezina, J., et al. Efficacy of a psychoeducative group program for caregivers of demented persons living at home: a randomized controlled trial. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences* 2003; 58(1): S58–S67.

Hepburn, K.W., Lewis, M., Narayan, S., et al. Partners in caregiving: A psychoeducation program affecting dementia family caregivers' distress and caregiving outlook. *Clinical Gerontologist* 2005; 29(1): 53–69.

Hepburn, K.W., Lewis, M., Sherman, C.W., et al. The Savvy Caregiver Program: Developing and Testing a Transportable Dementia Family Caregiver Training Program. *The Gerontologist* 2003; 43(6): 908–915.

Hirono, N., Kobayashi, H., Mori, E. Caregiver burden in dementia: evaluation with a Japanese version of the Zarit caregiver burden interview. *No To Shinkei* 1998; 50(6): 561–567.

Holst, G., Edberg, A.K. Wellbeing among people with dementia and their next of kin over a period of 3 years. *Scandinavian Journal of Caring Sciences* 2011; 25(3): 549–557.

Hooker, K., Bowman, S.R., Coehlo, D.P., et al. Behavioral change in persons with dementia: relationships with mental and physical health of caregivers. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences* 2002; 57(5): P453–P460.

Huang, S.S., Lee, M.C., Liao, Y.C., et al. Caregiver burden associated with behavioral and psychological symptoms of dementia (BPSD) in Taiwanese elderly. *Archives of Gerontology and Geriatrics* 2012; 55(1): 55–59.

Johnson, D.K., Niedens, M., Wilson, J., et al. Treatment Outcomes of a Crisis Intervention Program for Dementia With Severe Psychiatric Complications: The Kansas Bridge Project. *The Gerontologist* 2013; 53(1): 102–112.

Kaufer, D.I., Cummings, J.L., Christine, D., et al. Assessing the impact of neuropsychiatric symptoms in Alzheimer's disease: The neuropsychiatric inventory caregiver distress scale. *Journal of the American Geriatrics Society* 1998; 46(2): 210–215.

Kaufer, D.I., Cummings, J.L., Ketchel, P., et al. Validation of the NPI-Q, a brief clinical form of the Neuropsychiatric Inventory. *Journal of Neuropsychiatry and Clinical Neurosciences* 2000; 12(2): 233–239.

Khachiyants, N., Trinkle, D., Son, S.J., et al. Sundown syndrome in persons with dementia: An update. *Psychiatry Investigation* 2011; 8(4): 275–287.

Kim, K.W., Jeong, H., Kim, T.H., et al. Abusive behaviors in the caregivers of dementia patients: Results from the nationwide survey on dementia care in Korea (NASDECK). *Alzheimer's and Dementia* 2012; (1): 249–250.

Kim, S.Y., Choi, M.S. Neuropsychiatric symptoms in mild Alzheimer's disease and mild cognitive impairment. *Alzheimer's and Dementia* 2012; (1): 367.

Kochhann, R., Borba, E., Cerveira, M.O., et al. Neuropsychiatric symptoms as the main determinant of caregiver burden in Alzheimer's disease. *Dementia and Neuropsychologia* 2011; 5(3): 203–208.

Kramer, B., Gibson, J., Teri, L. Interpersonal family stress in Alzheimer's disease—Perceptions of patients and caregivers. *Clinical Gerontologist* 1993; 12(1): 57–75.

Kunik, M.E., Snow, A.L., Davila, J.A., et al. Causes of aggressive behavior in patients with dementia. *Journal of Clinical Psychiatry* 2010; 71(9): 1145–1152.

Kurasawa, S., Yoshimasu, K., Washio, M., et al. Factors influencing caregivers' burden among family caregivers and institutionalization of in-home elderly people cared for by family caregivers. *Environmental Health and Preventive Medicine* 2012; 17(6): 474–483.

Kurz, A., Wagenpfeil, S., Hallauer, J., et al. Evaluation of a brief educational program for dementia carers: The AENEAS Study. *International Journal of Geriatric Psychiatry* 2010; 25(8): 861–869.

Lavoie, J.P., Ducharme, F., Levesque, L., et al. Understanding the outcomes of a psycho-educational group intervention for caregivers of persons with dementia living at home: a process evaluation. *Aging and Mental Health* 2005; 9(1): 25–34.

Lee, D.R., Thomas, A.J. Sleep in dementia and caregiving-assessment and treatment implications: A review. *International Psychogeriatrics* 2011; 23(2): 190–201.

Leggett, A.N., Zarit, S., Taylor, A., et al. Stress and burden among caregivers of patients with Lewy body dementia. *The Gerontologist* 2011; 51(1): 76–85.

Levy, K., Lanctot, K.L., Farber, S.B., et al. Does pharmacological treatment of neuropsychiatric symptoms in Alzheimers disease relieve caregiver burden? *Drugs and Aging* 2012; 29(3): 167–179.

Lewis, M.L., Hobday, J.V., Hepburn, K.W. Internet-based program for dementia caregivers. *American Journal of Alzheimer's Disease and other Dementias* 2010; 25(8): 674–679.

Liddle, J., Smith-Conway, E.R., Baker, R., et al. Memory and communication support strategies in dementia: Effect of a training program for informal caregivers. *International Psychogeriatrics* 2012; 24(12): 1927–1942.

Lim, J., Goh, J., Chionh, H.L., et al. Why do patients and their families not use services for dementia? Perspectives from a developed Asian country. *International Psychogeriatrics* 2012; 24(10): 1571–1580.

Lin, W.C., Tsai, C.F., Wang, S.J., et al. Comparison of the burdens of family caregivers and foreign paid caregivers of the individuals with dementia. *International Psychogeriatrics* 2012; 24(12): 1953–1961.

Liu, Y. Impact of family caregiving upon caregivers of elders with dementia in China. *Dissertation Abstracts International: Section B: The Sciences and Engineering* 2010; 71(5-B).

Livingston, G., Mahoney, R., Regan, C., et al. The Caregivers for Alzheimer's disease Problems Scale (CAPS): development of a new scale within the LASER-AD study. *Age and Ageing* 2005; 34(3): 287–290.

Machnicki, G., Allegri, R., Dillon, C., et al. Cognitive, functional and behavioral factors associated with the burden of caring for geriatric patients with cognitive impairment or depression: evidence from a South American sample. *International Journal of Geriatric Psychiatry* 2009; 24(4): 382–389.

Mahoney, D.F., Tarlow, B.J., Jones, R.N., et al. Effects of an automated telephone support system on caregiver burden and anxiety: findings from the REACH for TLC intervention study. *The Gerontologist* 2003; 43(4): 556–567.

Marriott, A., Donaldson, C., Tarrier, N., et al. Effectiveness of cognitive-behavioural family intervention in reducing the burden of care in carers of patients with Alzheimer's disease. *British Journal of Psychiatry* 2000; 176: 557–562.

Matsumoto, N., Ikeda, M., Fukuhara, R., et al. Caregiver burden associated with behavioral and psychological symptoms of dementia in elderly people in the local community. *Dementia and Geriatric Cognitive Disorders* 2007; 23(4): 219–224.

McCurry, S.M., Gibbons, L.E., Logsdon, R.G., et al. Nighttime insomnia treatment and education for Alzheimer's disease: a randomized, controlled trial. *Journal of the American Geriatrics Society* 2005; 53(5): 793–802.

Melo, G., Maroco, J., De Mendonca, A. Influence of personality on caregiver's burden, depression and distress related to the BPSD. *International Journal of Geriatric Psychiatry* 2011; 26(12): 1275–1282.

Merritt, R.P. The decision making process of informal caregivers of dementia family members regarding nursing home placement. *Dissertation Abstracts International: Section B: The Sciences and Engineering* 2011; 72(4-B).

Mittelman, M.S., Haley, W.E., Clay, O.J., et al. Improving caregiver well-being delays nursing home placement of patients with Alzheimer disease. *Neurology* 2006; 67(9): 1592–1599.

Mittelman, M.S., Roth, D.L., Haley, W.E., et al. Effects of a caregiver intervention on negative caregiver appraisals of behavior problems in patients with Alzheimer's disease: results of a randomized trial. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences* 2004; 59(1): P27–P34.

Mohamed, S., Rosenheck, R., Lyketsos, C.G., et al. Caregiver burden in alzheimer disease: Cross-sectional and longitudinal patient correlates. *American Journal of Geriatric Psychiatry* 2010; 18(10): 917–927.

Moniz-Cook, E., Elston, C., Gardiner, E., et al. Can training community mental health nurses to support family carers reduce behavioural problems in dementia? An exploratory pragmatic randomised controlled trial. *International Journal of Geriatric Psychiatry* 2008; 23(2): 185–191.

Montgomery, R.J., Gonyea, J.G., Hooyman, N.R. Caregiving and the Experience of Subjective and Objective Burden. *Family Relations* 1985; 34(1): 19–26.

Monti, M.S., Vanacore, N., Bartorelli, L., et al. The savvy caregiver program: A probe, multicenter, controlled trial. *Journal of Alzheimer's Disease* 2012; 29: 90.

Moore, K., Ozanne, E., Ames, D., et al. How do family carers respond to behavioral and psychological symptoms of dementia? *International Psychogeriatrics* 2013; 25(5): 743–753.

Moreno, A., Lasprilla, J.C., Rogers, H., et al. Independent relationships between problems presented by individuals with dementia and caregiver psychosocial outcomes. *Brain Injury* 2010; 24(3): 143.

Mori, T., Ueno, S.I. Support provided to dementia patients by caregivers and the community. *Japan Medical Association Journal* 2011; 54(5): 301–304.

Morycz, R.K. Caregiving strain and the desire to institutionalize family members with Alzheimer's disease. Possible predictors and model development. *Research on Aging.* 1985; 7(3): 329–361.

Mougias, A.A., Politis, A., Lyketsos, C.G., et al. Quality of life in dementia patients in Athens, Greece: Predictive factors and the role of caregiver-related factors. *International Psychogeriatrics* 2011; 23(3): 395–403.

Napoles, A.M., Chadiha, L., Eversley, R., et al. Reviews: developing culturally sensitive dementia caregiver interventions: are we there yet? *American Journal of Alzheimer's Disease and Other Dementias* 2010; 25(5): 389–406.

Ng, A., Chua, E., Nyu, M.M., et al. Severity of psychiatric symptoms correlates with activities of daily living and caregiver burden in frontotemporal dementia. *Alzheimer's and Dementia* 2012; (1): P568.

NHMRC. *How to use the evidence: assessment and application of scientific evidence.* Canberra: National Health and Medical Research Council 2000.

NHMRC. *Additional levels of evidence and grades for recommendations for developers of guidelines—final draft.* Canberra: National Health and Medical Research Council 2009.

Nobili, A., Riva, E., Tettamanti, M., et al. The effect of a structured intervention on caregivers of patients with dementia and problem behaviors: A randomized controlled pilot study. *Alzheimer's Disease and Associated Disorders* 2004; 18(2): 75–82.

Novak, M., Guest, C. Application of a multidimensional caregiver burden inventory. *The Gerontologist* 1989; 29(6): 798–803.

O'Dwyer, S., Moyle, W., Zimmer-Gembeck, M., et al. Suicidal ideation in family carers of people with dementia: a pilot study. *International Journal of Geriatric Psychiatry* 2013;doi: 10.1002/gps.3941.

O'Rourke, N., Tuokko, H.A. Psychometric properties of an abridged version of the Zarit Burden Interview within a representative Canadian caregiver sample. *The Gerontologist* 2003a; 43(1): 121–127.

O'Rourke, N., Tuokko, H.A. The relative utility of four abridged versions of the Zarit Burden interview. *Journal of Mental Health and Aging* 2003b; 9(1): 55–64.

Oh, B.H. Treatment strategy of BPSD in Korean dementia patients. *Asia-Pacific Psychiatry* 2012; 4: 7–8.

Okura, T., Langa, K.M. Caregiver Burden and Neuropsychiatric Symptoms in Older Adults with Cognitive Impairment: The Aging, Demographics, and Memory Study (ADAMS). *Alzheimer Disease and Associated Disorders* 2011; 25(2): 116–121.

Ornstein, K., Gaugler, J.E. The problem with "problem behaviors": A systematic review of the association between individual patient behavioral and psychological symptoms and caregiver depression and burden within the dementia patient-caregiver dyad. *International Psychogeriatrics* 2012; 24(10): 1536–1552.

Ornstein, K.A. Caregiving over time: The impact of the behavioral and psychological symptoms of dementia on caregiver depression. *Dissertation Abstracts International: Section B: The Sciences and Engineering* 2012; 72(7-B).

Papastavrou, E., Tsangari, H., Karayiannis, G., et al. Caring and coping: the dementia caregivers. *Aging and mental health* 2011; 15(6): 702–711.

Patel, V., Prince, M. Ageing and mental health in a developing country: who cares? Qualitative studies from Goa, India. *Psychological Medicine* 2001; 31(1): 29–38.

Peisah, C. Practical application of family and systems theory in old age psychiatry: three case reports. *International Psychogeriatrics* 2006; 18(2): 345–353.

Pekkarinen, L., Sinervo, T., Perala, M.L., et al. Work stressors and the quality of life in long-term care units. *The Gerontologist* 2004; 44(5): 633–643.

Pinquart, M., Sörensen, S. Associations of stressors and uplifts of caregiving with caregiver burden and depressive mood: A meta-analysis. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences* 2003; 58(2): P112–P128.

Pinquart, M., Sörensen, S. Helping caregivers of persons with dementia: which interventions work and how large are their effects? *International Psychogeriatrics* 2006; 18(4): 577–595.

Poulshock, S.W., Deimling, G.T. Families caring for elders in residence: issues in the measurement of burden. *Journal of Gerontology* 1984; 39: 230–239.

Prince, M., Brodaty, H., Uwakwe, R., et al. Strain and its correlates among carers of people with dementia in low-income and middle-income countries. A 10/66 Dementia Research Group population-based survey. *International Journal of Geriatric Psychiatry* 2012; 27(7): 670–682.

Prince, M., Quraishi, S., Copeland, J., et al. Care arrangements for people with dementia in developing countries. *International Journal of Geriatric Psychiatry* 2004; 19(2): 170–177.

Robinson, B.C. Validation of a Caregiver Strain Index. *Journal of Gerontology* 1983; 38(3): 344–348.

Rocca, P., Leotta, D., Liffredo, C., et al. Neuropsychiatric symptoms underlying caregiver stress and insight in Alzheimer's disease. *Dementia and Geriatric Cognitive Disorders* 2010; 30(1): 57–63.

Romero-Moreno, R., Losada, A., Mausbach, B.T., et al. Analysis of the moderating effect of self-efficacy domains in different points of the dementia caregiving process. *Aging and mental health* 2011; 15(2): 221–231.

Ryan, K.A., Weldon, A., Persad, C., et al. Neuropsychiatric symptoms and executive functioning in patients with mild cognitive impairment: Relationship to caregiver burden. *Dementia and Geriatric Cognitive Disorders* 2012; 34(3–4): 206–215.

Saez, I., Oliveras, M., Ciudad, M.J., et al. Alladin project: A technology platform for the assisted living of dementia elderly individuals and their carers. *European Geriatric Medicine* 2011; 2: S151–S152.

Saeza, I., Masa, M.A., Santaeugenia, S. Organization of TeleHomeCare at the Home Setting: Different approaches to specific phenotypes. *European Geriatric Medicine* 2012; 3: S128–S129.

Saldanha, D., Mani, M.R., Srivastava, K., et al. An epidemiological study of dementia under the aegis of mental health program, Maharashtra, Pune chapter. *Indian Journal of Psychiatry* 2010; 52(2): 131–139.

Savundranayagam, M.Y., Hummert, M.L., Montgomery, R.J. Investigating the effects of communication problems on caregiver burden. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences* 2005; 60(1): S48–S55.

Savundranayagam, M.Y., Montgomery, R.J., Kosloski, K. A dimensional analysis of caregiver burden among spouses and adult children. *The Gerontologist* 2011; 51(3): 321–331.

Savundranayagam, M.Y., Montgomery, R.J., Kosloski, K., et al. Impact of a psychoeducational program on three types of caregiver burden among spouses. *International Journal of Geriatric Psychiatry* 2011; 26(4): 388–396.

Savundranayagam, M.Y., Montgomery, R.J. Impact of role discrepancies on caregiver burden among spouses. *Research on Aging* 2010; 32(2): 175–199.

Schoenmakers, B., Buntinx, F., De Lepeleire, J., et al. Can pharmacological treatment of behavioural disturbances in elderly patients with dementia lower the burden of their family caregiver? *Family Practice* 2009; 26(4): 279–286.

Schulz, R., Martire, L.M. Family caregiving of persons with dementia: prevalence, health effects, and support strategies. *American Journal of Geriatric Psychiatry* 2004; 12(3): 240–249.

Schulz, R., O'Brien, A.T., Bookwala, J., et al. Psychiatric and physical morbidity effects of dementia caregiving: prevalence, correlates, and causes. *The Gerontologist* 1995; 35(6): 771–791.

Schulz, R., Williamson, G.M. The measurement of caregiver outcomes in Alzheimer disease research. *Alzheimer Disease and Associated Disorders* 1997; 11: 117–124.

Schulz, R., Beach, S.R. Caregiving as a risk factor for mortality: The caregiver health effects study. *Journal of the American Medical Association* 1999; 282(23): 2215–2219.

Seeher, K., Brodaty, H., Low, L.F., et al. To what extent does cognitive and functional decline in older persons affect the psychological well-being of cohabiting family members? *Alzheimer's and Dementia* 2012; (1): P378–P379.

Seeher, K., Low, L.F., Reppermund, S., et al. Predictors and outcomes for caregivers of people with mild cognitive impairment—A systematic literature review. *Alzheimer's and Dementia* 2013; 9(3): 346–355.

Segerstrom, S.C., Schipper, L.J., Greenberg, R.N. Caregiving, repetitive thought, and immune response to vaccination in older adults. *Brain, Behavior and Immunity* 2008; 22: 744–752.

Senanarong, V., Jamjumras, P., Harmphadungkit, K., et al. A counseling intervention for caregivers: effect on neuropsychiatric symptoms. *International Journal of Geriatric Psychiatry* 2004; 19: 781–788.

Shahly, V., Chatterji, S., Gruber, M.J., et al. Cross-national differences in the prevalence and correlates of burden among older family caregivers in the World Health Organization World Mental Health (WMH) Surveys. *Psychological Medicine* 2013; 43(4): 865–879.

Shin, H., Youn, J., Kim, J.S., et al. Caregiver burden in Parkinson disease with dementia compared to Alzheimer disease in Korea. *Journal of Geriatric Psychiatry and Neurology* 2012; 25(4): 222–226.

Silvestre, A., Guarda, C. How do caregiver's features influence the sense of burden? *Alzheimer's and Dementia* 2011; (1): S431.

Sleath, B., Thorpe, J., Landerman, L.R., et al. African-American and white caregivers of older adults with dementia: differences in depressive symptomatology and psychotropic drug use. *Journal of the American Geriatric Society* 2005; 53(3): 397–404.

Sullivan, M.T. Caregiver Strain Index. *Journal of Gerontological Nursing* 2002; 28(8): 4–5.

Sumit, B., Daniel, S., Mani, R.N. Care giver burden and dementia. *Indian Journal of Psychiatry* 2012; 54: S64.

Tan, L.L., Wong, H.B., Allen, H. The impact of neuropsychiatric symptoms of dementia on distress in family and professional caregivers in Singapore. *International Psychogeriatrics* 2005; 17(2): 253–263.

Teri, L., Gibbons, L.E., McCurry, S.M., et al. Exercise plus behavioral management in patients with Alzheimer disease: a randomized controlled trial. *Journal of the American Medical Association* 2003; 290(15): 2015–2022.

Teri, L., Logsdon, R.G., McCurry, S.M., et al. Nonpharmacologic treatment of behavioral disturbance in dementia. *Medical Clinics of North America* 2002; 86(3) 641–656.

Teri, L., Logsdon, R.G., Peskind, E., et al. Treatment of agitation in Alzheimer's disease: a randomized placebo controlled clinical trial. *Neurology* 2000; 55: 1271–1278.

Teri, L., McCurry, S.M., Logsdon, R., et al. Training community consultants to help family members improve dementia care: a randomized controlled trial. *The Gerontologist* 2005; 45(6): 802–811.

Teri, L., Truax, P., Logsdon, R., et al. Assessment of behavioral problems in dementia: the revised memory and behavior problems checklist. *Psychology and Aging* 1992; 7(4): 622–631.

Teri, L., Logsdon, R.G., Uomoto, J., et al. Behavioral treatment of depression in dementia patients: A controlled clinical trial. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences* 1997; 52B(4): 159–166.

The 10/66 Dementia Research Group. Care arrangements for people with dementia in developing countries. *International Journal of Geriatric Psychiatry* 2004; 19: 170–177.

Thornton, M., Travis, S.S. Analysis of the reliability of the modified caregiver strain index. *The Journals of Gerontology, Series B: Psychological Sciences and Social Sciences* 2003; 58(2): S127–S132.

Tschanz, J., Hess, K., Corcoran, C., et al. Caregiver coping strategies predict neuropsychiatric symptoms in dementia: The Cache county dementia progression study. *Alzheimer's and Dementia* 2012; (1): P126.

Uett, S., Linnamagi, U. Neuropsychiatric and behavioural symptoms in patients with Alzheimer's disease as an effect to caregivers' state of mental health. *Alzheimer's and Dementia* 2011; (1): S626–S627.

Ulstein, I.D., Sandvik, L., Wyller, T.B., et al. A one-year randomized controlled psychosocial intervention study among family carers of dementia patients—effects on patients and carers. *Dementia and Geriatric Cognitive Disorders* 2007; 24(6): 469–475.

Ulstein, I., Wyller, T.B., Engedal, T.K. The relative stress scale, a useful instrument to identify various aspects of carer burden in dementia? *International Journal of Geriatric Psychiatry* 2007; 22(1): 61–67.

Van Den Heuvel, E., Jowitt, F., McIntyre, A. Awareness, requirements and barriers to use of Assistive Technology designed to enable independence of people suffering from Dementia (ATD). *Technology and Disability* 2012; 24(2): 139–148.

Van Der Linde, R.M., Stephan, B.C., Savva, G.M., et al. Systematic reviews on behavioural and psychological symptoms in the older or demented population. *Alzheimer's Research and Therapy* 2012; 4(4).

Van Der Mussele, S., Le Bastard, N., Vermeiren, Y., et al. Behavioral symptoms in mild cognitive impairment as compared to Alzheimer's disease and healthy elderly. *Alzheimer's and Dementia* 2011; (1): S547.

Van Durme, T., Macq, J., Jeanmart, C., et al. Tools for measuring the impact of informal caregiving of the elderly: a literature review. *International Journal of Nursing Studies* 2012; 49(4): 490–504.

Vedhara, K., Cox, N.K., Wilcock, G.K., et al. Chronic stress in elderly carers of dementia patients and antibody response to influenza vaccination. *Lancet* 1999; 3531: 627–631.

Vitaliano, P.P. , Russo, J., Young, H.M., et al. Predictors of burden in spouse caregivers of individuals with Alzheimer's disease. *Psychology and Aging* 1991; 6: 392–402.

Vitaliano, P.P., Russo, J., Young, H.M., et al. The Screen for Caregiver Burden. *The Gerontologist* 1991; 31(1): 76–83.

Vitaliano, P.P., Zhang, J., Scanlan, J.M. Is caregiving hazardous to one's physical health? A meta-analysis. *Psychological Bulletin* 2003; 129(6): 946–972.

Vitaliano, P.P., Scanlan, J.M., Zhang, J., et al. A path model of chronic stress, the metabolic syndrome, and coronary heart disease. *Psychosomatic Medicine* 2002; 64(3): 418–435.

Werner, P. Mild cognitive impairment and caregiver burden: A critical review and research agenda. *Public Health Reviews* 2012; 34(2).

Westphal, A., Dingjan, P., Attoe, R. What can low and high technologies do for late-life mental disorders? *Current Opinion in Psychiatry* 2010; 23(6): 510–515.

Whitlatch, C.J., Zarit, S.H., von Eye, A. Efficacy of interventions with caregivers: A reanalysis. *The Gerontologist* 1991; 31(1): 9–14.

Winterton, R., Warburton, J. Models of care for socially isolated older rural carers: barriers and implications. *Rural and Remote Health* 2011; 11(3): 1678.

Wood, S., Cummings, J.L., Barclay, T., et al. Assessing the impact of neuropsychiatric symptoms on distress in professional caregivers. *Aging and Mental Health* 1999; 3(3): 241–245.

Wood, S., Cummings, J.L., Hsu, M.A., et al. The use of the neuropsychiatric inventory in nursing home residents. Characterization and measurement. *American Journal of Geriatric Psychiatry* 2000; 8(1): 75–83.

Wortmann, M. An intervention tool for lower and middle-income countries: Helping carers to care'. *Alzheimer's and Dementia* 2011; (1): S493.

Yaffe, K., Fox, P., Newcomer, R., et al. Patient and Caregiver Characteristics and Nursing Home Placement in Patients with Dementia. *Journal of the American Medical Association* 2002; 287(16): 2090–2097.

Yan, E., Kwok, T. Abuse of older Chinese with dementia by family caregivers: An inquiry into the role of caregiver burden. *International Journal of Geriatric Psychiatry* 2011; 26(5): 527–535.

Zarit, S.H., Femia, E.E., Kim, K., et al. The structure of risk factors and outcomes for family caregivers: implications for assessment and treatment. *Aging and Mental Health* 2010; 14(2): 220–231.

Zarit, S.H., Reever, K.E., Bach-Peterson, J. Relatives of the impaired elderly: correlates of feelings of burden. *The Gerontologist* 1980; 20: 649–655.

Zawadzki, L., Mondon, K., Peru, N., et al. Attitudes towards Alzheimer's disease as a risk factor for caregiver burden. *International Psychogeriatrics* 2011; 23(9): 1451–1461.

Zekry, D., Graf, C.E., Giannelli, S.V., et al. Non-cognitive outcomes in trials of disease-modifying drugs for Alzheimer's disease. *European Geriatric Medicine* 2012; 3(1): 37–42.

Zhao, H., Zhao, Z., Huang, L., et al. Diagnosis and assessment of apathy in Chinese patients with Alzheimer's disease. *Journal of Psychosomatic Research* 2012; 72(5): 405–407.

Zucchella, C., Bartolo, M., Pasotti, C., et al. Caregiver burden and coping in early-stage Alzheimer disease. *Alzheimer Disease and Associated Disorders* 2012; 26(1): 55–60.

Zweig, Y., Thaipisuttikul, P., Gurnani, A.S., et al. A retrospective review of clinical and psychometric characteristics of patients with and without Capgras syndrome in dementia with Lewy bodies. *Journal of the American Geriatrics Society* 2012; 60: S63–S64.

INTERNATIONAL PSYCHOGERIATRIC ASSOCIATION

www.ipa-online.org

MODULE 5

Non-pharmacological treatments

The IPA Complete Guides to Behavioral and Psychological Symptoms of Dementia

BPSD

Specialists Guide

Specialists • Primary Care Physicians • Nurses

MODULE 5: Non-pharmacological treatments

Contents

Key messages	**5.2**
Introduction	**5.2**
Understanding BPSD	**5.2**
Underlying principles	**5.3**
Assessment methods	**5.4**
Mapping symptoms	5.5
Treatment principles	**5.5**
Further tips	5.6
Ensuring safety	5.6
Individual treatments	**5.6**
Activity and recreation	5.7
Aromatherapy	5.7
Family tape-recordings	5.7
Music and sound	5.7
One-to-one interaction	5.8
Physical activity	5.8
Treatment of particular symptoms	**5.8**
Exit-seeking	5.8
Repeated questioning	5.8
Sleep disturbance	5.9
Physical environment	**5.9**
Conclusions	**5.10**
References and recommended reading	**5.10**

Key messages

- There is now a substantial body of evidence supporting the use of non-pharmacological treatments of the behavioral and psychological symptoms of dementia (BPSD).
- Even when BPSD are caused by physical discomfort, major depression or psychosis, psychosocial interventions will prove helpful when offered in combination with analgesic, antidepressant or antipsychotic medications.
- Psychosocial approaches are indicated as first-line approaches to all emotional and behavioral disturbances in people with dementia.
- All of the psychosocial interventions described here work best when they are tailored to people's backgrounds, interests and capacity.
- Family and professional caregivers are key collaborators. It is important to provide them with necessary information and education and to support them as they test and refine their responses to challenging symptoms.
- The physical environment can help prevent or minimize BPSD by reducing distress, encouraging meaningful activity, maximizing independence and promoting safety.

Introduction

In Western countries, many people with serious, persistent BPSD live in nursing homes. Much of the information in this module is directed to medical, nursing and allied health clinicians who work in that setting but the principles expressed here apply equally well to the family carers of people with dementia who live in their own homes.

This module examines:

- Psychosocial models of BPSD
- Principles of dementia care
- Assessment methods
- Specific treatments
- Physical environment

Additional information on responses to BPSD can be found on the web sites listed at the end of this module.

Understanding BPSD

While changes in brain structure and function certainly contribute to BPSD (See Module 3), psychological processes also play a part. People with dementia may feel great distress as a result of their condition and the responses of those around them are critical. Caregivers typically seek to provide what support is required in a calm, affirming and respectful manner. Sometimes, though, they respond inadvertently in ways that make distress worse. Three different models have been put forward to explain how this works:

- **Learning theory** states that behaviors are reinforced if they lead to people being given more attention. Yelling, for example, will increase in frequency if staff members attend to residents when they are noisy and ignore them when they are quiet (Teri et al., 1998). Paying more attention to people when they are quiet should therefore lead to a reduction in yelling.
- According to the **unmet needs theory**, so-called challenging behaviors stem from normal human needs for meaningful activity, emotional validation and social interaction (Cohen-Mansfield, 2001). Since people with advanced dementia cannot always voice these needs, or take action to address them, their carers must take the initiative. A need for physical movement and social engagement, for example, might be addressed by a carefully tailored exercise program.
- According to the **stress threshold model**, dementia reduces people's capacity to cope with stress, resulting in inappropriate behaviors when levels of stress are excessive (Hall and Buckwalter, 1987). Stress can be reduced to tolerable levels by attending to signs of tension and providing opportunities for relaxation.

In reality, most psychosocial treatments blend elements of all three models. For example, a music therapy session in a nursing home might lead to a reduction in BPSD by:

- Generating positive attention from staff members and co-residents while participating in the group, thereby reinforcing normal social behavior
- Meeting a resident's need for creative, enjoyable activity
- Providing an optimal level of stimulation

Other factors that increase stress and might therefore worsen BPSD, include:

- Poor vision or hearing
- Limited mobility
- Pain or physical discomfort
- Incontinence
- Lack of fluency in the local language

Underlying principles

Since BPSD are triggered in part by psychological forces, it follows that family and professional caregivers can interact with people with dementia in ways that prevent symptoms emerging, or at least reduce their frequency and severity. Based on the models described above, caregivers should aim to:

- Encourage socially appropriate behaviors
- Create opportunities for social interaction and meaningful activity
- Ensure that levels of stimulation are neither too high nor too low

To help reduce the impact of sensory handicap, functional incapacity and cultural isolation, caregivers can assist by:

- Correcting vision and hearing deficits by ensuring that spectacles and hearing aids are worn and adjusted correctly

- Promoting mobility via walking aids and regular exercise
- Relieving pain by means of regular analgesia, physical exercise and change of position
- Minimizing incontinence through regular toileting regimes and incontinence aids
- Using short, simple sentences and making word or icon cards for people who do not share the local language

If caregivers are to meet these various needs of people with dementia in a way that is truly therapeutic, they must have a detailed knowledge of each person's:

- Cultural and family background
- Personal life story
- Previous interests and skills
- Likes and dislikes (e.g., food, activities, personal care)
- Physical well-being

People with mild dementia can provide much of this information themselves. Family members will need to be questioned about the backgrounds of those with more severe levels of impairment.

The term "person-centered care" is used to describe a style of engaging with people with dementia that encapsulates all of the above points. There is evidence that behavioral symptoms are reduced when:

- Nursing home staff are trained in person-centered care (Chenoweth et al., 2009)
- Personal care is designed to maintain residents' abilities and to help them compensate for lost ones (Wells et al., 2000)
- Residents are bathed in their preferred way while carers speak to them calmly and minimize discomfort (Sloane et al., 2004)

Nursing home staff can rate their ability to deliver dementia-sensitive care using the Person-centered Care Assessment Tool (P-CAT) (Edvardsson et al., 2010). The tool allows staff to rate the professional, organisational and environmental factors that promote or impede a focus on residents' individuality and autonomy.

Assessment methods

When treating BPSD, success rates will be higher if a full assessment is made beforehand. To make sense of symptoms, and devise strategies to make their expression unnecessary, it is necessary to:

- Identify what symptom(s) most trouble the resident and present the greatest challenge to carers
- Describe each symptom in detail; note what exactly the resident does or says that is concerning
- Specify the **A**ntecedents of **B**ehaviors (the circumstances that spark them) and their **C**onsequences (what makes them better or worse)—this is called the **ABC** approach

Caregivers often believe symptoms come 'out of the blue' but careful observation of the events immediately preceding them will usually identify trigger factors. Symptoms are rarely simple. Usually several factors are involved in triggering symptoms and the more caregivers understand their inter-relationship, the more likely it is that interventions will prove successful. The following examples use the **ABC** approach to understand symptoms:

- A resident is too confused to shower herself. She is incontinent of urine overnight and needs a shower each morning. When carers help her to undress and wash (**A**ntecedent), she hits them and pushes them away (**B**ehavior). Carers tend to leave her alone as a result (**C**onsequence). This relieves her agitation temporarily but her groin area is becoming abraded through neglect.
- When another resident is left alone for long periods in the morning (**A**ntecedent), he becomes anxious and irritable and asks repeatedly when his daughter will come to see him (**B**ehavior). Staff members respond to his questions (**C**onsequence). This helps only for a few minutes.

Mapping symptoms

Mapping the frequency and severity of symptoms shows patterns in occurrence during the day, from one day to another, as well as changes before and after an intervention is introduced. It provides an objective rating of what is happening over time. Symptoms can be mapped in the following ways:

- Keeping a daily diary, using the carer's own words
- Graphing a symptom on paper, marking if it is absent or present to a mild, moderate or severe degree on an hour by hour (or shift by shift) basis
- Using a rating scale. The two scales used most often in research studies are the following:
  - The Cohen-Mansfield Agitation Inventory—CAMI (Cohen-Mansfield, 1991) rates the frequency of 29 individual behaviors (e.g., hitting, calling out) in the previous two weeks. A shorter 14-item version is also available.
  - The Neuropsychiatric Inventory (NPI) rates the frequency and severity of a wider range of symptoms including delusions, hallucinations, agitation, apathy, and sleep disturbance in the previous one month (Cummings, 1997).

Treatment principles

When devising an approach to help a person with a behavioral or psychological symptom, experts recommend that carers should:

- Address one symptom at a time
- Follow the ABC approach
- Measure the symptom before and after making an intervention to confirm that it is effective
- Start with a small achievable goal and proceed step-by-step
- Apply the intervention consistently. Do not expect immediate change, improvement takes time

- Continually evaluate and modify plans. Decide in advance what "success" means for this person
- Think in advance of an alternative strategy if the first one fails

There is evidence that teaching family caregivers to follow these principles can prove just as effective as psychotropic medications in reducing agitation (Teri et al., 2000).

Further tips

It is important to respond sensitively and constructively when people with dementia feel anxious, frustrated or overwhelmed. Strategies that experts have often found to be successful include the following:

- Identifying situations that trigger distress and avoiding them whenever possible
- Recognizing that the person's stress levels are rising and taking action to prevent them escalating further
- Approaching an anxious, agitated person from the front
- Speaking at eye level, and using a gentle, non-threatening posture and tone of voice
- Telling the person what is happening and why
- Defusing the situation once stress levels rise by changing activities, tempo or space
- Avoiding arguments whenever possible as they usually make things worse
- If all else fails, telling an untruth (e.g., "Your daughter will be here later") as a means of relieving distress
- Avoiding physical restraint since it can lead to escalating levels of agitation

Ensuring safety

It is important for carers to have the knowledge, skills and resources to maintain the safety of all concerned—the person with dementia, the carers themselves and co-residents:

- A medication box helps carers check that essential medications are being taken correctly
- People at risk of wandering and becoming lost should carry a card or wear a bracelet with their address and telephone number
- Gas or electrical appliances may need to be disabled if people use them dangerously
- Carers must know what to do and how to get help urgently if a situation becomes dangerous
- If a significant risk is identified, strategies should be written in the care plan in an obvious place.

Individual treatments

This section describes psychosocial treatments of physical agitation, aggression and anxiety. Treatments of specific symptoms are discussed later. There are now hundreds of published reports of different non-pharmacological treatments of BPSD (Opie et al., 1999; Cohen-Mansfield, 2001; O'Connor et al., 2009a; O'Connor et al., 2009b).

In most studies, a treatment is compared with "usual care". If it proves superior, it is promoted as having a special therapeutic effect. In reality, its benefits might simply reflect the personal attention that follows from participating in a scientific study. For reasons of space, the focus here is on evidence from well-designed trials in which a treatment reduced agitation or distress better than personal attention. Only a small number of published reports met this requirement (O'Connor et al., 2009a). The fact that a treatment does not qualify for inclusion in this brief outline (e.g. pet therapy) does not mean that it lacks value. A lack of evidence is not the same as a lack of effectiveness.

The material presented below focuses more on treatments of physical agitation than anxiety and depression, reflecting researchers' interests.

Activity and recreation

Enjoyable, meaningful activities improve quality of life, mood and behavior. Activities can take the form of daily chores, hobbies or shared pastimes. Two studies have shown that:

- Activities offering art, rhythm and touch led to greater contentment and interest (Beck et al., 2002)
- Recreational activities elicited more pleasure and interest when they were matched to people's previous interests (Kolanowski et al., 2005).

Aromatherapy

Lavender (*Lavendula angustifolia*) and lemon balm (*Melissa officinalis*) have both been tested as treatments for BPSD. Lavender oil is quickly absorbed through skin and respiration (Jäger, 1992) and acts on brain neurotransmitter systems in a similar way to sedative medications (Elisabetsky et al., 1995). When administered to mice, they become much less active for approximately an hour (Buchbauer et al., 1993). The evidence from controlled trials is mixed but two trials found that:

- Agitated behaviors reduced in frequency when 2% lavender oil was sprayed in a dementia care unit (Holmes et al., 2002)
- Massage on the face and arms with lemon balm led to a reduction in agitated behaviors (Ballard et al., 2002).

Family tape-recordings

The voice or image of a family member can have a calming effect on confused nursing home residents who quickly forget visits. One study found that a 15-minute audiotape made by a family member reduced agitated behaviors when played through headphones (Garland et al., 2007).

Music and sound

Music can engage interest and generate positive emotions. It also provides an opportunity for enjoyable social interaction. Research studies found that:

- Music that was carefully matched to people's interests reduced agitated behaviors more than "off the shelf" relaxing classical music (Gerdner, 2000)

- Playing soothing audiotapes of a mountain stream or ocean waves reduced verbally disruptive behaviors (Burgio et al., 1996)
- Live music resulted in higher rates of arousal, engagement and well-being than pre-recorded music (Sherratt et al., 2004)
- Playing tapes of people's preferred music during baths reduced rates of verbal and physical aggression (Clark et al., 1998)

One-to-one interaction

Empathic, attentive contact with another person may be the key ingredient in many psychosocial interventions. In support of this view, one-to-one interaction with a therapist who sought to engage people in conversation, gentle exercise, a sensory kit or manual activities shaped by their interests and skills worked as well in reducing verbally disruptive behaviors as a family-made videotape (Cohen-Mansfield and Werner, 1997).

Physical activity

Physical activity lifts mood and has a calming effect in younger age groups. In a nursing home study, a daily, 30-minute active exercise program led to a greater improvement in mood than either a gentle walking group or a conversation group (Williams and Tappen, 2007).

Treatment of particular symptoms

Exit-seeking

Some people with dementia try leave their home or a residential facility without heed to their safety. This presents a challenge to carers to minimize risk while still encouraging activity and independence. Evidence shows that:

- The number of locked doors in residential facilities should be kept to a minimum since locking doors makes it more likely that residents will try to leave (Namazi and Johnson, 1992)
- Attempts to leave residential units are reduced if exit doors do not have glass panels and if doors and door handles are obscured so as not to draw residents' attention (Dickinson et al., 1995)

Repeated questioning

Repeated questioning (e.g., "What time is my daughter coming?) can be stressful to caregivers. Suggested strategies include:

- Recognizing the worry that prompts the question (e.g., a fear of abandonment) and providing reassurance ("Your daughter phoned earlier. She's really concerned about you.")
- Giving comfort in a culturally-appropriate way (e.g., hand holding, neck massage)
- Starting an enjoyable activity

People with mild to moderate dementia who ask a question repeatedly (e.g., "What day is it"?) can be taught to look at a card in their pocket that has the answer written on it. Once the behavior is learned, the intervals between instructions are spaced further and further apart. This technique is called spaced retrieval (Malone et al., 2007).

Sleep disturbance

Dementia is sometimes accompanied by a profound disturbance of the daily sleep-wake cycle resulting in broken or limited sleep. Sleeping tablets sometimes have limited effectiveness.

There is evidence that a sleep hygiene program slightly reduces the length of time spent awake at night and greatly reduces the amount of time spent sleeping by day (Alessi et al., 2005). A sleep hygiene program includes the following steps:

- Encouraging activity during the day
- Having a set, personalized bedtime routine
- Keeping nighttime noise and light to a minimum
- Avoiding unnecessary nighttime interruptions

There is no strong evidence that bright light therapy assists with sleep-wake disturbances (Forbes et al., 2004).

Physical environment

A calm, supportive physical environment helps to prevent or minimize BPSD by the following means:

- Ensuring that help is readily available
- Encouraging independence while preserving safety
- Promoting meaningful activity and social engagement

Experts advise that these goals are best achieved by providing:

- Small, home-like residential units
- Ready access to staff members
- A range of shared areas with varied ambience
- Single bedrooms for most people
- Clearly marked access to conveniently situated bathrooms
- Adequate lighting
- A calm environment free of loud music and television
- Access to safe walking paths and gardens
- Maintenance of personal identity, background and culture through use of photographs, mementoes, furnishings and reading materials

Each residential facility is unique and it is difficult to prove that a single design feature has a distinct effect on residents' mood, activity levels and independence. Even so, there is evidence that:

- Home-like environments with single bedrooms are linked to lower rates of anxiety and aggression (Zeisel et al., 2003)

- Residential facilities that offer privacy, a home-like setting, visual and tactile stimulation, and outdoor areas have lower rates of agitation and other symptoms (Bicket et al., 2010)
- Residents spend more time in settings enriched with pleasing sounds, smells and photographs (Cohen-Mansfield and Werner, 1998)

Fleming and Purandare (2010) give an overview of the relationship between the physical environment and the mental well-being of people with dementia.

Nursing home staff members can rate the quality of their physical environment (e.g., its opportunities for social interaction, levels of stimulation and provision for wandering) using the Environmental Audit Tool (Fleming, 2011).

Conclusions

- Many of the benefits of psychosocial treatments stem more from the person who delivers the treatment than from the treatment itself. This is not a problem. Any activity that is enjoyable, healthy and culturally appropriate is to be encouraged.
- The treatments outlined above do appear to have some additional specific benefits. These benefits tend to fade quite quickly once the treatment stops. Once again, this need not be a problem. Few symptoms are present continuously throughout the day. Some are present just at particular times (e.g., "sundowning"). Others arise just in particular circumstances (e.g., personal care). It makes sense, therefore, to target treatments at these times.
- There is good evidence that treatments work best when tailored to people's interests and skills. For those with advanced dementia, this information must be sought from a family member.

References and recommended reading

Alessi, C.A., Martin, J.L., Webber, A.P., Kim, E.C., Harker, J.O., Josephson, K.R. Randomized, controlled trial of a nonpharmacological intervention to improve sleep/wake patterns in nursing home residents. *Journal of the American Geriatrics Society* 2005; 53: 803–810.

Ballard, C.G., O'Brien, J.T., Reichelt, K., Perry, E.K. Aromatherapy as a safe and effective treatment for the management of agitation in severe dementia: the results of a double-blind, placebo-controlled trial with Melissa. *Journal of Clinical Psychiatry* 2002; 63: 553–558.

Beck, C.K., Vogelpohl, T.S., Rasin, J.H., Uriri, J.T., O'Sullivan, P., Walls, R., Phillips, R., Baldwin, B. Effects of behavioral interventions on disruptive behavior and affect in demented nursing home residents. *Nursing Research* 2002; 51: 219–228.

Buchbauer, G., Jirovetz, L., Jager, W., Plank, C., Dietrich, H. Fragrance compounds and essential oils with sedative properties. *Journal of Pharmaceutical Sciences* 1993; 82: 660–664.

Burgio, L., Scilley, K., Hardin, J.M., Hsu, C., Yancey, J. Environmental "white noise": an intervention for verbally agitated nursing home residents. *Journal of Gerontology* 1996; 51: P364–P373.

Clark, M.E., Lipe, A.W., Bilbrey, M. Use of music to decrease aggressive behaviors in people with dementia. *Journal of Gerontological Nursing* 1998; 24: 10–17.

Cohen-Mansfield, J. Instruction manual for the Cohen-Mansfield Agitation Inventory (CMAI). Access: http://www.dementia-assessment.com.au/symptoms/CMAI_Manual.pdf

Cohen-Mansfield, J. Nonpharmacologic interventions for inappropriate behaviors in dementia: a review, summary, and critique. *American Journal of Geriatric Psychiatry* 2001; 9: 361–381.

Cohen-Mansfield, J., Werner, P., Management of verbally disruptive behaviours in nursing home residents. *Journal of Gerontology* 1997; 52A: M369–M377.

Cohen-Mansfield, J., Werner, P. The effects of an enhanced environment on nursing home residents who pace. *Gerontologist* 1998; 38: 199–208.

Cummings, J.L. The Neuropsychiatric Inventory: assessing psychopathology in dementia patients. *Neurology* 1997; 48: S10–S16.

Dickinson, J.I., McLain, J., Marshall-Baker, A. The effects of visual barriers on exiting behavior in a dementia care unit. *Gerontologist* 1995; 35: 127–130.

Edvardsson, D., Fetherstonhaugh, D., Nay, R., Gibson, S. Development and initial testing of the Person-Centered Care Assessment Tool (P-CAT). *International Psychogeriatrics* 2010; 22: 101–108.

Elisabetsky, E., Marschner, J., Souza, D.O. Effects of linalool on glutamatergic system in the rat cerebral cortex. *Neurochemical Research* 1995; 20: 461–465.

Fleming, R. An environmental audit tool suitable for use in homelike facilities for people with dementia. *Australasian Journal on Ageing* 2011; 30: 108–112.

Fleming, R., Purandare, N. Long-term care for people with dementia: environmental design guidelines. *International Psychogeriatrics* 2010; 22: 1084–1096.

Forbes, D., Morgan, D.G., Bangma, J., Peacock, S., Adamson, J. Light therapy for managing sleep, behaviour and mood disturbances in dementia. Cochrane Database of Systematic Reviews 2004: doi: 10.1002/14651858.CD003946.pub2.

Garland, K., Beer, E., Eppingstall, B., O'Connor, D.W. A comparison of two treatments of agitated behavior in nursing home residents with dementia: simulated presence and preferred music. *American Journal of Geriatric Psychiatry* 2007; 15: 514–521.

Gerdner, L.A. Effects of individualized versus classical "relaxation" music on the frequency of agitation in elderly persons with Alzheimer's disease and related disorders. *International Psychogeriatrics* 2000; 12: 49–65.

Holmes, C., Hopkins, V., Hensford, C., MacLaughlin, V., Wilkinson, D., Rosenvinge, H. Lavender oil as a treatment for agitated behaviour in severe dementia: a placebo controlled study. *International Journal of Geriatric Psychiatry* 2002; 17: 305–308.

Jäger, W., Buchbauer, G., Jorovetz, L., Fritzer, M. Percutaneous absorption of lavender oil from a massage oil. *Journal of the Society of Cosmetic Chemists* 1992; 43: 49–54.

Kolanowski, A.M., Litaker, M., Buettner, L. Efficacy of theory-based activities for behavioral symptoms of dementia. *Nursing Research* 2005; 54: 219–228.

Malone, M.L., Skrajner, M.J., Camp, C.J., Neundorfer, M., Gorzelle, G.J. Research in practice II: Spaced retrieval, a memory intervention. *Alzheimer's Care Quarterly* 2007; 8: 65–74.

Namazi, K.H., Johnson, B.D. Pertinent autonomy for residents with dementias: modification of the physical environment to enhance independence. *American Journal of Alzheimer's Disease and Research* 1992; 1: 16–21.

O'Connor, D.W., Ames, D., Gardner, B., King, M. Psychosocial treatments of behavior symptoms in dementia: a systematic review of reports meeting quality standards. *International Psychogeriatrics* 2009a; 21: 225–240.

O'Connor, D.W., Ames, D., Gardner, B., King, M. Psychosocial treatments of psychological symptoms in dementia: a systematic review of reports meeting quality standards. *International Psychogeriatrics* 2009b; 21: 241–251.

Opie, J., Rosewarne, R., O'Connor, D.W. The efficacy of psychosocial approaches to behaviour disorders in dementia: a systematic literature review. *Australian and New Zealand Journal of Psychiatry* 1999; 33: 789–799.

Sherratt, K., Thornton, A., Hatton, C. Emotional and behavioural responses to music in people with dementia: an observational study. *Aging and Mental Health* 2004; 8: 233–241.

Sloane, P.D., Hoeffer, B., Mitchell, C.M., McKenzie, D.A., Barrick, A.L., Rader, J., Stewart, B.J., Talerico, K.A., Rasin, J.H., Zink, R.C., Koch, G.G. Effect of person-centered showering and the towel bath on bathing-associated aggression, agitation, and discomfort in nursing home residents with dementia: a randomized, controlled trial. *Journal of the American Geriatrics Society* 2004; 52: 1795–1804.

Teri, L., Logsdon, R.G., Peskind, E., Raskind, M., Weiner, M.F., Tractenberg, R.E., Foster, N.L., Schneider, L.S., Sano, M., Whitehouse, P., Tariot, P., Mellow, A.M., Auchus, A.P., Grundman, M., Thomas, R.G., Schafer, K., Thal, L.J. Treatment of agitation in AD: a randomized, placebo-controlled clinical trial. *Neurology* 2000; 55: 1271–1278.

Wells, D.L., Dawson, P., Sidani, S., Craig, D., Pringle, D. Effects of an abilities-focused program of morning care on residents who have dementia and on caregivers. *Journal of the American Geriatrics Society* 2000; 48: 442–449.

Williams, C.L., Tappen, R.M. Effect of exercise on mood in nursing home residents with Alzheimer's disease. *American Journal of Alzheimer's Disease and Other Dementias* 2007; 22: 389–397.

Zeisel, J., Silverstein, N.M., Hyde, J., Levkoff, S., Lawton, M.P., Holmes, W. Environmental correlates to behavioral health outcomes in Alzheimer's special care units. *Gerontologist* 2003; 43: 697–711.

Other resources

The following resources are suitable for family and professional caregivers:

Dementia Gateway

Access: http://www.scie.org.uk/publications/dementia/index.asp

The British Social Care Institute for Excellence provides online modules on dementia care. Topics include communication, activities, nutrition and the physical environment. With respect to challenging behaviors, there is detailed information on constructive responses to aggression, repetitive questions, disorientation and refusal of help.

Alzheimer's Australia

Access: http://www.fightdementia.org.au/understanding-dementia/help-sheets-and-update-sheets.aspx

Alzheimer's Australia publishes online fact sheets on a range of challenging behaviors including wandering, sundowning, aggression, agitation and disinhibited behaviors. Each two-page fact sheet addresses the causes of behaviors, prevention and recommended responses.

INTERNATIONAL PSYCHOGERIATRIC ASSOCIATION

www.ipa-online.org

MODULE 6

Pharmacological management

The IPA Complete Guides to Behavioral and Psychological Symptoms of Dementia

BPSD

Specialists Guide

Specialists • Primary Care Physicians • Nurses

MODULE 6: Pharmacological management

Contents

Key messages	**6.3**
General principles	**6.3**
Drug classes and target symptoms	**6.4**
Antipsychotics	6.5
Atypical antipsychotics	6.6
Efficacy of atypical antipsychotics	6.6
Discontinuation of antipsychotics	6.7
Side effect profile of atypical antipsychotics	6.7
Mortality and cerebrovascular events with antipsychotics	6.8
Guidelines for prescribing antipsychotics in BPSD	6.8
Typical antipsychotics	6.9
Side effect profile of typical antipsychotics	6.10
Effects of typical antipsychotics on cognition and function	6.10
Antidepressants	6.11
Trazodone	6.11
Selective serotonin reuptake inhibitors (SSRIs)	6.11
Discontinuation of antidepressants	6.11
Antidepressants used in dementia patients with depression	6.11
Antidepressant dosing recommendations	6.12
Cognitive enhancers	6.13
Cholinesterase inhibitors	6.13
Memantine	6.14
Anticonvulsants	6.15
Carbamazepine	6.15
Valproic acid	6.16
Other anticonvulsants	6.16
Anxiolytics	6.17
Benzodiazepines	6.17
Buspirone	6.17
Miscellaneous drug classes	**6.18**
Lithium	6.18

Adrenergic blockers	6.18
Selegiline	6.18
Melatonin	6.18
Cannabinoids	6.18
Treatment of sleep disturbances in dementia	6.18
Pain management in dementia	6.19
Electroconvulsive therapy for BPSD and depression	**6.19**
Special populations	**6.20**
Dementia with Lewy bodies and Parkinson's disease dementia	6.20
Frontotemporal dementia	6.21
Treatments for inappropriate sexual behaviors	6.21
Treatment of apathy	6.21
References and recommended reading	**6.22**

Key messages

- In general, non-pharmacological approaches are first-line treatment for behavioral and psychological symptoms of dementia (BPSD).
- Medication is indicated for BPSD that are moderate to severe and that impact on a patient's or caregiver's quality of life, functioning, or that pose a safety concern, often in conjunction with non-pharmacological interventions.
- All patients should be informed of the potential risks associated with pharmacological treatments of BPSD and monitored accordingly.
- In elderly patients with dementia, dosages of medication will generally be lower than those used in younger patients and in older people, although the elderly are a heterogeneous group requiring an individualized approach to dosing.
- Antipsychotic medications are most effective in the treatment of psychotic symptoms (hallucinations, delusions), agitation, and aggression.
- Both atypical and typical antipsychotics appear to carry an increased risk for mortality and stroke in patients with dementia. These should be prescribed only after discussing risks and benefits, and their use should be re-evaluated frequently when prescribed.
- Atypical antipsychotics are preferred over typical antipsychotics for BPSD.
- Antidepressants may be used in for the treatment of agitation in dementia as well as for depression in dementia.
- Cholinesterase inhibitors and memantine may be useful in treating BPSD; these medications may also provide cognitive benefits unlike other medications.
- Anticonvulsant medications, especially carbamazepine, may be an option for the treatment of agitation when other medications have failed; current evidence does not favor the use of valproic acid.

General principles

The first step in the management of behavioral and psychological symptoms of dementia (BPSD) involves the careful assessment and correction of any physical, psychosocial, or environmental precipitating or perpetuating factors for the observed behaviors. The clinical presentation and diagnostic criteria for BPSD are presented in Module 2, and etiology is discussed in Module 3. There have been several BPSD review articles (Sink et al., 2005a; Schneider et al., 1990; Schneider et al., 2006a; Herrmann and Lanctôt, 2007; Snowden et al., 2003; Bharani and Snowden, 2005; Trinh et al., 2003; Ballard et al., 2009a; Ballard et al., 2009b) and guidelines (Canadian Coalition for Seniors' Mental Health, 2006b; American Geriatrics and American Association for Geriatric, 2003; Jeste et al., 2008; Herrmann et al., 2007a) that would serve to provide additional details on this topic to complement *The IPA Complete Guides to BPSD*.

- In general, non-pharmacological approaches are the first-line treatment for BPSD (see Module 5)
- Medications are indicated for BPSD symptoms that are refractory to non-pharmacological interventions, severe, or jeopardize the safety of a patient or others, often in conjunction with non-pharmacological interventions
- Prescribing must involve an assessment of patient capacity, informed consent, and judicious dosages
- Dose adjustment should involve slow and cautious dose titration, with careful monitoring for the emergence of side effects
- When using drugs in a population with dementia, due consideration must be given to the age and disease-related changes in the pharmacokinetics, pharmacodynamics, nutritional status, and renal and hepatic function
- Older adults with dementia are more sensitive than younger individuals to the side effects of many drugs, particularly medications that can cause sedation, cognitive-impairment, central anticholinergic side effects, or extrapyramidal symptoms (EPS)
- Many dementia patients, especially those with dementia with Lewy bodies and Parkinson's disease dementia, will demonstrate increased sensitivity to antipsychotics (typical antipsychotics in particular) due to deficits in dopaminergic pathways
- Before deciding whether to treat BPSD with medication, the following questions must be addressed:
  - Does the particular symptom or behavior warrant drug treatment, and why?
  - Is this symptom or behavior likely to respond to pharmacotherapy?
  - Which class of medication is most suitable for this symptom or behavior?
  - What are the predictable and potential side effects of a particular drug treatment?
  - How long should the treatment be continued?

Drug treatment for BPSD should only be initiated after discussion of the risks and benefits of treatment with the patient or a substitute decision maker, and when symptoms have been found to:

- Have no physical cause
- Not be caused by the effects of other medication
- Not be caused by environmental factors
- Have failed to respond to or be appropriate for non-pharmacological interventions

Drug classes and target symptoms

The issue of whether a particular drug is effective can be a difficult one. Pharmacological treatment is indicated, however, where there is evidence from research and practice that particular symptoms or behaviors respond to a particular drug intervention. The use of different pharmacological agents in the management of BPSD is outlined in Table 6.1.

Table 6.1: Pharmacological therapy and BPSD.

Drug category	Target symptom
Atypical antipsychotics	Psychosis, aggression, agitation, sleep-wake cycle disturbances
Typical antipsychotics	Psychosis, aggression, agitation, sleep-wake cycle disturbances
Antidepressants	
Trazodone	Sleep-wake cycle disturbances, agitation, aggression, anxiety, depressive syndromes
Selective Serotonin Reuptake Inhibitors (SSRIs)	Depressive syndromes, agitation, irritability, psychosis
Other antidepressants (i.e., mirtazapine, bupropion)	Depressive syndromes
Tricyclic antidepressants (TCAs)	Depressive syndromes
Cognitive Enhancers	
Cholinesterase inhibitors	Cognition, apathy, aberrant motor behavior, anxiety, depressive syndromes, psychosis (delusions, hallucinations)
Memantine	Cognition, aggression, agitation, irritability, psychosis
Other Medications	
Anticonvulsants	Agitation, aggression, manic-like symptoms, sleep disturbance
Benzodiazepines	Anxiety, agitation, sleep disturbance

It is important to identify target symptoms or behaviors, and to use medications that may address several different symptoms to avoid unnecessary polypharmacy (sedating atypical antipsychotic for individuals with agitation, psychosis, and sleep disturbance).

Drug treatment for BPSD should be time-limited when possible. Drug dosages should be reviewed and reduced or discontinued when possible, and all psychotropics should be reviewed at a minimum of every three months. The outcome of a pharmacological treatment should be monitored on a routine basis for both efficacy and side effects.

Antipsychotics

There are two broad categories of antipsychotic medications that are used in dementia patients with BPSD:

1. Atypical antipsychotics have broad, drug specific effects on dopaminergic, serotonergic, and other receptors with a decreased propensity to cause EPS. Clozapine was the first atypical antipsychotic available, but there are now a number of agents available including risperidone, olanzapine, quetiapine, aripiprazole, and ziprasidone.
2. Typical (conventional) antipsychotics—Actions are primarily mediated through dopamine D2-antagonism and are more likely to cause extrapyramidal symptoms (EPS). Examples of such agents are haloperidol, perphenazine, and loxapine.

Typical antipsychotics were once the most common psychotropic medication prescribed to agitated patients in nursing homes and long-stay institutions (Ray et al., 1980; Gilleard et al., 1983). However, only a modest evidence base exists to support their use, and atypical antipsychotics are now being prescribed much more frequently to this population (Kamble et al., 2008).

Atypical antipsychotics

There are several randomized controlled double-blind studies to suggest that antipsychotics are effective in the treatment of BPSD and may have improved side effect profiles when compared to typical antipsychotics (De Deyn et al., 1999; Chan et al., 2001). In particular, atypical antipsychotics are associated with less EPS and a lower propensity to cause tardive dyskinesia.

Efficacy of atypical antipsychotics. There are published randomized controlled trials for risperidone, olanzapine, aripiprazole, and quetiapine for the treatment of BPSD in older adults with Alzheimer's disease. There have been several systematic reviews and meta-analyses of atypical antipsychotics for BPSD (Ballard and Waite, 2006; Schneider et al., 2006a; Lee et al., 2004; Herrmann and Lanctôt, 2007; Sink et al., 2005b) that contain additional information on unpublished studies.

The largest trial to-date investigating the efficacy and safety of atypical antipsychotics for BPSD is the CATIE-AD trial. This multicenter trial compared risperidone, olanzapine, quetiapine, and placebo for agitation in Alzheimer's disease. The primary outcome was time to discontinuation of therapy for any reason. Overall rates of discontinuation for any cause were similar among the four groups, although the time to discontinuation of therapy for lack of efficacy favored olanzapine and risperidone (Schneider et al., 2006b) over placebo and quetiapine. Symptoms most likely to respond to treatment were anger, aggression, and psychosis (Sultzer et al., 2008).

Risperidone at a dose of approximately 1 mg/day has been found to be superior to placebo in the treatment of BPSD, particularly for aggressive behaviors in dementia patients and for psychotic symptoms (Katz et al., 1999; De Deyn et al., 1999; Brodaty et al., 2003; Chan et al., 2001). Risperidone at this dose is well tolerated and has an EPS profile similar to placebo (Katz et al., 1999; De Deyn et al., 1999; Brodaty et al., 2003) and superior to haloperidol (De Deyn et al., 1999; Chan et al., 2001). There is also at least one published, randomized controlled trial that did not demonstrate significant benefit of risperidone over placebo (Mintzer et al., 2006). Another trial comparing flexibly dosed risperidone (0.5-2.0 mg) or olanzapine (2.5-10 mg) to placebo found no significant benefit of either active drug when compared to placebo (Deberdt et al., 2005). The rate of discontinuation was lowest in the placebo group, and olanzapine had significantly higher rates of discontinuation when compared to both placebo and risperidone.

A multicenter nursing home study of olanzapine in BPSD has shown that 5 and 10 mg/day doses of olanzapine was significantly superior to placebo and well tolerated in treating agitation/aggression. Curiously, the 5 mg dose showed greater efficacy than the 10 mg dose (Street et al., 2000). A second trial of olanzapine found that olanzapine in doses of 5 and 7.5 mg did not result in significant improvement in BPSD when compared to placebo in the primary outcome of the study (De Deyn et al., 2004).

A fixed dose, randomized controlled trial compared quetiapine 200 mg daily, 100 mg daily, and placebo for BPSD. The group receiving 200 mg daily had improvement over the placebo group on the primary outcome (Zhong et al., 2007). A second randomized controlled trial of quetiapine (mean dose 96 mg), haloperidol (mean dose 1.9 mg), or placebo did not find any significant difference among the three groups on global measures of BPSD, although agitation may have been improved with the two drug groups when compared to placebo (Tariot et al., 2006). Quetiapine tended to be better tolerated than haloperidol. A third trial of quetiapine (50–100 mg) compared to rivastigmine and placebo did not find that either active treatment was superior to placebo. Greater cognitive decline was observed with quetiapine when compared to placebo (Ballard et al., 2005).

At least two randomized placebo-controlled trials of aripiprazole for BPSD have been completed. The first found no difference in the primary endpoint of psychosis as measured on the NPI or on global measures of change (De Deyn et al., 2005). The second trial found that 10 mg of aripiprazole was superior to placebo on measures of psychosis, agitation, and global improvement, while lower doses (2 mg or 5 mg) were not effective (Mintzer et al., 2007). Adverse event rates were not statistically significant between the treatment groups.

Open-label trials of ziprasidone have also demonstrated efficacy, although adverse events were also commonly observed (Rocha et al., 2006).

Discontinuation of antipsychotics. There are a number of studies to show that dementia patients' symptoms actually remain stable or improve when they are withdrawn from a conventional neuroleptic (Thapa et al., 1994; Horowitz et al., 1995; Bridges-Parlet et al., 1997). There are several randomized, placebo-controlled studies examining the effects of discontinuing long-term treatment with antipsychotics (van Reekum et al., 2002; Cohen-Mansfield et al., 1999; Ruths et al., 2008; Ballard et al., 2008; Devanand et al., 2012). Most studies have found that many individuals can have antipsychotics safely discontinued without worsening of behavioral symptoms. One recent trial, however, reported a significantly increased risk of relapse up to four months after discontinuation of risperidone in patients with psychosis or agitation and aggression (Devanand et al., 2012). Predictors of successful discontinuation antipsychotics include lower daily doses of antipsychotics (van Reekum et al., 2002; Ruths et al., 2008) and lower baseline severity of behavioral symptoms (Ballard et al., 2008). Most studies have examined relatively short-term behavioral outcomes, although one study found no significant difference in behavioral symptoms following discontinuation at six months (Ballard et al., 2008). No differences in other outcomes, including cognition and adverse events, were noted between continuation and discontinuation groups in the placebo-controlled trials (Declercq et al., 2013), but long-term mortality follow-up data from one study indicated that discontinuation of antipsychotics was associated with reduced mortality at 12, 24, and 36 months (Ballard et al., 2009c).

Side effect profile of atypical antipsychotics. Like all medications, side effects need to be monitored during drug treatment with atypical antipsychotics. Most atypicals may be associated with dyslipidemia, impaired glucose tolerance, and weight gain. The risk of weight gain may be greatest in females treated with olanzapine or quetiapine, and olanzapine may be associated with the greatest adverse effects on cholesterol (Schneider et al., 2009). All antipsychotics are associated with an increased risk of falls and fractures. In addition, clozapine has significant anticholinergic and postural hypotensive effects, and it is associated with a

risk of agranulocytosis that requires weekly white blood cell count monitoring. Olanzapine, like clozapine, also possesses anticholinergic activity. Risperidone can be associated with the emergence of EPS, postural hypotension, and sedation at higher doses. Quetiapine can be associated with sedation and postural hypotension. Ziprasidone can also cause prolongation of the QT interval, although it likely has the most benign metabolic side effect profile.

Mortality and cerebrovascular events with antipsychotics. European, American, and Canadian regulatory agencies have issued warnings regarding an increased risk of adverse events in patients with dementia receiving these drugs for management of BPSD. The initial 2005 warning issued by the United States Food and Drug Administration (FDA, 2005) was based upon a meta-analysis of 17 trials of atypical antipsychotics in patients with dementia. The trials showed an increased relative risk of death of approximately 1.7, mainly due to vascular or infectious causes (Schneider et al., 2005). The risk of ischaemic stroke in particular was emphasized by the FDA based upon studies predating this meta-analysis. The FDA warning was subsequently extended to cover all antipsychotics (FDA, 2008) after retrospective population-based studies of American (Wang et al., 2005) and Canadian (Schneeweiss et al., 2007; Gill et al., 2007) data demonstrated that typical antipsychotics also showed a similar increased risk of death. More recent studies have even suggested that the risk of death with typical antipsychotics may even be greater than with the atypical ones (Liperoti et al., 2009; Hollis et al., 2007) and that those who remain on long-term (12 months and more) antipsychotic therapy have an increased and persistent risk of mortality with decreased survival at up to 3 years follow-up (Ballard et al., 2009).

It should be noted that, although antipsychotics are associated with increased risk of death, the absolute increase in mortality is between 1–2% (Meeks and Jeste, 2008). A prudent recommendation is that antipsychotics should be used more judiciously than they have been in the past. Studies examining rates of antipsychotic prescribing in the United States after the FDA warnings demonstrated that the prescription of these medications for patients with BPSD has decreased (Dorsey et al., 2010). However, some authors believe that current prescription practices are still not cautious enough (Rochon and Anderson, 2010), and certainly more research needs to be urgently conducted regarding these concerns. In the meantime, before initiating the use of these medications, patients and substitute decision-makers should be informed about the warnings regarding them and the data supporting these warnings.

Guidelines for prescribing antipsychotics in BPSD. On the basis of evidence from the literature, the following clinical guidelines for the use of antipsychotics are recommended:

- Use in conjunction with non-pharmacological interventions
- Moderate to severe BPSD, especially agitation, aggression, or psychosis
- Discuss risk of common side effects (e.g., falls, postural hypotension, sedation) and less common but serious side effects (e.g., cerebrovascular accidents, mortality)
- Use antipsychotics for as short a time period as possible and attempt to reduce dosages and discontinue antipsychotics when possible
- Check for a history of antipsychotic sensitivity, and consider the diagnosis of dementia with Lewy bodies before prescribing any antipsychotic

The suggested starting doses and maximum dosages are listed in Table 6.2. In general, increases in dosage should occur at a maximum once weekly unless more rapid dose titration is required. Patients should be monitored carefully for the development of adverse effects including EPS, postural hypotension, anticholinergic side effects, sedation, and falls.

Set duration for treatment and monitor. A duration of 12-weeks treatment is recommended and should be reviewed. If a 4- to 6-week trial of one agent at an adequate dose fails to decrease the frequency, severity, or impact of a target symptom, a trial of a second agent would be indicated.

Table 6.2: Clinical recommendations for dosing of typical and atypical antipsychotics for BPSD

Drug	Starting Dose (mg)	Dose range (mg) Schedule
Risperidone	0.25	0.5–2 once daily
Olanzapine	2.5	5–10 once daily
Aripiprazole	2.0	5–10 daily
Quetiapine	25.0	25–150 daily divided doses
Haloperidol	0.5	0.5–2 once daily
Ziprasidone*	20.0	40–80 in divided doses, administered with meals (ECG monitoring of QTc required)
Clozapine*	6.25	12.5–100 once or twice daily

*Information from open-label trials only

Typical antipsychotics

Three systematic reviews have evaluated the effects of typical antipsychotics on symptoms of BPSD. The first review included 17 placebo-controlled studies, 7 of which were of sufficient quality to be included in meta-analysis (Schneider et al., 1990). The doses of medications in these studies were modest (chlorpromazine equivalent 66–267/mg day). There was a small, but statistically significant difference between all antipsychotics and placebo in the meta-analysis. At the time of this meta-analysis, haloperidol and thioridazine were the most commonly utilized antipsychotics for BPSD. Meta-analysis comparing thioridazine or haloperidol to comparator antipsychotics did not find any significant difference between these two agents and all other antipsychotics.

A more recent meta-analysis included 16 studies of typical antipsychotics (Lanctôt et al., 1998). Overall, 61% of individuals treated with typical antipsychotics had a clinical response, compared to 34% of individuals who received placebo. The trials tended to have fair quality in terms of potential risk of bias. Dosages of medication were relatively low in most studies, defined by daily dose equivalents. There were no differences noted in response rates for different classes of antipsychotic potency. However, higher rates of side effects were observed for all antipsychotics when compared to placebo, although there were no differences in trial withdrawals. There was no significant difference in side effects or drop-outs for butyrylphenones when compared to other antipsychotics.

A review of five studies examining haloperidol for agitation in dementia found that haloperidol was effective in reducing symptoms of aggression but not overall levels of agitation (Lonergan et al., 2002). There was no statistically significant difference in dropout rates for haloperidol when compared to placebo.

There are relatively few studies comparing typical antipsychotics to atypical antipsychotics. Most trials have found similar efficacy for typical antipsychotics when compared to atypical antipsychotics, although some studies have found greater efficacy of atypicals when compared to typicals. Atypical antipsychotics also seem to be associated with less extrapyramidal side effects when compared to typical antipsychotics.

Based on the evidence (Schneider et al., 1990; Barnes et al., 1982; Petrie et al., 1982; Devanand et al., 1989; Finkel et al., 1995), the symptoms that appear to be most responsive to typical antipsychotic medications include agitation, hallucinations, and hostility.

Side effect profile of typical antipsychotics. The most common side effects of antipsychotics are the following:

- Extrapyramidal side effects (EPS) (e.g., bradykinesia, tremor, mask-like facies), especially with high-potency conventional agents such as haloperidol and thiothixene, although EPS can occur with low-potency typical antipsychotics as well.
- Postural hypotension and anticholinergic side effects (e.g., dry mouth, constipation, urinary retention, and delirium) are more likely with low-potency conventional agents such as chlorpromazine.
- Elevated risk of tardive dyskinesia with long-term treatment. The estimated incidence of tardive dyskinesia in the elderly following conventional neuroleptic treatment is 25% following one year of treatment (Woerner et al., 1998). For this reason an 8–12 week (time-limited) exposure of dementia patients to typical antipsychotics is to be encouraged.

When side effects occur, the dose of conventional neuroleptic should be reduced or discontinued, depending on the severity of the adverse event, and an alternative agent considered. The use of anticholinergic agents to treat drug-induced EPS is discouraged, because they are likely to increase delirium and other anticholinergic adverse effects.

Effects of typical antipsychotics on cognition and function. It is possible that long-term exposure to conventional neuroleptics, while improving behavioral disturbance, results in a deterioration in functional ability and a progression of dementia. Treatment with haloperidol over 6–8 weeks was associated with a decline in cognition as measured with the Mini-Mental State Examination (MMSE) (Devanand et al., 1989).

A number of studies have reported an association between the presence of psychosis or psychiatric symptoms and a more rapid rate of progression (McShane et al., 1997). The association between psychosis and a more rapid cognitive deterioration could also be explained by a worsening of cognition and functional abilities with typical antipsychotics (McShane et al., 1997; Stern et al., 1987; Chui et al., 1994). It has also been suggested that the worsening of cognitive impairment in patients with Alzheimer's disease could result through central anticholinergic side effects of low-potency conventional antipsychotics.

Antidepressants

Trazodone. Serotonin has an important role in the development of behavioral symptoms in dementia (Lawlor, 1990), and a number of antidepressants have been utilized for BPSD. Both open-label studies (Pinner and Rich, 1988; Aisen et al., 1993; Lawlor et al., 1994) and three placebo-controlled trials (Lawlor et al., 1994; Sultzer et al., 1997; Teri et al., 2000) found that trazodone may have modest effects for the treatment of agitation in patients with BPSD. Trazodone has sedative properties and thus may also be useful in treating sleep disturbances associated with dementia. Doses varying from 50–250 mg/day have been used in studies, and the recommended dose range for patients with severe BPSD would generally not exceed 300 mg/day. The main side effects of trazodone are somnolence and postural hypotension, and more rarely trazodone can be associated with priapism.

Selective serotonin reuptake inhibitors (SSRIs). Placebo-controlled trials of citalopram (Nyth and Gottfries, 1990) and sertraline (Finkel et al., 2004) have found some benefit on symptoms of BPSD while one small trial of fluoxetine was negative (Auchus and Bissey-Black, 1997). Studies comparing fluoxetine (Auchus and Bissey-Black, 1997) and sertraline (Gaber et al., 2001) to haloperidol found similar effects for antidepressants with trends towards improved tolerability. Studies of citalopram compared to perphenazine (Pollock et al., 2002) and risperidone (Pollock et al., 2007) have also shown that the effects of citalopram are similar to antipsychotics for BPSD. A recent pilot study comparing escitalopram and risperidone found both effective at reducing behavioral and psychotic symptoms. Although improvement was earlier with risperidone, escitalopram was better tolerated (Barak et al., 2011).

Discontinuation of antidepressants. Few studies have examined the effect of withdrawing antidepressants in patients with dementia. A small, open-label trial and a subsequent placebo-controlled discontinuation trial have suggested that selective serotonin reuptake inhibitors can be safely discontinued in most patients (Bergh and Engedal, 2008; Bergh et al., 2012). In the placebo-controlled trial, the majority of nursing home patients on selective serotonin reuptake inhibitors tolerated antidepressant discontinuation without change however a small but significant increase in depressive symptoms was noted (Bergh et al., 2012). Patients with prior history of depressive disorders were excluded but the indication for the antidepressant treatment was not specified. An increase in neuropsychiatric symptoms was also observed but the difference did not reach significance.

Side effects associated with SSRIs can include gastrointestinal upset, diarrhea, akathisia, restlessness, sleep disturbance (insomnia/somnolence), hyponatremia, and increased risk of bleeding, especially in patients taking anti-platelet agents. SSRIs are also associated with falls and fractures.

Antidepressants used in dementia patients with depression. A randomized placebo-controlled study found that paroxetine was as effective, and better tolerated, than imipramine in treating depression in dementia (Katona et al., 1998). An initial study of sertraline in treating dementia found significant benefits over placebo (Lyketsos et al., 2000); however, a recent large-scale replication of this trial failed to show significant benefit for sertraline over placebo (Rosenberg et al., 2010). Another large trial of sertraline (or sertraline) and mirtazapine in combination

similarly failed to demonstrate an advantage over placebo (Banerjee et al., 2011), and an older placebo-controlled trial of sertraline also failed to show a significant benefit (Magai et al., 2000). A placebo-controlled study of fluoxetine for depression in dementia also failed to find significant benefit of drug over placebo (Petracca et al., 2001).

A systematic review concluded that due to small sample sizes and few trials of newer and more commonly used antidepressants, evidence to confirm the efficacy of antidepressants in treating depression in dementia was insufficient (Bains et. al., 2009). Likewise, results of a more recent meta-analysis were suggestive but did not confirm benefit, although the authors noted that this may reflect the paucity of evidence as opposed to ineffectiveness (Nelson and Devanand, 2009).

There is anecdotal evidence supporting the use of tricyclic antidepressants in depressed dementia patients (Reynolds et al., 1987). Results of a trial with imipramine (Reifler et al., 1989) for depression in dementia were negative, while clomipramine (Petracca et al., 1996) showed benefit over placebo. Tricyclic antidepressants are associated with problematic and frequent side effects in dementia patients, and must be used with caution. Tricyclic antidepressants can cause side effects including postural hypotension, blurred vision, urinary hesitancy and intracardiac conduction defects, and central anticholinergic side effects including delirium and falls. If tricyclic antidepressants are to be used in depressed dementia patients, secondary (e.g., nortriptyline, desipramine) rather than tertiary amines (e.g., amitriptyline, doxepin) are preferred, due to better tolerability.

When an antidepressant is selected, overall tolerability as well as favorable effects on anxiety, sleep disturbance, and agitation should also be considered. Mirtazapine may also be a useful treatment for use in depressed patients with dementia, given its sedative, anxiolytic, and appetite-stimulating properties (Raji and Brady, 2001; Cakir and Kulaksizoglu, 2008).

In addition, other placebo-controlled trials carried out with antidepressants such as maprotiline and minaprine have indicated that depressed dementia patients respond to antidepressants (Passeri et al., 1987; Fuchs et al., 1993). Other agents such as moclobemide, a reversible inhibitor of monoamine oxidase A, at doses of 150–600 mg/day have a proven favorable side effect profile in elderly dementia patients and can be useful in the treatment of depression (Roth et al., 1996).

Antidepressant dosing recommendations. If an antidepressant is to be prescribed, selective serotonin reuptake inhibitors should be used as first line agents. Like all medications in this population, doses should start low and be increased gradually. A dosing schedule for selected antidepressants is shown in Table 6.3. Patients with depression should be treated for one to two years to prevent relapse (Canadian Coalition for Seniors' Mental Health, 2006a).

The following antidepressants should be preferentially used in patient with dementia due to decreased anticholinergic activity, decreased potential for drug-drug interactions, and decreased likelihood of accumulation in renal or hepatic impairment: citalopram, escitalopram, sertraline, venlafaxine, or mirtazapine.

Table 6.3: Dosing schedule for selected antidepressants in patients with dementia

Drug	Starting Dose (mg)	Dose range (mg) Schedule
Trazodone	25	50–300
Citalopram	10	10–40
Escitalopram	5	10–20
Sertraline	25	50–100
Venlafaxine	37.5	75–150
Mirtazapine	15	15–45
Duloxetine	20	20–60
Bupropion	100	150–300
Moclobemide	150	150–600
Nortriptyline	10	25–100

Cognitive enhancers

Cholinesterase inhibitors. Three cholinesterase inhibitors (donepezil, galantamine, and rivastigmine) are currently indicated for the treatment of cognitive symptoms in Alzheimer's disease, where they have proven clinically modest effects on dementia at various levels of severity (Birks, 2006). These medications are used "off-label" to treat BPSD.

There has been one trial of cholinesterase inhibitors for the treatment of BPSD. This trial studied the effect of donepezil 10 mg daily on symptoms of agitation during a 12-week trial. The study failed to demonstrate a significant effect of donepezil on treating symptoms of agitation in individuals with Alzheimer's disease (Howard et al., 2007b) as measured by change in symptoms of agitation or proportion of individuals with significant improvement in agitation.

A recent, systematic review of 14 randomized controlled studies examining the use of cholinesterase inhibitors in BPSD found three studies that showed a significant effect of cholinesterase inhibitors on reducing BPSD as measured on NPI scores (Rodda et al., 2009). However, the eleven other trials reviewed showed no significant reduction of various BPSD for cholinesterase inhibitors when compared to placebo. Included among the negative trials was the only prospective trial to examine the effect of cholinesterase inhibitors on BPSD as a primary outcome (Howard et al., 2007a). A meta-analysis of nine randomized trials found that cholinesterase inhibitors were statistically significant over placebo in reducing NPI scores, but the magnitude of the effect was of questionable clinical significance (Campbell et al., 2008). The authors noted that the result became non-significant when only trials examining moderate-to-severe dementia were analyzed. A recent observational study of 938 Italian patients starting cholinesterase inhibitors for cognitive enhancement failed to show any improvement in BPSD symptom measures at 36 weeks, although the lack of a comparator group means that this study could not address whether the patients would have deteriorated more rapidly if not taking the medications (Santoro et al., 2010). Importantly, there were no differences shown among the three different medications.

Clinical observation suggests that cholinesterase inhibitors may be useful in targeting specific BPSD symptoms. Subgroup analyses of larger trials, and uncontrolled studies that have specifically investigated specific symptoms in addition to global measures of BPSD, suggest that apathy, aberrant motor behavior, hallucinations and delusions, and anxiety and depression may all be specifically improved with cholinesterase inhibitors (Gauthier et al., 2002; Feldman et al., 2005; Holmes et al., 2004; Aupperle et al., 2004; Cummings et al., 2004). The reviews mentioned earlier look more at global measures and may not capture this pattern of symptom response. There is also some suggestion that rivastigmine may be more useful in reducing hallucinations in Lewy body disease compared to Alzheimer's disease, although the evidence to support this is preliminary (Rozzini et al., 2007).

Additional studies have found that withdrawal of cholinesterase inhibitors may lead to worsening of BPSD. A trial of donepezil in participants with Alzheimer's disease and significant BPSD received open-label treatment for 12 weeks after which they were randomized to either placebo or continued treatment (Holmes et al., 2004). Individuals who received continued treatment with donepezil had decreased levels of BPSD when compared to placebo.

All three of the cholinesterase inhibitors are initially prescribed at subtherapeutic doses, on a slow dose-escalation regimen, in order to habituate patients to any potential side effects. The dosing schedules allow achievement of steady plasma levels of the medication before proceeding to a higher dose. A transdermal rivastigmine patch that has recently become available in some countries was equivalent to oral rivastigmine in the treatment of cognitive symptoms, and patients reported fewer gastrointestinal side effects (Winblad et al., 2007).

Common side effects of cholinesterase inhibitors include gastrointestinal symptoms such as diarrhea, gastrointestinal upset, and anorexia. Cholinomimetic cardiac effects have the potential to exacerbate pre-existing arrhythmias, including heart block. Some clinicians advocate obtaining an electrocardiogram prior to the prescription of these medications.

Memantine. Memantine is an NMDA glutamate receptor antagonist that is moderately effective in the symptomatic treatment of cognitive symptoms of dementia. As with cholinesterase inhibitors, there is a modest but growing body of evidence suggesting that this medication may also be useful in treating concurrent BPSD.

As of yet, only two prospective trials have examined the use of memantine in treating BPSD as a primary outcome. A randomized placebo-controlled trial of memantine added to donepezil in institutionalized patients with AD and clinically significant agitation found no effect of memantine on the CMAI score at 6 or 12 weeks. A statistically significant reduction in NPI score, a secondary outcome, favored memantine, but the clinical relevance of the 7–10 point decrease compared to placebo remained unclear as no significant change in global clinical improvement was noted (Fox et al., 2012). A similar trial in community dwelling AD patients with agitation and aggression at baseline showed no significant benefit of memantine compared to placebo on NPI score or secondary measures of behavior but lacked statistical power to detect an effect (Hermann et al., 2013).

Data from retrospective analyses and secondary outcome of trials provide additional information on the potential effects of memantine on BPSD (Grossberg et al., 2009; Cummings et al., 2006; Gauthier et al., 2005; Wilcock et al., 2008; Gauthier et al., 2008; Winblad and Poritis, 1999; van Marum, 2009). In a recent study in patients with moderate to severe AD, memantine was associated with a statistically significant four point reduction on the NPI as compared to placebo, while a meta-analysis of five trials (including three previously unpublished trials) concluded that memantine treatment was associated with a two point reduction on the NPI (Howard et al., 2012; Maidment et al., 2008). This was consistent with the results obtained in the Cochrane review sub-analysis looking at the effects of memantine for treating BPSD (McShane et al., 2006). The clinical significance of such a modest reduction in NPI scores is unclear. Studies that have investigated individual symptoms suggest that memantine can be useful in treating specifically delusions and hallucinations, agitation and aggression, and irritability (Cummings et al., 2006; Gauthier et al., 2008; Wilcock et al., 2008). In the largest of these studies, the effect size of memantine on agitation was approximately equivalent to that seen for antipsychotics (Wilcock et al., 2008). Importantly, one large observational study performed in France demonstrated that prescribing memantine resulted in reduced prescription of other psychotropic medications (Vidal et al., 2008), which provides further indirect evidence of its usefulness.

In some studies it has been observed that memantine, when compared to placebo, appeared to delay the emergence of BPSD, especially agitation, in patients without agitation at baseline (Wilcock et al., 2008; Gauthier et al., 2008). This has also been observed in patients who were concurrently taking donepezil (Cummings et al., 2006). These observations were from retrospective, post-hoc analyses, and need confirmation in prospective controlled trials. Thus, memantine may be effective in delaying the emergence of agitation, although this drug should not be prescribed with only this goal in mind.

Memantine is generally well-tolerated with the most commonly reported side effects being constipation, somnolence, dizziness, hypertension, headache, and anorexia. Confusion and anxiety may also arise as side effects of this treatment. In some cases, memantine may precipitate psychosis, especially in patients who have dementia with Lewy bodies (Ridha et al., 2005; Menendez-Gonzalez et al., 2005). Thus, while memantine is potentially useful for the treatment of BPSD, it also has the potential to precipitate such symptoms.

Anticonvulsants

Anticonvulsants may represent a useful alternative in cases where medications from other drug classes are found to be ineffective. Limited evidence for their efficacy comes from open-label studies, as well as some randomized controlled trials as reviewed in other articles (Konovalov et al., 2008; Amann et al., 2009). In general, the older anticonvulsants, especially carbamazepine, have the most evidence and experience for use in BPSD, but evidence is slowly beginning to accumulate for the use of some of the newer anticonvulsants.

Carbamazepine. Case reports (Essa, 1986; Leibovici and Tariot, 1988; Patterson, 1988; Marin and Greenwald, 1989), as well as open-label prospective studies (Gleason and Schneider, 1990; Lemke and Stuhlmann, 1994; Tariot et al., 1994) suggested that carbamazepine can be used to treat aggression, hostility, agitation, and mania-like symptoms. There is a case report of

its use for treating sexual disinhibition (Freymann et al., 2005). There have also been smaller randomized controlled trials examining this drug showing an effect on aggression, but these were open-label or had other methodological limitations (Olin et al., 2001; Cooney et al., 1996; Tariot et al., 1998). Importantly, this drug has been studied in patients who failed to respond to neuroleptics, where it was found to be useful in open-label studies (Lemke and Stuhlmann, 1994; Gleason and Schneider, 1990) and one randomized controlled trial (Olin et al., 2001). Thus, there is limited evidence that carbamazepine may be useful in BPSD, particularly in treating aggression and agitation. However, its side effects and drug interactions can, at times, limit the usefulness of this drug. Carbamazepine may be associated with a decreased risk of mortality when compared to antipsychotics in at least one large observational study (Hollis et al., 2007).

Valproic acid. Case reports have suggested that valproic acid preparations were useful in controlling aggression, agitation, and other mania-like symptoms in Alzheimer's disease (Sandborn et al., 1995; Takahashi and Akagi, 1996) and vascular dementia (Buchalter and Lantz, 2001). This observation has been repeated in several larger retrospective case series (Sival et al., 1994; Narayan and Nelson, 1997; Kunik et al., 1998; Meinhold et al., 2005) and small open-label trials (Lott et al., 1995; Mellow et al., 1993; Haas et al., 1997; Porsteinsson et al., 1997; Sival et al., 2004; Forester et al., 2007; Kasckow et al., 1997; Herrmann, 1998; Porsteinsson et al., 2003), mainly in patients with Alzheimer's disease. Some studies have suggested that patients on valproate required lesser doses of antipsychotics (Narayan and Nelson, 1997; Meinhold et al., 2005). However, some studies also reported that patients suffered side effects from valproate, especially somnolence and ataxia (Forester et al., 2007).

There have been five prospective, blinded, randomized controlled trials carried out examining the use of valproic acid derivatives for the treatment of agitation and mania-like symptoms (Porsteinsson et al., 2001; Tariot et al., 2001; Sival et al., 2002; Tariot et al., 2005; Herrmann et al., 2007b). None of these have shown a statistically significant effect of valproic acid to reduce BPSD, although one showed a trend toward reduced agitation (Porsteinsson et al., 2001). More importantly, most of these randomized controlled trials revealed a trend toward greater numbers of adverse events (Tariot et al., 2001; Konovalov et al., 2008). It would therefore appear that despite some promising observational evidence, the best evidence available does not support the use of valproic acid in the management of BPSD (Lonergan and Luxenberg, 2009).

Other anticonvulsants. A double-blind, randomized, placebo-controlled trial has been carried out examining the use of oxcarbazepine to treat agitation in patients with dementia (Sommer et al., 2009). This trial, which was among the most methodologically sound trials examining anticonvulsants for BPSD, did not show any significant effect.

Several case reports and case series have reported success using gabapentin to treat BPSD (Kim et al., 2008). In most patients, sedation is the main side effect. As a cautionary note, there has been a report of two patients with dementia with Lewy bodies who demonstrated a dramatic worsening of their illness (Rossi et al., 2002). Gabapentin may present a useful alternative in patients with agitation, hypersexuality, or sleep disturbance who are not responding to other classes of medication, but much more research is needed on its use.

Case reports (Devarajan and Dursun, 2000; De Leon, 2004; Tekin et al., 1998) and retrospective reviews (Aulakh et al., 2005) have suggested that lamotrigine may also be useful in treating BPSD. In all of the studies, lamotrigine was well tolerated. It can be prescribed at dosages of 12.5–25 mg daily, increasing up to 300 mg-per-day divided in two doses.

Topiramate has been studied in one open-label retrospective study of 15 dementia patients with BPSD (Fhager et al., 2003). It was used as monotherapy or as adjunctive therapy in doses ranging from 25–150mg per day, and caused a significant reduction in agitation.

A recent retrospective, open-label study of 37 patients with mania-like symptoms (defined as disinhibition, emotional lability, irritability, aggression, and agitation) refractory to other medications showed a marked improvement in symptoms with this levetiracetam treatment (Kyomen et al., 2007). An open-label prospective study found reductions in the NPI scores, but importantly also found significant reductions in MMSE scores and had patients with side effects including lethargy and paradoxically increased agitation (Weiner et al., 2005).

Anxiolytics

Benzodiazepines. Benzodiazepines are a commonly prescribed medication class for BPSD. A number of controlled studies have shown that benzodiazepines decrease agitated behaviors compared with placebo to the same extent as typical antipsychotics during short-term use (Chesrow et al., 1965; Kirven and Montero, 1973; Covington, 1975; Coccaro et al., 1990). There has been one study comparing intramuscular olanzapine, lorazepam, and placebo for the acute treatment of agitation in dementia. Both olanzapine (2.5 or 5 mg) and lorazepam (1 mg) produced significant acute reductions in agitation when compared to placebo. Side effects were similar between both active treatments and placebo (Meehan et al., 2002).

Short-acting benzodiazepines such as oxazepam or lorazepam that do not accumulate are preferred, and are most effective if used for short periods at low doses (e.g., lorazepam 0.5–2.0 mg/day). Lorazepam may be especially useful as a premedication for infrequent periodic episodic symptoms or where agitation or distress can be anticipated (e.g., minor surgical procedures or dental visits).

Side effects are common, and most often include excessive sedation (drowsiness), ataxia, amnesia, and confusion. The risk of falls with benzodiazepines is similar for short-acting when compared to long half-life medications with the greatest risk of falls associated with recent initiation of treatment (Cumming and Couteur, 2003). After patients have been maintained on benzodiazepines for more than 4–6 weeks, a gradual taper is advised prior to discontinuation to avoid withdrawal symptoms.

Buspirone. Buspirone is a serotonin 5-HT1a partial agonist that has been found to be helpful in agitated dementia patients in case reports and open-label studies (Herrmann and Eryavec, 1993; Levy et al., 1994). A small double-blind trial found that buspirone was associated with decreases in agitation and tension when compared to haloperidol (Cantillon et al., 1996). However, a placebo-controlled crossover study of buspirone (at doses of 30 mg/day), trazodone, or placebo found that buspirone was well tolerated, but had limited effects on agitation (Lawlor et al., 1994).

Miscellaneous drug classes

Lithium

Published data on the use of lithium in BPSD are limited, and there are no controlled studies of its use. One open study (Williams and Goldstein, 1979) reported decreased agitation in six out of eight patients with mixed chronic brain syndromes, but another reported little benefit and prominent toxicity (Randels et al., 1984).

Adrenergic blockers

There have been two uncontrolled studies of β-blockers in dementia that found some benefit (Petrie and Ban, 1981; Weiler et al., 1988). One small randomized trial of propranolol for agitation in nursing home residents with dementia found significant benefits for propranolol when compared to placebo (Peskind et al., 2005). A recent placebo-controlled trial of the alpha adrenergic antagonist prazosin (1–6 mg daily) for agitation or aggression in Alzheimer's dementia found significant benefits in favor of the drug (Wang et al., 2009).

Selegiline. Selegiline, at low doses, is an irreversible inhibitor of monoamine oxidase B. It has been suggested that decreasing or normalizing monoamine oxidase B activity in Alzheimer's disease might result in asymptomatic improvement in this illness (Tariot et al., 1987). The results to date with selegiline in the treatment of BPSD in Alzheimer's disease have been mixed. Although some small, open-label studies have shown beneficial effects on BPSD (Goad et al., 1991; Schneider et al., 1991), two large and placebo-controlled studies showed no effect of selegiline in patients with dementia (Freedman et al., 1998; Burke et al., 1993). In a study of Alzheimer's disease patients with depression and agitation, selegiline has been shown to improve BPSD, although the effect size was small (Lawlor et al., 1997).

Melatonin. Melatonin has been proposed as a treatment for agitation and sleep disturbances in dementia due to the known disruptions in melatonin that accompany dementia. There is limited evidence for melatonin in treating cognitive symptoms of dementia although melatonin may have modest effects on behavioral symptoms of dementia (Jansen et al., 2006).

Cannabinoids. Case-reports (Passmore and Passmore, 2008) and open-label studies (Walther et al., 2006) have suggested that cannabinoid medications may be beneficial in the treatment of agitation in dementia. A systematic review, however, concluded that the results of the only randomized controlled trial available could not be validated and that there was no evidence to support the efficacy of cannabinoids in the treatment of BPSD (Krishnan et al., 2009).

Treatment of sleep disturbances in dementia. No intervention studies exist on the use of sedative hypnotics for the treatment of sleep disturbances in AD (Salami et al., 2011), but in general, agents with short-to-intermediate half-lives and few active metabolites are favored (e.g., zopiclone 3.75–7.5 mg, zolpidem 5–10 mg, lorazepam 0.5–1.0 mg, oxazepam 7.5–15 mg, temazepam 10 mg). Sedative hypnotics should only be used for the short-term management of sleep disturbance in BPSD. When long-term treatment is necessary, an alternative agent with sleep-enhancing properties such as trazodone is recommended.

Antipsychotics have not been examined in the treatment of sleep specifically, but evidence from trials targeting behavioral symptoms suggests that sedative side effects of the atypicals may have a secondary effect on sleep (Salami et al., 2011). Given the associated risks in the elderly, their routine use in the treatment of sleep disturbance is not recommended, but could be considered in the context of psychotic symptoms or other BPSD requiring treatment. Similarly, evidence for the use of sedating antidepressants such as trazodone and mirtazapine is very limited, but these may be an option when sleep disturbance is co-morbid with depressive symptoms (Salami et al., 2011).

Acetylcholinesterase inhibitors have shown beneficial effects on sleep architecture (Moraes et al., 2008; Mizuno et al., 2004), but results from placebo-controlled studies on their use in the treatment in sleep disturbances have been mixed (Ancoli-Israeli et al., 2005; Markowitz et al., 2003; Moraes et al., 2008).

Melatonin has been proposed as a treatment option for sleep disturbances in dementia, but of four placebo-controlled clinical trials, three failed to find a significant effect. Two studies have reported that it may be more efficacious when combined with bright light therapy (Salami et al., 2010).

Pain management in dementia. It has been proposed that pain, common in people with dementia but often under recognized, may contribute to behavioral disturbances and may be an important target in the treatment of BPSD (Corbett et al., 2012; Husebo et al., 2011). More controlled trials are needed, but the most recent results suggest that it may be beneficial to adequately manage pain in patients with agitation and either obvious signs of discomfort or commonly painful comorbid medical conditions. A large cluster randomized controlled trial on the use of analgesics in dementia supported the efficacy of treating pain in reducing agitation, with a statistically significant improvement in agitation and aggression in patients receiving a stepwise pain treatment protocol including opioids (Husebo et al., 2011). A follow-up analysis reported that verbal agitation and physically non-aggressive behaviors, including restlessness and pacing, showed the greatest response (Husebo et al., 2013).

Other studies on the use of analgesics in the treatment of BPSD are few and have been equivocal. In a study aimed at addressing unmet needs employing both a non-pharmacological treatment program and analgesics in nursing home patients, there was an improvement in discomfort but not in behavioral symptoms (Kovach et al., 2006). In a small placebo-controlled trial, acetaminophen was not effective in reducing agitation but some improvement in social interaction was noted (Chibnall et al., 2005), while a statistically significant reduction in agitation was observed in only a subset of patients over 85 years old in a crossover trial with opioid analgesics (Manfredi et al., 2003).

Electroconvulsive therapy for BPSD and depression

Electroconvulsive therapy (ECT) may be an option in the management of severe depression complicating dementia. The use of ECT in individuals with dementia is limited due to the frequent occurrence of delirium following treatment. Increasing the time interval between

treatments can reduce this risk. Less cognitive impairment would be expected if unilateral treatment were used, but balanced against this is the need for more sessions with unilateral treatment compared with bilateral treatment.

Case reports and retrospective studies suggest that ECT is effective in individuals with dementia and depression (Price and McAllister, 1989; Rao and Lyketsos, 2000; Liang et al., 1988). Case series also suggest that ECT may be a useful treatment for refractory cases of BPSD (Carlyle et al., 1991; Grant and Mohan, 2001). Capacity for informed consent for ECT in a dementia patient is difficult, and it is advisable to obtain the consent of a substitute decision maker.

Special populations

Dementia with Lewy bodies and Parkinson's disease dementia

Dementia with Lewy bodies can be a relatively common clinical problem that has been observed in approximately 15% of dementia patients. Dementia also affects up to 25% of individuals with Parkinson's disease (Aarsland et al., 2005). Visual hallucinations and other psychotic symptoms can be present early in the course of the disease. Severe and sometimes fatal sensitivity to conventional neuroleptics is a feature of dementia with Lewy bodies (McKeith et al., 2005), and patients with Parkinson's disease dementia are also sensitive to neuroleptic medications.

Currently the best-supported evidence for treating behavioral symptoms associated with dementia with Lewy bodies is for cholinesterase inhibitors. Randomized controlled-trial evidence for rivastigmine in dementia with Lewy bodies (McKeith et al., 2000) has demonstrated improvement in BPSD symptoms with treatment. One study of rivastigmine for behavioral symptoms in Parkinson's disease also found benefit on BPSD symptoms (Emre et al., 2004). In contrast, donepezil was not shown to be effective for BPSD in Parkinson's disease dementia (Ravina et al., 2005).

There is limited information on the efficacy of atypical antipsychotics for dementia with Lewy bodies. Reports on the use of risperidone in patients with dementia with Lewy bodies have been mixed (Lee et al., 1994; Allen et al., 1995; McKeith et al., 1995). Post hoc analysis of individuals with dementia with Lewy bodies who were enrolled in a larger trial of olanzapine for BPSD found that 5 mg and 10 mg of olanzapine were more effective than placebo in reducing BPSD symptoms without worsening of motor symptoms (Cummings et al., 2002).

A retrospective chart review study of quetiapine in patients with Parkinson's disease dementia or dementia with Lewy bodies found that the majority of individuals had reductions in psychosis during treatment, although motor worsening was observed in a third of patients (Fernandez et al., 2002). However, a small placebo-controlled trial of quetiapine for psychosis in dementia associated with Parkinsonism did not find any benefit of quetiapine over placebo (Kurlan et al., 2007). Clozapine currently is the best supported treatment for psychosis secondary to dopaminergic therapy in Parkinson's disease (Pollak et al., 2004; Parkinson Study Group, 1999).

For severe BPSD, low doses of the newer antipsychotics such as quetiapine (6.25 mg), olanzapine (2.5 mg), or clozapine (6.25 mg) could be used, but patients must be monitored closely for treatment-emergent EPS and other adverse effects.

Frontotemporal dementia

Frontotemporal dementia (FTD) also has important differences in terms of symptom presentation and management when compared to Alzheimer's disease. Individuals with FTD tend to have an earlier onset of illness and more pronounced behavioral symptoms or language impairment early in the course of illness when compared to Alzheimer's disease (McKhann et al., 2001). Behaviors frequently observed in FTD include personality changes early in the course of illness, loss of social awareness and self-care, abnormal eating, and rigidity or repetitive and stereotyped interests and behaviors (Bozeat et al., 2000).

There have been relatively few high-quality studies examining pharmacological interventions for frontotemporal dementia. Serotonergic antidepressants are currently the best supported treatments for FTD (Kaye et al., 2010; Huey et al., 2006; Freedman, 2007). The only medication to demonstrate benefit in any placebo-controlled trial is trazodone (Lebert et al., 2004).

Other antidepressants that have demonstrated benefit in uncontrolled studies have included fluoxetine, and sertraline with mixed results reported for two studies of paroxetine. Atypical antipsychotics including aripiprazole, olanzapine, and quetiapine have also demonstrated some benefits in case reports and open-label studies. The use of cholinesterase inhibitors and memantine in FTD is uncertain at the present time. Some studies have reported improvement in cognitive symptoms of FTD with cholinesterase inhibitors, although there may also be behavioral worsening. An open-label study of memantine for FTD suggested cognitive and behavioral benefits, although further studies are required (Boxer et al., 2009).

Treatments for inappropriate sexual behaviors

Inappropriate sexual behaviors may be observed in dementia. An important distinction must be made between normal sexual behaviors performed in an abnormal context, which may be related to disinhibition and impaired judgment, and hypersexual behaviors that may indicate an abnormal sexual drive (Ozkan et al., 2008). There are no randomized controlled trials of pharmacotherapies for inappropriate sexual behaviors. There is some evidence from open-label trials and case reports to support the use of gabapentin, carbamazepine, trazodone, paroxetine, citalopram, and cimetidine (Ozkan et al., 2008). Antiandrogens including medroxyprogesterone, cyproterone acetate, and finasteride may reduce inappropriate hypersexual behavior in men with dementia, but consideration should be given to the ethical concerns associated with their use in this context (Joller et al., 2013).

Treatment of apathy

Despite being widely recognized as one of the most prevalent and persistent behavioral symptoms of AD and other forms of dementia, studies of effective pharmacologic treatment options for apathy are relatively few. Evidence has been largely derived from trials investigating treatment of behavioral disturbances in general and rarely designed to assess apathy specifically.

Cholinesterase inhibitors are currently the best supported treatment option. Several open-label trials and one placebo-controlled trial demonstrated an improvement in neuropsychiatric symptoms including apathy in patients with AD treated with donepezil while only one study, in patients with AD or mixed dementia residing in nursing homes, found no benefit (Berman et al., 2012; Tariot et al., 2001). Galantamine was likewise effective in improving apathy in large

trial including patients with vascular and mixed dementia, and has been associated with a positive effect on apathy and fewer new behavioral symptoms in patients with mild to moderate AD (Cummings et al., 2004; Erkinjuntti et al., 2002; Herrmann et al., 2005). Two small studies of rivastigmine have supported its use for apathy and other behavioral symptoms in DLB, while open-label and observational studies have also demonstrated a benefit for treating apathy in AD (Berman et al., 2012).

Although evidence linking dysfunction in dopaminergic transmission with symptoms of apathy has suggested a potential role for psychostimulants, evidence for their routine use remains very limited (Herrmann et al., 2008; Berman et al., 2010). Only methylphenidate has been studied in placebo-controlled trials in patients with dementia. A small trial in AD patients showed an improvement as measured by the Apathy Evaluation Scale (AES), the best validated scale for measuring apathy in dementia (Herrmann et al., 2008). In a recent trial of patients with AD selected for clinically significant apathy, methylphenidate was associated with a modest but significant reduction in the NPI apathy score and a larger clinical impact with 21% of methylphenidate treated patients versus 3% of placebo-treated considered to have moderate to markedly improved (Rosenberg et al., 2013).

Evidence for other pharmacotherapy options is sparse, of poor quality, or has not yielded promising results. Of note, antidepressant medications including selective serotonin reuptake inhibitors and trazodone have demonstrated no benefit in the treatment of apathy (Berrman et al., 2010). Similarly, studies of typical antipsychotics have been largely negative, and while retrospective analyses and one open-label trial have suggested atypical antipsychotics may be effective, this has not been confirmed in placebo-controlled trials (Berrman et al., 2010).

References and recommended reading

General principles

American Geriatrics S, American Association for Geriatric P. Consensus statement on improving the quality of mental health care in U.S. nursing homes: management of depression and behavioral symptoms associated with dementia. *Journal of the American Geriatrics Society* 2003; 51: 1287.

Ballard, C., Corbett, A., Chitramohan, R., Aarsland, D. Management of agitation and aggression associated with Alzheimer's disease: controversies and possible solutions. *Current Opinion in Psychiatry* 2009; 22: 532–540.

Ballard, C., Gauthier, S., Cummings, J.L., et al. Management of agitation and aggression associated with Alzheimer disease. *Nature Reviews Neurology* 2009; 5: 245–255.

Bharani, N., Snowden, M. Evidence-based interventions for nursing home residents with dementia-related behavioral symptoms. *Psychiatric Clinics of North America* 2005; 28: 985.

Canadian Coalition for Seniors' Mental Health. National Guidelines for Seniors' *Mental Health: The Assessment and Treatment of Mental Health Issues in Long Term Care Homes* 2006.

Herrmann, N., Gauthier, S., Lysy, P.G. Clinical practice guidelines for severe Alzheimer's disease. *Alzheimer's & Dementia* 2007; 3: 385–397.

Herrmann, N., Lanctôt, K.L. Pharmacologic management of neuropsychiatric symptoms of Alzheimer disease. *Canadian Journal of Psychiatry* 2007; 52: 630.

Jeste, D.V., Blazer, D., Casey D, et al. ACNP White Paper: update on use of antipsychotic drugs in elderly persons with dementia. *Neuropsychopharmacology* 2008; 33: 957–970.

Schneider, L.S., Pollock, V.E., Lyness, S.A. A metaanalysis of controlled trials of neuroleptic treatment in dementia. *Journal of the American Geriatrics Society* 1990; 38: 553.

Schneider, L.S., Dagerman, K., Insel, P.S. Efficacy and adverse effects of atypical antipsychotics for dementia: meta-analysis of randomized, placebo-controlled trials. *American Journal of Geriatric Psychiatry* 2006; 14: 191–210.

Sink, K.M., Holden, K.F., Yaffe, K. Pharmacological treatment of neuropsychiatric symptoms of dementia: a review of the evidence *JAMA* 2005; 293: 596–608.

Snowden, M., Sato, K., Roy-Byrne, P. Assessment and treatment of nursing home residents with depression or behavioral symptoms associated with dementia: a review of the literature. *Journal of the American Geriatrics Society* 2003; 51: 1305.

Trinh, N.H., Hoblyn, J., Mohanty, S., Yaffe, K. Efficacy of Cholinesterase Inhibitors in the Treatment of Neuropsychiatric and Functional Impairment in Alzheimer Disease. *JAMA* 2003; 289: 210–216.

Antipsychotics

United States Food and Drug Administration. Public Health Advisory: Deaths with antipsychotics in elderly patients with behavioral disturbances Volume 2010 2005.

United States Food and Drug Administration. Information for Healthcare Professionals: Conventional Antipsychotics Volume 2010 2008.

Ballard, C., Margallo-Lana, M., Juszczak, E., et al. Quetiapine and rivastigmine and cognitive decline in Alzheimer's disease: randomised double blind placebo-controlled trial. *BMJ* 2005; 330: 874.

Ballard, C. Hanney, M.L., Theodoulou, M., et al. The dementia antipsychotic withdrawal trial (DART-AD): long-term follow-up of a randomised placebo-controlled trial. *Lancet Neurology* 2009; 8: 151–157.

Ballard, C., Lana, M.M., Theodoulou, M., et al. A randomised, blinded, placebo-controlled trial in dementia patients continuing or stopping neuroleptics (the DART-AD trial). *PLoS Medicine/ Public Library of Science* 2008; 5: e76.

Ballard, C., Waite, J. The effectiveness of atypical antipsychotics for the treatment of aggression and psychosis in Alzheimer's disease. *Cochrane database of systematic reviews (Online)* 2006 (1): CD003476.

Barnes, R., Veith, R., Okimoto, J., Raskind, M., Gumbrecht, G. Efficacy of antipsychotic medications in behaviorally disturbed dementia patients. *American Journal of Psychiatry* 1982; 139: 1170–1174.

Bridges-Parlet, S., Knopman, D., Steffes, S. Withdrawal of neuroleptic medications from institutionalized dementia patients: results of a double-blind, baseline-treatment-controlled pilot study. *Journal of Geriatric Psychiatry & Neurology* 1997; 10: 119–126.

Brodaty, H., Ames, D., Snowdon, J., et al. A randomized placebo-controlled trial of risperidone for the treatment of aggression, agitation, and psychosis of dementia. *Journal of Clinical Psychiatry* 2003; 64: 134–143.

Chan, W.C., Lam, L.C., Choy, C.N., Leung, V.P., Li, S.W., Chiu, H.F. A double-blind randomised comparison of risperidone and haloperidol in the treatment of behavioral and psychological symptoms in Chinese dementia patients. *International Journal of Geriatric Psychiatry* 2001; 16: 1156–1162.

Chui, H.C., Lyness, S.A., Sobel, E., Schneider, L.S. Extrapyramidal signs and psychiatric symptoms predict faster cognitive decline in Alzheimer's disease. *Archives of Neurology* 1994; 51: 676–681.

Cohen-Mansfield, J., Lipson, S., Werner, P., Billig, N., Taylor, L., Woosley, R. Withdrawal of haloperidol, thioridazine, and lorazepam in the nursing home: a controlled, double-blind study. *Archives of Internal Medicine* 1999; 159: 1733–1740.

Deberdt, W.G., Dysken, M.W., Rappaport, S.A., et al. Comparison of olanzapine and risperidone in the treatment of psychosis and associated behavioral disturbances in patients with dementia. *American Journal of Geriatric Psychiatry* 2005; 13: 722–730.

Declercq, T., Petrovic, M., Azermai, M., Vander Stichele, R., De Sutter, A.I., van Driel, M.L., et al. Withdrawal versus continuation of chronic antipsychotic drugs for behavioral and psychological symptoms in older people with dementia. *Cochrane Database of Systematic Reviews (Online)* 2013: CD007726.

De Deyn, P.P., Carrasco, M.M., Deberdt, W., et al. Olanzapine versus placebo in the treatment of psychosis with or without associated behavioral disturbances in patients with Alzheimer's disease. *International Journal of Geriatric Psychiatry* 2004; 19: 115–126.

De Deyn, P.P., Jeste, D.V., Swanink, R., et al. Aripiprazole for the treatment of psychosis in patients with Alzheimer's disease: a randomized, placebo-controlled study. *Journal of Clinical Psychopharmacology* 2005; 25: 463–467.

De Deyn, P.P., Rabheru, K., Rasmussen, A., et al. A randomized trial of risperidone, placebo, and haloperidol for behavioral symptoms of dementia. *Neurology* 1999; 53: 946–955.

Devanand, D.P., Sackeim, H.A., Brown, R.P., Mayeux, R. A pilot study of haloperidol treatment of psychosis and behavioral disturbance in Alzheimer's disease. *Archives of Neurology* 1989; 46: 854–857.

Devanand, D.P., Mintzer, J., Schultz, S.K., Andrews, H.F., Sultzer, D.L., de la Pena, D., et al. Relapse risk after discontinuation of risperidone in Alzheimer's disease. *New England Journal of Medicine* 2012; 367: 1497–1507.

Dorsey, E.R., Rabbani, A., Gallagher, S.A., Conti, R.M., Alexander, G.C. Impact of FDA black box advisory on antipsychotic medication use. *Archives of Internal Medicine* 2010; 170: 96–103.

Finkel S.I., Lyons, J.S., Anderson, R.L., et al. A randomized, placebo-controlled trial of thiothixene in agitated, demented nursing home elderly. *International Journal of Geriatric Psychiatry* 1995; 10: 129–136.

Gilleard, C.J., Morgan, K., Wade, B.E. Patterns of neuroleptic use among the institutionalized elderly. *Acta Psychiatrica Scandinavica* 1983; 68: 419–425.

Gill, S.S., Bronskill, S.E., Normand, S-L.T., et al. Antipsychotic drug use and mortality in old adults with dementia. *Annals of Internal Medicine* 2007; 146: 775–786.

Hollis, J.M.B.B.S., Grayson, D.P.D., Forrester, L., Brodaty, H.D.S., Touyz, S.P.D., Cumming, R.P.D. Antipsychotic medication dispensing and risk of death in veterans and war widows 65 years and older. *American Journal of Geriatric Psychiatry* 2007; 15: 932–941.

Horowitz, A., Balistreri, E., Stuen, C., Fangmeier, R. Visual impairment and rehabilitation needs for nursing home residents. *Journal of Visual Impairment & Blindness* 1995; 89: 7–15.

Kamble, P., Chen, H., Sherer, J., Aparasu, R.R. Antipsychotic drug use among elderly nursing home residents in the United States. *American Journal of Geriatric Pharmacotherapy* 2008; 6: 187–197.

Katz, I.R., Jeste, D.V., Mintzer, J.E., Clyde, C., Napolitano, J., Brecher, M. Comparison of risperidone and placebo for psychosis and behavioral disturbances associated with dementia: a randomized, double-blind trial. Risperidone Study Group. *Journal of Clinical Psychiatry* 1999; 60: 107–115.

Lanctôt, K.L., Best, T.S., Mittmann, N., et al. Efficacy and safety of neuroleptics in behavioral disorders associated with dementia. *Journal of Clinical Psychiatry* 1998; 59: 550–561.

Lee, P.E., Gill, S.S., Freedman, M., Bronskill, S.E., Hillmer, M.P., Rochon, P.A. Atypical antipsychotic drugs in the treatment of behavioral and psychological symptoms of dementia: systematic review. *BMJ* 2004; 329: 75.

Liperoti, R., Onder, G., Landi, F., et al. All-cause mortality associated with atypical and conventional antipsychotics among nursing home residents with dementia: a retrospective cohort study. *Journal of Clinical Psychiatry* 2009; 70: 1340–1347.

Lonergan, E., Luxenberg, J., Colford, J. Haloperidol for agitation in dementia. *Cochrane database of systematic reviews (Online)* 2002; (2): CD002852.

Meeks, T.W., Jeste, D.V. Beyond the black box: what is the role for antipsychotics in dementia? *Current Psychiatry* 2008; 7: 50–65.

Mintzer, J., Greenspan, A., Caers, I., et al. Risperidone in the treatment of psychosis of Alzheimer disease: results from a prospective clinical trial. *American Journal of Geriatric Psychiatry* 2006;14: 280–291.

Mintzer, J.E., Tune, L.E., Breder, C.D., et al. Aripiprazole for the treatment of psychoses in institutionalized patients with Alzheimer dementia: a multicenter, randomized, double-blind, placebo-controlled assessment of three fixed doses. *American Journal of Geriatric Psychiatry* 2007; 15: 918–931.

McShane, R., Keene, J., Gedling, K., Fairburn, C., Jacoby, R., Hope, T. Do neuroleptic drugs hasten cognitive decline in dementia? Prospective study with necropsy follow up. *BMJ* 1997; 314: 266–270.

Petrie, W.M., Lawson, E.C., Hollender, M.H. Violence in geriatric patients. *JAMA* 1982; 248: 443–444.

Ray, W.A., Federspiel, C.F., Schaffner, W. A study of antipsychotic drug use in nursing homes: epidemiologic evidence suggesting misuse. *American Journal of Public Health* 1980; 70: 485–491.

Rocha, F.L., Hara, C., Ramos, M.G., et al. An exploratory open-label trial of ziprasidone for the treatment of behavioral and psychological symptoms of dementia. *Dementia and Geriatric Cognitive Disorders* 2006; 22: 445–448.

Rochon, P.A., Anderson, G.M. Prescribing optimal drug therapy for older people: sending the right message: comment on "impact of FDA black box advisory on antipsychotic medication use". *Archives of Internal Medicine* 2010; 170: 103–106.

Ruths, S., Straand, J., Nygaard, H.A., et al. Stopping antipsychotic drug therapy in demented nursing home patients: a randomized, placebo-controlled study—the Bergen District Nursing Home Study (BEDNURS). *International Journal of Geriatric Psychiatry* 2008; 23: 889–895.

Schneeweiss, S., Setoguchi, S., Brookhart, A., Dormuth, C., Wang, P.S. Risk of death associated with the use of conventional versus atypical antipsychotic drugs among elderly patients. *CMAJ* 2007; 176: 627–632.

Schneider, L.S., Dagerman, K.S., Insel, P. Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. *JAMA* 2005; 294: 1934–1943.

Schneider, L.S., Mack, W., Dagerman, K., et al. Second generation antipsychotics for Alzheimer's disease patients and metabolic abnormalities: The CATIE-AD Study. American Association for Geriatric Psychiatry Annual Meeting. Honolulu, Hawaii, United States 2009, pp. A75–A76.

Schneider, L.S., Tariot, P.N., Dagerman, K.S., et al. Effectiveness of atypical antipsychotic drugs in patients with Alzheimer's disease. *New England Journal of Medicine* 2006b; 355: 1525–1538.

Sink, K.M., Holden, K..F, Yaffe, K. Pharmacological treatment of neuropsychiatric symptoms of dementia: a review of the evidence. *JAMA* 2005; 293: 596.

Stern, Y., Mayeux, R., Sano, M., Hauser, W.A., Bush, T. Predictors of disease course in patients with probable Alzheimer's disease. *Neurology* 1987; 37: 1649–1653.

Street, J.S., Clark, W.S., Gannon, K.S., et al. Olanzapine treatment of psychotic and behavioral symptoms in patients with Alzheimer disease in nursing care facilities: a double-blind, randomized, placebo-controlled trial. The HGEU Study Group. *Archives of General Psychiatry* 2000, pp. 968–976.

Sultzer, D.L., Davis, S.M., Tariot, P.N., et al. Clinical symptom responses to atypical antipsychotic medications in Alzheimer's disease: phase 1 outcomes from the CATIE-AD effectiveness trial. *American Journal of Psychiatry* 2008; 165: 844–854.

Tariot, P.N., Schneider, L., Katz, I.R., et al. Quetiapine treatment of psychosis associated with dementia: a double-blind, randomized, placebo-controlled clinical trial. *American Journal of Geriatric Psychiatry* 2006; 14: 767–776.

Thapa, P.B., Meador, K.G., Gideon, P., Fought, R.L., Ray, W.A. Effects of antipsychotic withdrawal in elderly nursing home residents. *Journal of the American Geriatrics Society* 1994; 42: 280–286.

van Reekum, R., Clarke, D., Conn, D., et al. A randomized, placebo-controlled trial of the discontinuation of long-term antipsychotics in dementia. *International Psychogeriatrics* 2002; 14: 197–210.

Wang, P.S., Schneeweiss, S., Avorn, J., et al. Risk of death in elderly users of conventional vs. atypical antipsychotic medications. *New England Journal of Medicine* 2005; 353: 2335–2341.

Woerner, M.G., Alvir, J.M., Saltz, B.L., Lieberman, J.A., Kane, J.M. Prospective study of tardive dyskinesia in the elderly: rates and risk factors. *American Journal of Psychiatry* 1998; 155: 1521–1528.

Zhong, K.X., Tariot, P.N., Mintzer, J., Minkwitz, M.C., Devine, N.A., Zhong, K.X. Quetiapine to treat agitation in dementia: a randomized, double-blind, placebo-controlled study. *Current Alzheimer's Research* 2007; 4: 81–93.

Antidepressants

Aisen, P.S., Johanssen. D.J., Marin. D. Trazodone for behavioral disturbance in dementia. *American Journal of Geriatric Psychiatry* 1993; 1: 349–350.

Auchus, A.P., Bissey-Black, C. Pilot study of haloperidol, fluoxetine, and placebo for agitation in Alzheimer's disease. *The Journal of Neuropsychiatry and Clinical Neurosciences* 1997; 9: 591–593.

Bains, J., Birks, J.S., Dening, T.R. The efficacy of antidepressants in the treatment of depression in dementia. *Cochrane Database of Systematic Reviews* 2002: CD003944.

Banerjee, S., Hellier, J., Dewey, M., Romeo, R., Ballard, C., Baldwin, R., et al. Sertraline or mirtazapine for depression in dementia (HTA-SADD): A randomised, multicentre, double-blind, placebo-controlled trial. *Lancet* 2011; 378: 403–411.

Barak, Y., Plopski, I., Tadger, S., Paleacu, D. Escitalopram versus risperidone for the treatment of behavioral and psychotic symptoms associated with Alzheimer's disease: A randomized double-blind pilot study. *International Psychogeriatrics* 2011; 23:1–5.

Bergh, S., Engedal, K. The withdrawal of antipsychotics and antidepressants from patients with dementia and BPSD living in nursing homes: An open pilot study. *International Journal of Geriatric Psychiatry* 2008; 23: 877–879.

Bergh, S., Selbaek, G., Engedal, K. Discontinuation of antidepressants in people with dementia and neuropsychiatric symptoms (DESEP study): Double blind, randomised, parallel group, placebo-controlled trial. *British Medical Journal* 2012 Mar 9; 344: e1566, doi:e1566.

Cakir, S., Kulaksizoglu, I.B. The efficacy of mirtazapine in agitated patients with Alzheimer's disease: A 12-week open-label pilot study. *Neuropsychiatric Disease and Treatment* 2008; 4: 963–966.

Canadian Coalition for Seniors' Mental Health. National Guidelines for Seniors' Mental Health: The Assessment and Treatment of Depression 2006.

Finkel, S.I., Mintzer, J.E., Dysken, M,. Krishnan, K.R., Burt, T., McRae, T. A randomized, placebo-controlled study of the efficacy and safety of sertraline in the treatment of the behavioral manifestations of Alzheimer's disease in outpatients treated with donepezil. *International Journal of Geriatric Psychiatry* 2004; 19: 9–18.

Gaber, S., Ronzoli, S., Bruno, A., Biagi, A. Sertraline versus small doses of haloperidol in the treatment of agitated behavior in patients with dementia. *Archives of Gerontology and Geriatrics* 2001; 33: 159–162.

Katona, C.L., Hunter, B.N., Bray, J. A double-blind comparison of the efficacy and safely of paroxetine and imipramine in the treatment of depression with dementia. *International Journal of Geriatric Psychiatry* 1998; 13: 100–108.

Lawlor, B.A. Serotonin and Alzheimer's disease. Psychiatric Annals. 1990;20: 567–570. Lawlor, B.A., Radcliffe. J., Molchan. S.E., Martinez. R.A., Hill, J.L., Sunderland, T. A pilot placebo-controlled study of trazodone and buspirone in Alzheimer's disease. *International Journal of Geriatric Psychiatry* 1994; 9: 55–59.

Lyketsos, C.G., Sheppard, J.M., Steele, C.D., et al. Randomized, placebo-controlled, double-blind clinical trial of sertraline in the treatment of depression complicating Alzheimer's disease: initial results from the Depression in Alzheimer's Disease study. *American Journal of Psychiatry* 2000; 157: 1686–1689.

Magai, C., Kennedy, G., Cohen, C.I., Gomberg, D. A controlled clinical trial of sertraline in the treatment of depression in nursing home patients with late-stage Alzheimer's disease. *The American Journal of Geriatric Psychiatry* 2000, 66–74.

Nelson, J. C., Devanand, D. P. A systematic review and meta-analysis of placebo-controlled antidepressant studies in people with depression and dementia. *Journal of the American Geriatrics Society* 2009; 59: 577–585.

Nyth, A.L., Gottfries, C.G. The clinical efficacy of citalopram in treatment of emotional disturbances in dementia disorders. A Nordic multicenter study. *British Journal of Psychiatry* 1990; 157: 894–901.

Passeri, M., Cucinotta, D., de Mello, M., Biziere, K. Comparison of minaprine and placebo in the treatment of Alzheimer's disease and multi-infarct dementia. *International Journal of Geriatric Psychiatry* 1987; 2: 97–103.

Petracca, G.M., Chemerinski, E., Starkstein, S.E. A double-blind, placebo-controlled study of fluoxetine in depressed patients with Alzheimer's disease. *International Psychogeriatrics* 2001; 13: 233–240.

Petracca, G., Teson, A., Chemerinski, E., Leiguarda, R., Starkstein, S.E. A double-blind placebo-controlled study of clomipramine in depressed patients with Alzheimer's disease. *Journal of Neuropsychiatry & Clinical Neurosciences* 1996; 8: 270–275.

Pinner, E., Rich, C.L. Effects of trazodone on aggressive behavior in seven patients with organic mental disorders. *American Journal of Psychiatry* 1988; 145: 1295–1296.

Pollock, B.G., Mulsant, B.H., Rosen, J., et al. Comparison of citalopram, perphenazine, and placebo for the acute treatment of psychosis and behavioral disturbances in hospitalized, demented patients. *The American Journal of Psychiatry* 2002; 159: 460–465.

Raji, M.A., Brady, S.R. Mirtazapine for treatment of depression and comorbidities in Alzheimer disease. *Annals of Pharmacotherapy* 2001; 35: 1024–1027.

Reifler, B.V., Teri, L., Raskind, M., et al. Double-blind trial of imipramine in Alzheimer's disease patients with and without depression. *American Journal of Psychiatry* 1989; 146: 45–49.

Reynolds III, C.F., Perel, J.M., Kupfer, D.J,. Zimmer, B., Stack, J.A., Hoch, C.C. Open-trial response to antidepressant treatment in elderly patients with mixed depression and cognitive impairment. *Psychiatry Research* 1987; 21: 111–122.

Rosenberg, P.B., Drye, L.T., Martin, B.K., et al. Sertraline for the treatment of depression in Alzheimer's disease. *American Journal of Geriatric Psychiatry* 2010; 18: 136–145.

Roth, M., Mountjoy, C.Q., Amrein, R. Moclobemide in elderly patients with cognitive decline and depression: an international double-blind, placebo-controlled trial. *British Journal of Psychiatry* 1996; 168: 149–157.

Sultzer, D.L., Gray, K.F., Gunay, I., Berisford, M.A., Mahler, M.E. A double-blind comparison of trazodone and haloperidol for treatment of agitation in patients with dementia. *American Journal of Geriatric Psychiatry* 1997; 5: 60–69.

Teri, L., Logsdon, R.G., Peskind, E., et al. Treatment of agitation in AD: a randomized, placebo-controlled clinical trial. *Neurology* 2000; 55: 1271–1278.

Cognitive enhancers

Aupperle, P.M., Koumaras, B., Chen, M., Rabinowicz, A,. Mirski, D. Long-term effects of rivastigmine treatment on neuropsychiatric and behavioral disturbances in nursing home residents with moderate to severe Alzheimer's disease: results of a 52-week open-label study. *Current Medical Research and Opinion* 2004; 20: 1605–1612.

Birks, J. Cholinesterase inhibitors for Alzheimer's disease. *Cochrane Database of Systematic Reviews* 2006: CD005593.

Campbell, N., Ayub, A., Boustani, M.A., et al. Impact of cholinesterase inhibitors on behavioral and psychological symptoms of Alzheimer's disease: a meta-analysis. *Clinical Interventions In Aging* 2008; 3: 719–728.

Cummings, J.L., Schneider, E., Tariot, P.N., Graham, S.M., for the Memantine MEM-MD-02 Study Group. Behavioral effects of memantine in Alzheimer disease patients receiving donepezil treatment. *Neurology* 2006; 67: 57–63.

Cummings, J.L., Schneider, L., Tariot, P.N., Kershaw, P.R., Yuan, W. Reduction of behavioral disturbances and caregiver distress by galantamine in patients with Alzheimer's disease. *American Journal of Psychiatry* 2004; 161: 532–538.

Feldman, H., Gauthier, S., Hecker, J., et al. Efficacy and safety of donepezil in patients with more severe Alzheimer's disease: a subgroup analysis from a randomized, placebo-controlled trial. *International Journal of Geriatric Psychiatry* 2005; 20: 559–569.

Fox, C., Crugel, M., Maidment, I., Auestad, B. H., Coulton, S., Treloar, A., et al. (2012). Efficacy of memantine for agitation in alzheimer's dementia: A randomised double-blind placebo-controlled trial. *PloS One* 2012; 7: e35185.

Gauthier, S., Feldman, H,. Hecker, J., et al. Efficacy of donepezil on behavioral symptoms in patients with moderate to severe Alzheimer's disease. *International Psychogeriatrics* 2002; 14: 389–404.

Gauthier, S., Loft, H., Cummings, J. Improvement in behavioral symptoms in patients with moderate to severe Alzheimer's disease by memantine: a pooled data analysis. *International Journal of Geriatric Psychiatry* 2008; 23: 537–545.

Gauthier, S., Wirth, Y., Mobius, H.J. Effects of memantine on behavioral symptoms in Alzheimer's disease patients: an analysis of the Neuropsychiatric Inventory (NPI) data of two randomised, controlled studies. *International Journal of Geriatric Psychiatry* 2005; 20: 459–464.

Grossberg, G.T., Pejovic, V., Miller, M.L., Graham, S.M. Memantine therapy of behavioral symptoms in community-dwelling patients with moderate to severe Alzheimer's disease. *Dementia and Geriatric Cognitive Disorders* 2009; 27: 164–172.

Hermann, N., Gauthier S., Boneva N., Lemming O.M. A randomized, double-blind, placebo-controlled trial of memantine in a behaviorally enriched sample of patients with moderate-to-severe Alzheimer's disease. *International Psychogeriatrics* 2013; 25; 919–927.

Holmes, C., Wilkinson, D., Dean, C., et al. The efficacy of donepezil in the treatment of neuropsychiatric symptoms in Alzheimer disease. *Neurology* 2004; 63: 214–219.

Howard, R.J., Juszczak, E., Ballard, C.G., et al. Donepezil for the treatment of agitation in Alzheimer's disease. *New England Journal of Medicine* 2007; 357: 1382–1392.

Howard, R., McShane R., Lindesay J., et al.. Donepezil and memantine for moderate-to-severe Alzheimer's disease. *New England Journal of Medicine* 2012; 366: 893–903.

Maidment, I.D., Fox, C.G., Boustani,M., Rodriguez, J., Brown, R.C., Katona, C.L. Efficacy of memantine on behavioral and psychological symptoms related to dementia: A systematic meta-analysis. *Annals of Pharmacotherapy* 2008; 42: 32–38.

McShane, R., Areosa Sastre, A., Minakaran, N. Memantine for dementia. *Cochrane Database of Systematic Reviews* 2006.

Menendez-Gonzalez, M., Calatayud, M.T., Blazquez-Menes, B. Exacerbation of Lewy bodies dementia due to memantine. *Journal of Alzheimer's Disorders* 2005; 8: 289–291.

Ridha, B.H., Josephs, K.A., Rossor, M.N. Delusions and hallucinations in dementia with Lewy bodies: worsening with memantine. *Neurology* 2005; 65: 481–482.

Rodda, J., Morgan, S., Walker, Z. Are cholinesterase inhibitors effective in the management of the behavioral and psychological symptoms of dementia in Alzheimer's disease? A systematic review of randomized, placebo-controlled trials of donepezil, rivastigmine and galantamine. *International Psychogeriatrics* 2009; 21: 813–824.

Rozzini, L., Chilovi, B.V., Bertoletti, E., et al. Cognitive and psychopathologic response to rivastigmine in dementia with Lewy bodies compared to Alzheimer's disease: a case control study. *American Journal of Alzheimer's Disease and Other Dementias* 2007; 22: 42–47.

Santoro, A., Siviero, P., Minicuci, N., et al. Effects of donepezil, galantamine and rivastigmine in 938 italian patients with Alzheimer's disease: a prospective, observational study. *CNS Drugs* 2010; 24: 163–176.

van Marum, R.J. Update on the use of memantine in Alzheimer's disease. *Neuropsychiatric Disease and Treatment* 2009; 5: 237–247.

Vidal, J-S, Lacombe, J-M, Dartigues, J-F, et al. Evaluation of the impact of memantine treatment initiation on psychotropics use: a study from the French national health care database. *Neuroepidemiology* 2008; 31: 193–200.

Wilcock, G.K., Ballard, C.G., Cooper, J.A., Loft, H. Memantine for agitation/aggression and psychosis in moderately severe to severe Alzheimer's disease: a pooled analysis of 3 studies. *Journal of Clinical Psychiatry* 2008; 69: 341–348.

Winblad, B., Grossberg, G., Frölich, L., et al. IDEAL: A 6-month, double-blind, placebo-controlled study of the first skin patch for Alzheimer disease. *Neurology* 2007; 69: S14–S22.

Winblad, B., Poritis, N. Memantine in severe dementia: results of the 9M-Best Study (Benefit and efficacy in severely demented patients during treatment with memantine). *International Journal of Geriatric Psychiatry* 1999; 14: 135–146.

Anticonvulsants

Amann, B., Pantel, J., Grunze, H., et al. Anticonvulsants in the treatment of aggression in the demented elderly: an update. *Clinical Practice and Epidemiology in Mental Health* 2009; 5: 14.

Aulakh, J.S., Hawkins, J.W., Athwal, H.S., Sheikh, J.I,. Yesavage, J., Tinklenberg, J.R. Tolerability and effectiveness of lamotrigine in complex elderly patients. *Journal of Geriatric Psychiatry and Neurology* 2005; 18: 8–11.

Buchalter, E.N., Lantz, M.S. Treatment of impulsivity and aggression in a patient with vascular dementia. *Geriatrics* 2001; 56: 53–54.

Cooney, C., Mortimer, A., Smith, A., Newton, K., Wrigley, M. Carbamazepine use in aggressive behavior associated with senile dementia. *International Journal of Geriatric Psychiatry* 1996; 11: 901–905.

De Leon, O.A. Treatment of psychotic symptoms with lamotrigine in Alzheimer disease. *Journal of Clinical Psychopharmacology* 2004; 24: 232–233.

Devarajan, S., Dursun, S.M. Aggression in dementia with lamotrigine treatment. *American Journal of Psychiatry* 2000; 157: 1178.

Essa, M. Carbamazepine in dementia. *Journal of Clinical Pharmacology* 1986; 6: 234–236.

Fhager, B., Meiri, I-M, Sjogren, M., Edman, A. Treatment of aggressive behavior in dementia with the anticonvulsant topiramate: a retrospective pilot study. *International Psychogeriatrics* 2003; 15: 307–309.

Forester, B., Vanelli, M., Hyde, J., et al. Report on an open-label prospective study of divalproex sodium for the behavioral and psychological symptoms of dementia as monotherapy and in combination with second-generation antipsychotic medication. *American Journal of Geriatric Pharmacotherapy* 2007; 5: 209–217.

Freymann, N., Michael, R., Dodel, R., Jessen, F. Successful treatment of sexual disinhibition in dementia with carbamazepine—a case report. *Pharmacopsychiatry* 2005; 38: 144–145.

Gleason, R.P., Schneider, L.S. Carbamazepine treatment of agitation in Alzheimer's outpatients refractory to neuroleptics. *Journal of Clinical Psychiatry* 1990; 51: 115–118.

Haas, S., Vincent, K., Holt, J., Lippmann, S. Divalproex: a possible treatment alternative for demented, elderly aggressive patients. *Annals of Clinical Psychiatry* 1997; 9: 145–147.

Herrmann, N. Valproic acid treatment of agitation in dementia. *Canadian Journal of Psychiatry* 1998; 43: 69–72.

Herrmann, N., Lanctôt, K.L., Rothenburg, L.S., Eryavec, G. A placebo-controlled trial of valproate for agitation and aggression in Alzheimer's disease. *Dementia & Geriatric Cognitive Disorders* 2007; 23: 116–119.

Kasckow, J.W., McElroy, S.L., Cameron, R.L., Mahler, L.L., Fudala, S.J. A pilot study on the use of divalproex sodium in the treatment of behavioral agitation in elderly patients with dementia: assessment with the behave-ad and CGI rating scales. *Current Therapeutic Research* 1997; 58: 981–989.

Kim, Y., Wilkins, K.M., Tampi, R.R. Use of gabapentin in the treatment of behavioral and psychological symptoms of dementia: a review of the evidence. *Drugs & Aging* 2008; 25: 187–196.

Konovalov, S., Muralee, S., Tampi, R.R. Anticonvulsants for the treatment of behavioral and psychological symptoms of dementia: a literature review. *International Psychogeriatrics* 2008; 20: 293–308.

Kunik, M.E., Puryear, L., Orengo, C.A., Molinari, V., Workman, R.H,. Jr. The efficacy and tolerability of divalproex sodium in elderly demented patients with behavioral disturbances. *International Journal of Geriatric Psychiatry* 1998; 13: 29–34.

Kyomen, H.H., Whitfield, T.H., Baldessarini, R.J. Levetiracetam for manic behavior in hospitalized geriatric patients with dementia of the Alzheimer's type. *Journal of Clinical Psychopharmacology* 2007; 27: 408–410.

Leibovici, A., Tariot, P.N. Carbamazepine treatment of agitation associated with dementia. *Journal of Geriatric Psychiatry and Neurology* 1988; 1: 110–112.

Lemke, M.R., Stuhlmann, W. [Therapeutic use of carbamazepine for treatment of agitation and affective disorders in geriatric psychiatry patients]. *Psychiatrische Praxis* 1994; 21: 147–150.

Lonergan, E., Luxenberg, J. Valproate preparations for agitation in dementia. *Cochrane Database of Systematic Reviews* 2009: CD003945.

Lott, A.D,. McElroy, S.L., Keys, M.A. Valproate in the treatment of behavioral agitation in elderly patients with dementia. *Journal of Neuropsychiatry & Clinical Neurosciences* 1995; 7: 314–319.

Marin, D.B., Greenwald, B.S. Carbamazepine for aggressive agitation in demented patients during nursing care. *American Journal of Psychiatry* 1989; 146: 805.

Meinhold, J.M., Blake, L.M., Mini, L.J,. Welge, J.A., Schwiers, M., Hughes, A. Effect of divalproex sodium on behavioral and cognitive problems in elderly dementia. *Drugs & Aging* 2005; 22: 615–626.

Mellow, A.M., Solano-Lopez, C., Davis, S. Sodium valproate in the treatment of behavioral disturbance in dementia. *Journal of Geriatric Psychiatry and Neurology* 1993; 6: 205–209.

Narayan, M., Nelson, J.C. Treatment of dementia with behavioral disturbance using divalproex or a combination of divalproex and a neuroleptic. *Journal of Clinical Psychiatry* 1997; 58: 351–354.

Olin, J.T., Fox, L.S., Pawluczyk, S., Taggart, N.A., Schneider, L.S. A pilot randomized trial of carbamazepine for behavioral symptoms in treatment-resistant outpatients with Alzheimer disease. *American Journal of Geriatric Psychiatry* 2001; 9: 400–405.

Patterson, J.F. A preliminary study of carbamazepine in the treatment of assaultive patients with dementia. *Journal of Geriatric Psychiatry and Neurology* 1988; 1: 21–23.

Porsteinsson, A.P., Tariot, P.N., Erb, R., et al. Placebo-controlled study of divalproex sodium for agitation in dementia. *American Journal of Geriatric Psychiatry* 2001; 9: 58–66.

Porsteinsson, A.P., Tariot, P.N., Erb, R., Gaile, S. An open trial of valproate for agitation in geriatric neuropsychiatric disorders. *American Journal of Geriatric Psychiatry* 1997; 5: 344–351.

Porsteinsson, A.P., Tariot, P.N., Jakimovich, L.J., et al. Valproate therapy for agitation in dementia: open-label extension of a double-blind trial. *American Journal of Geriatric Psychiatry* 2003; 11: 434–440.

Rossi, P., Serrao, M., Pozzessere, G. Gabapentin-induced worsening of neuropsychiatric symptoms in dementia with lewy bodies: case reports. *European Neurology* 2002; 47: 56–57.

Sandborn, W.D., Bendfeldt, F., Hamdy, R. Valproic acid for physically aggressive behavior in geriatric patients. *American Journal of Geriatric Psychiatry* 1995; 3: 242–243.

Sival, R.C., Duivenvoorden, H.J., Jansen, P.A..F, Haffmans, P.M.J., Duursma, S.A., Eikelenboom, P. Sodium valproate in aggressive behavior in dementia: a twelve-week open-label follow-up study. *International Journal of Geriatric Psychiatry* 2004; 19: 305–312.

Sival, R.C., Haffmans, P.M.J., Jansen, P.A..F, Duursma, S.A., Eikelenboom, P. Sodium valproate in the treatment of aggressive behavior in patients with dementia—a randomized placebo-controlled clinical trial. *International Journal of Geriatric Psychiatry* 2002; 17: 579–585.

Sival, R.C., Haffmans, P.M., van Gent, P.P., van Nieuwkerk, J.F. The effects of sodium valproate on disturbed behavior in dementia. *Journal of the American Geriatric Society* 1994; 42: 906–907.

Sommer, O.H., Aga, O., Cvancarova, M., Olsen, I.C., Selbaek, G., Engedal, K. Effect of oxcarbazepine in the treatment of agitation and aggression in severe dementia. *Dementia & Geriatric Cognitive Disorders* 2009; 27: 155–163.

Takahashi, M., Akagi, M. Case report of sodium valproate treatment of aggression associated with Alzheimer's disease. *No To Shinkei* 1996; 48: 757–760.

Tariot, P.N., Erb, R., Leibovici, A., et al. Carbamazepine treatment of agitation in nursing home patients with dementia: a preliminary study. *Journal of the American Geriatric Society* 1994; 42: 1160–1166.

Tariot, P.N., Erb, R., Podgorski, C.A., et al. Efficacy and tolerability of carbamazepine for agitation and aggression in dementia. *American Journal of Psychiatry* 1998; 155: 54–61.

Tariot, P.N., Raman, R., Jakimovich, L., et al. Divalproex sodium in nursing home residents with possible or probable Alzheimer Disease complicated by agitation: a randomized, controlled trial. *American Journal of Geriatric Psychiatry* 2005; 13: 942–949.

Tariot, P.N., Schneider, L.S., Mintzer, J.E., et al. Safety and tolerability of divalproex sodium in the treatment of signs and symptoms of mania in elderly patients with dementia: results of a double-blind, placebo-controlled trial. *Current Therapeutic Research* 2001; 62: 51–67.

Tekin, S., Aykut-Bingol, C., Tanridag, T., Aktan, S. Antiglutaminergic therapy in Alzheimer's disease-effects of lamotrigine. *Journal of Neural Transmission* 1998; 105: 295–303.

Weiner, M.F., Womack, K.B., Martin-Cook, K., Svetlik, D.A., Hynan, L.S. Levetiracetam for agitated Alzheimer's disease patients. *International Psychogeriatrics* 2005; 17: 327–328.

Anxiolytics

Cantillon, M., Brunswick, R., Molina, D., Bahro, M. Buspirone vs. haloperidol: A double-blind trial for agitation in a nursing home population with Alzheimer's disease. *American Journal of Geriatric Psychiatry* 1996; 4: 263–267.

Chesrow, E.J., Kaplitz, S.E., Vetra, H. Double-blind study of oxazepam in the management of geriatric patients with behavioral problems. *Clinical Medicine* 1965; 72: 1001–1005.

Coccaro, E.F., Kramer, E., Zemishlany, Z., et al. Pharmacologic treatment of noncognitive behavioral disturbances in elderly demented patients. *American Journal of Psychiatry* 1990; 147: 1640–1645.

Covington, J.S. Alleviating agitation, apprehension, and related symptoms in geriatric patients: A double-blind comparison of a phenothiazine and a benzodiazepien. *Southern Medical Journal* 1975; 68: 719–724.

Cumming, R.G., Couteur, D.G.L. Benzodiazepines and Risk of Hip Fractures in Older People: A Review of the Evidence. *CNS Drugs* 2003; 17: 825–837.

Herrmann, N., Eryavec, G. Buspirone in the management of agitation and aggression associated with dementia. *American Journal of Geriatric Psychiatry* 1993; 1.

Kirven, L.E., Montero, E.F. Comparison of thioridazine and diazepam in the control of non-psychotic symptoms associated with senility: double-blind study. *Journal of the American Geriatric Society* 1973; 21: 546–551.

Levy, M.A., Burgio, L.D., Sweet, R., Bonino, P., Janosky, J., Perel, J. A trial of buspirone for the control of disruptive behaviors in community-dwelling patients with dementia. *International Journal of Geriatric Psychiatry* 1994; 9: 841–848.

Meehan, K.M., Wang, H., David, S.R., et al. Comparison of rapidly acting intramuscular olanzapine, lorazepam, and placebo: a double-blind, randomized study in acutely agitated patients with dementia. *Neuropsychopharmacology* 2002; 26: 494–504.

Miscellaneous drug classes

Burke, W.J., Ranno, A.E., Roccaforte, W.H., Wengel, S.P., Bayer, B.L., Willcockson, N.K. L-deprenyl in the treatment of mild dementia of the Alzheimer type: preliminary results. *Journal of the American Geriatrics Society* 1993; 41: 367–370.

Freedman, M., Rewilak, D., Xerri, T., et al. L-deprenyl in Alzheimer's disease: Cognitive and behavioral effects. *Neurology* 1998; 50: 660–668.

Goad, D.L., Davis, C.M., Liem, P., Fuselier, C.C., McCormack, J.R., Olsen, K.M. The use of selegiline in Alzheimer's patients with behavior problems. *Journal of Clinical Psychiatry* 1991; 52: 342–345.

Jansen, S.L., Forbes, D.A., Duncan, V., Morgan, D.G. Melatonin for cognitive impairment. *Cochrane Database of Systematic Reviews* 2006: CD003802.

Krishnan, S., Cairns, R., Howard, R. Cannabinoids for the treatment of dementia. *Cochrane Database of Systematic Reviews (Online)* 2009(2): CD007204.

Lawlor, B.A., Aisen, P.S., Green, .C, Fine, E., Schmeidler, J. Selegiline in the treatment of behavioral disturbance in Alzheimer's disease. *International Journal of Geriatric Psychiatry* 1997; 12: 319–322.

Manfredi, P.L., Breuer, B., Wallenstein, S., et al. Opioid treatment for agitation in patients with advanced dementia. *International Journal of Geriatric Psychiatry* 2003; 18: 700–705.

Passmore, M.J., Passmore, M.J. The cannabinoid receptor agonist nabilone for the treatment of dementia-related agitation. *International Journal of Geriatric Psychiatry* 2008; 23: 116–117.

Peskind, E.R., Tsuang, D.W., Bonner, L.T., et al. Propranolol for disruptive behaviors in nursing home residents with probable or possible Alzheimer disease: a placebo-controlled study. *Alzheimer Disease & Associated Disorders* 2005; 19: 23–28.

Petrie, W.M., Ban, T.A. Propranolol in organic agitation. *Lancet* 1981; 1: 324.

Randels, P.M., Marco, L.A,. Ford, D.I., Mitchell, R., Scholl, M., Plesnarski, J. Lithium and lecithin treatment in Alzheimer's disease: a pilot study. *Journal of Clinical Psychiatry* 1984; 6: 139–147.

Schneider, L.S., Pollock, V.E., Zemansky, M.F., Gleason, R.P., Palmer, R., Sloane, R.B. A pilot study of low-dose L-deprenyl in Alzheimer's disease. *Journal of Geriatric Psychiatry & Neurology* 1991; 4: 143–148.

Serfaty, M., Kennell-Webb, S., Warner, J., et al. Double blind randomised placebo-controlled trial of low dose melatonin for sleep disorders in dementia. *International Journal of Geriatric Psychiatry* 2002; 17: 1120–1127.

Singer, C., Tractenberg, R.E., Kaye, J., et al. A multicenter, placebo-controlled trial of melatonin for sleep disturbance in Alzheimer's disease. *Sleep* 2003; 26: 893–901.

Tariot, P.N., Cohen, R.M., Sunderland, T, et al. L-deprenyl in Alzheimer's disease. Preliminary evidence for behavioral change with monoamine oxidase B inhibition. *Archives of General Psychiatry* 1987; 44: 427–433.

Walther, S., Mahlberg, R., Eichmann, U., et al. Delta-9-tetrahydrocannabinol for nighttime agitation in severe dementia. *Psychopharmacology* 2006; 185: 524–528.

Wang, L.Y., Shofer, J.B., Rohde, K., et al. Prazosin for the treatment of behavioral symptoms in patients with Alzheimer disease with agitation and aggression. *American Journal of Geriatric Psychiatry* 2009; 17: 744–751.

Weiler, P.G., Mungas, D., Bernick, C. Propranolol for the control of disruptive behavior in senile dementia. *Journal of Geriatric Psychiatry & Neurology* 1988; 1: 226–230.

Williams, K.H., Goldstein, G. Cognitive and affective responses to lithium in patients with organic brain syndrome. *American Journal of Psychiatry* 1979; 136: 800–803.

Treatment of sleep disturbances in dementia

Ancoli-Israel, S., Amatniek, J., Ascher, S,. Sadik, K., Ramaswamy, K. Effects of galantamine versus donepezil on sleep in patients with mild to moderate alzheimer disease and their caregivers: A double-blind, head-to-head, randomized pilot study. *Alzheimer Disease and Associated Disorders* 2005 19: 240–245.

Markowitz, J.S., Gutterman, E.M., Lilienfeld, S., Papadopoulos G. Sleep-related outcomes in persons with mild to moderate Alzheimer disease in a placebo-controlled trial of galantamine. *Sleep* 2003; 26: 602–606.

Mizuno, S., Kameda, A., Inagaki, T., Horiguchi, J. Effects of donepezil on alzheimer's disease: The relationship between cognitive function and rapid eye movement sleep. *Psychiatry and Clinical Neurosciences* 2004; 58: 660–665.

Moraes Wdos, S., Poyares, D.R., Guilleminault, C., Ramos, L.R., Bertolucci, P.H., Tufik, S. The effect of donepezil on sleep and REM sleep EEG in patients with alzheimer disease: A double-blind placebo-controlled study. *Sleep* 2006; 29: 199–205.

Salami, O., Lyketsos, C., Rao, V. Treatment of sleep disturbance in Alzheimer's dementia. *International Journal of Geriatric Psychiatry* 2011; 26: 771–782.

Pain management in dementia

Chibnall, J. T., Tait, R. C., Harman, B., Luebbert, R. A. Effect of acetaminophen on behavior, well-being, and psychotropic medication use in nursing home residents with moderate-to-severe dementia. *Journal of the American Geriatrics Society* 2005; 53: 1921–1929.

Corbett, A., Husebo, B., Malcangio, M., Staniland, A., Cohen-Mansfield, J., Aarsland, D., et al. Assessment and treatment of pain in people with dementia. *Nature Reviews Neurology* 2013 May 28.

Husebo, B.S., Ballard, C., Cohen-Mansfield, J., Seifert, R., Aarsland, D. The response of agitated behavior to pain management in persons with dementia. *American Journal of Geriatric Psychiatry* 2013 Apr 20.

Husebo, B.S., Ballard, C., Sandvik, R., Nilsen, O.B., Aarsland, D. Efficacy of treating pain to reduce behavioral disturbances in residents of nursing homes with dementia: Cluster randomised clinical trial. *BMJ (Clinical Research Edition)* 2011; 343: d4065.

Kovach, C.R., Logan, B.R., Noonan, P.E., Schlidt, A.M., Smerz, J., Simpson, M., et al. Effects of the serial trial intervention on discomfort and behavior of nursing home residents with dementia. *American Journal of Alzheimer's Disease and Other Dementias* 2006; 21: 147–155.

Manfredi, P.L., Breuer, B., Wallenstein, S., et al. Opioid treatment for agitation in patients with advanced dementia. *International Journal of Geriatric Psychiatry* 2003; 18: 700–705.

Electroconvulsive therapy for BPSD and depression

Carlyle, W., Killick, L., Ancill, R. ECT: an effective treatment in the screaming demented patient. *Journal of the American Geriatrics Society* 1991; 39: 637.

Grant, J.E., Mohan, S.N. Treatment of agitation and aggression in four demented patients using ECT. *The Journal of ECT* 2001; 17: 205–209.

Liang, R.A., Lam, R.W., Ancill, R.J. ECT in the treatment of mixed depression and dementia. *British Journal of Psychiatry* 1988; 152: 281–284.

Price, T.R., McAllister, T.W. Safety and efficacy of ECT indepressed patients with dementia: A Review of Clinical Experience. *Convulsive Therapy* 1989; 5: 6174.

Rao, V., Lyketsos, C.G. The benefits and risks of ECT for patients with primary dementia who also suffer from depression. *International Journal of Geriatric Psychiatry* 2000; 15: 729–735.

Dementia with Lewy bodies and Parkinson's disease dementia

Aarsland, D., Zaccai, J., Brayne, C., Aarsland, D., Zaccai, J., Brayne, C. A systematic review of prevalence studies of dementia in Parkinson's disease. *Movement Disorders* 2005; 20: 1255–1263.

Allen, R..L, Walker, Z., D'Ath, P.J., Katona, C.L. Risperidone for psychotic and behavioral symptoms in Lewy body dementia. *Lancet* 1995; 346: 185.

Cummings, J.L., Street, J., Masterman, D., et al. Efficacy of olanzapine in the treatment of psychosis in dementia with Lewy bodies. *Dementia & Geriatric Cognitive Disorders* 2002; 13: 67–73.

Emre, M., Aarsland, D., Albanese, A., et al. Rivastigmine for dementia associated with Parkinson's disease. *New England Journal of Medicine* 2004; 351: 2509–2518.

Fernandez, H.H., Trieschmann, M.E., Burke, M.A., et al. Quetiapine for psychosis in Parkinson's disease versus dementia with Lewy bodies. *Journal of Clinical Psychiatry* 2002; 63: 513–515.

Kurlan, R., Cummings, J., Raman, R., et al. Quetiapine for agitation or psychosis in patients with dementia and parkinsonism. *Neurology* 2007; 68: 1356–1363.

Lee, H., Cooney, J.M., Lawlor, B.A. The use of risperidone, an atypical neuroleptic, in Lewy body disease. *International Journal of Geriatric Psychiatry* 1994; 9: 415–417.

McKeith, I.G., Ballard, C.G., Harrison, R.W. Neuroleptic sensitivity to risperidone in Lewy body dementia. *Lancet* 1995; 346: 699.

McKeith, I., Del Ser, T., Spano, P., et al. Efficacy of rivastigmine in dementia with Lewy bodies: a randomised, double-blind, placebo-controlled international study. *Lancet* 2000; 356: 2031–2036.

McKeith, I.G., Dickson, D.W., Lowe, J., et al. Diagnosis and management of dementia with Lewy bodies: third report of the DLB Consortium. *Neurology* 2005; 65: 1863–1872.

Parkinson Study Group. Low-dose clozapine for the treatment of drug-induced psychosis in Parkinson's disease. *New England Journal of Medicine* 1999; 340: 757–763.

Pollak, P., Tison, F., Rascol, O., et al. Clozapine in drug induced psychosis in Parkinson's disease: a randomised, placebo-controlled study with open follow up. *Journal of Neurology, Neurosurgery, and Psychiatry* 2004; 75: 689–695

Ravina, B., Putt, M., Siderowf, A., et al. Donepezil for dementia in Parkinson's disease: a randomised, double-blind, placebo-controlled, crossover study. *Journal of Neurology, Neurosurgery, and Psychiatry* 2005; 76: 934–939.

Frontotemporal dementia

Boxer, A.L., Lipton, A.M., Womack, K., et al. An open-label study of memantine treatment in 3 subtypes of frontotemporal lobar degeneration. *Alzheimer Disease & Associated Disorders* 2009; 23: 211–217.

Bozeat, S., Gregory, C.A., Ralph, M.A., Hodges, J.R. Which neuropsychiatric and behavioral features distinguish frontal and temporal variants of frontotemporal dementia from Alzheimer's disease? *Journal of Neurology, Neurosurgery, and Psychiatry* 2000; 69: 178–186.

Freedman, M. Frontotemporal dementai: recommendations for therapeutic studies, designs, and approaches. *Canadian Journal of Neurological Science* 2007; 34: S118–S124.

Huey, E.D., Taylor,J.L., Luu, P., Oehlert, J., Tinklenberg, J.R. Factors associated with use of medications with potential to impair cognition or cholinesterase inhibitors among Alzheimer's disease patients. *Alzheimer's and Dementia* 2006; 2: 314–321.

Kaye, E.D., Petrovic-Poljak, A., Verhoeff, N.P., et al. Frontotemporal dementia and pharmacologic interventions. *Journal of Neuropsychiatry & Clinical Neurosciences* 2010; 22: 19–29.

Lebert, F., Stekke, W., Hasenbroekx, C., Pasquier, F. Frontotemporal dementia: a randomised, controlled trial with trazodone. *Dementia & Geriatric Cognitive Disorders* 2004; 17: 355–359.

McKhann, G.M., Albert, M.S., Grossman, M., et al. Clinical and pathological diagnosis of frontotemporal dementia: report of the Work Group on Frontotemporal Dementia and Pick's Disease. *Archives of Neurology* 2001; 58: 1803–1809.

Treatments for inappropriate sexual behavior

Joller, P., Gupta, N., Seitz, D.P., Frank, C., Gibson, M., Gill, S.S. Approach to inappropriate sexual behavior in people with dementia. *Canadian Family Physician* 2013; 59: 255–260.

Ozkan, B., Wilkins, K., Muralee, S., et al. Pharmacotherapy for inappropriate sexual behaviors in dementia: a systematic review of literature. *American Journal of Alzheimer's Disease & Other Dementias* 2008; 23: 344–354.

Treatment of apathy

Berman, K., Brodaty, H., Withall, A., Seeher, K. Pharmacologic treatment of apathy in dementia. *The American Journal of Geriatric Psychiatry* 2012; 20: 104–122.

Cummings, J.L., Schneider, L., Tariot, P.N., Kershaw, P.R., Yuan, W. Reduction of behavioral disturbances and caregiver distress by galantamine in patients with Alzheimer's disease. *American Journal of Psychiatry* 2004; 161: 532–538.

Erkinjuntti, T. Treatment options: The latest evidence with galantamine (reminyl). *Journal of the Neurological Sciences* 2002; 203–204:125–130.

Herrmann, N., Rabheru, K., Wang, J., Binder, C. Galantamine treatment of problematic behavior in Alzheimer disease: Post-hoc analysis of pooled data from three large trials. *American Journal of Geriatric Psychiatry* 2005; 13: 527–534.

Herrmann, N., Rothenburg, L.S., Black, S.E., Ryan, M., Liu, B.A., Busto, U.E., et al. Methylphenidate for the treatment of apathy in Alzheimer disease: Prediction of response using dextroamphetamine challenge. *Journal of Clinical Psychopharmacology* 2008; 28: 296–301.

Rosenberg, P.B., Lanctôt, K.L., Drye, L.T., Herrmann, N., Scherer, R.W. Bachman, D.L., Mintzer, J.E. Safety and efficacy of methylphenidate for apathy in Alzheimer's disease: A randomized, placebo-controlled trial. *Journal of Clinical Psychiatry* 2013; 74: e1–7.

Tariot, P.N., Cummings, J.L., Katz, I.R., Mintzer, J., Perdomo, C.A., Schwam, E.M., et al. A randomized, double-blind, placebo-controlled study of the efficacy and safety of donepezil in patients with Alzheimer's disease in the nursing home setting. *Journal of the American Geriatrics Society* 2001; 49:1590–1599.

INTERNATIONAL PSYCHOGERIATRIC ASSOCIATION

www.ipa-online.org

MODULE 7

Cross-cultural and transnational considerations

The IPA Complete Guides to Behavioral and Psychological Symptoms of Dementia

BPSD

Specialists Guide

Specialists • Primary Care Physicians • Nurses

MODULE 7: Cross-cultural and transnational considerations

Contents

Key messages	**7.3**
Introduction	**7.3**
Aspects of BPSD likely to vary across cultures	**7.3**
Prevalence and presentation	7.4
BPSD in people of African descent living in Nigeria, Jamaica and the United States	7.5
Neuropsychiatric symptoms in MCI	7.7
Approaches to assessment	7.7
Approaches to management	7.10
Research methodological considerations	7.12
BPSD in minority elders in the United States	**7.12**
Prevalence and presentation of BPSD in minority elders	7.13
Assessment of dementia and BPSD	7.15
Approaches to management	7.16
BPSD in the Middle East	**7.16**
BPSD in Turkey	7.16
Assessment and frequency of BPSD	7.17
BPSD in Iran	7.18
BPSD in Asia	**7.19**
BPSD in India	7.19
Historical background	7.19
Demography of India	7.19
Economic conditions and social security for older people	7.19
Impact on family	7.20
Globalization and marginalization	7.20
Impact of 'Graying Nation' on health issues	7.20
Dementia prevalence, cost of care and services	7.20
BPSD and the burden of care	7.20
Nature and prevalence of BPSD	7.21
Approaches to management	7.22
Barriers to dementia care in India	7.23
Dementia care services in India	7.23
BPSD in China, Hong Kong SAR and Taiwan	7.24
Prevalence and presentation	7.24
Approaches to management	7.26
BPSD in South Korea	7.27
South Korea in 2013	7.27
Prevalence of BPSD in South Korea	7.27

Awareness of dementia including BPSD	7.28
Assessment of dementia	7.28
Management of dementia	7.28
Challenges	7.29
BPSD in Japan	7.29
Society aging	7.29
Rapid transition from aging to aged society	7.29
BPSD	7.30
Management of BPSD	7.30
Government policy to improve care for dementia patients	7.31
Conclusions	7.32
BPSD in Latin America	**7.32**
BPSD in Argentina	7.32
Frequency of BPSD	7.33
BPSD and caregiver burden	7.33
Approaches to management	7.33
BPSD in Mexico	7.34
Background	7.34
BPSD prevalence and caregiver burden	7.34
BPSD in Brazil	7.35
BPSD prevalence and measurement	7.35
BPSD treatment	7.36
Conclusions	7.37
BPSD in Africa	**7.37**
BPSD in Nigeria	7.37
References and recommended reading	**7.38**

Key messages

- Studying behavioral and psychological symptoms of dementia (BPSD) across cultures allows the identification of similarities and differences that may be useful to determine the best approach to managing these symptoms in different populations.
- An effective approach to management in one culture may not necessarily work in another, given the different prevalence of various BPSD and the level of tolerance for these symptoms within that culture.
- A patient's and caregiver's location can affect the impact and subsequent management of BPSD. Symptoms that pose difficulties in an urban setting (such as pacing or wandering) may not be regarded as problematic in a rural setting (where most patients will have room to pace and are less vulnerable if they wander).
- Comorbid conditions such as schizophrenia, depression, and alcoholism may vary in frequency across communities and could alter the presentation of BPSD in people with dementia.

Introduction

This module reviews cross-cultural and transnational aspects of BPSD and gives a series of snapshots from different ethnic groups, cultures, and nations around the world. It begins with a discussion of aspects of BPSD likely to vary across cultures and examines the reasons behind real or apparent differences. Each of the cross-cultural perspectives comes from physicians who all understand the culture described.

Dementia and associated BPSD are already recognized as a major medical challenge for the aging populations of the Western world. Although in many developing countries, BPSD are not yet regarded as a central focus, there is no doubt that in time these symptoms will present a management issue for these countries. The groundwork in observing similarities and differences in dementia and BPSD across cultures discussed herein will likely prove valuable in the future. In addition, studies examining neuropsychiatric symptoms in mild cognitive impairment (MCI) have emerged. This research will allow further investigations into the course of neuropsychiatric symptoms in the development of dementia.

Aspects of BPSD likely to vary across cultures

The study of BPSD across cultures and nations allows the identification of similarities and differences to determine the best approach to management. However, it is possible that an effective approach to management in one culture may not necessarily work in another, given the varying levels of prevalence and tolerance of BPSD within the communities in which they occur. As Shah pointed out, comparisons among different studies are problematic, because different studies have used different samples and settings, diagnostic groups, measurement instruments, methods of data collection, and methodology (Shah, et al., 2005).

In the following section, cultural factors critical to our understanding of the prevalence and presentation of BPSD and neuropsychiatric symptoms in MCI, and its assessment and management will be reviewed. Included in this is a comparison of BPSD in people of African descent residing in the United States, Jamaica and Nigeria. Further, the impact of research methodology on our understanding of these areas will be evaluated. Lastly, cross-cultural perspectives pertaining to BPSD in Turkey, India, Argentina, Brazil, Nigeria, Iran, Mexico, Japan, China, Hong Kong SAR, Taiwan, South Korea and minority elders in the United States will be highlighted.

Prevalence and presentation

Prevalence and presentation of BPSD in different communities are affected by a variety of illness-related and cultural factors. Illness-related factors include the rates of dementing disorders in the community and the expected life span. In some African and Asian countries, the lifespan of the general population is shorter than in some Western countries. This lessened life span may influence:

- The development of BPSD
- Caregiver perceptions of the severity of symptoms

In addition to prevalence and survival rates, BPSD may vary according to the predominant dementia subtype(s) found in the community. The comorbid conditions of schizophrenia, depression, and alcoholism may also vary in frequency across communities and could alter the presentation of BPSD in persons with dementia. The 10/66 Dementia Research Group found that there were regional differences for individual behaviors with high rates of agitation, wandering, and sleep disturbance among Indian participants, and high rates of vocalization among Latin-American people with dementia. Overall, numbers of reported BPSD were highest in India, intermediate in Latin America, and lowest in China (10/66 Dementia Research Group, 2004). Culture-related factors may also influence the prevalence and presentation of BPSD. In some countries, caregivers deny BPSD to avoid the stigma of mental illness.

Although it is important to evaluate the cultural factors among various countries, it is important to recognize the cultural variations within a country. In the section on Argentina, the authors report a mixture of ethnic cultures. In Buenos Aires, for example, caregivers are more apt to inquire about BPSD treatment. Argentineans descending from the Volga region of Germany, in comparison, are more likely to deny BPSD as these symptoms are stigmatizing. Additionally, in many studies examining neuropsychiatric symptoms among black patients with dementia in the United States, black populations are treated as homogeneous groups (Cohen and Magai, 1999). This treatment is problematic due to intraracial differences in psychiatric symptom expression (Cohen and Magai, 1999). Therefore, it is important to consider the possibility of intraracial differences when making comparisons about the prevalence and presentation of BPSD.

Table 7.1: Population-based prevalence (%) of BPSD in persons with dementia

	US Lyketsos et al., 2002	UK Savva et al., 2009	Spain Fernandez-Martinez et al., 2008	Brazil Tatsch et al., 2006	China Xie et al., 2004	Japan Ikeda et al., 2004	Nigeria Baiyewu et al., 2003
Symptoms in NPI	(n = 362)	(n = 587)[a]	(n = 108)	(n = 60)	(n = 373)	(n = 60)	(n = 40)
Delusions	18.0	25.4	16.7	11.7	11.0	26.7	17.5
Hallucinations	10.5	15.1	15.7	8.3	10.7	15.0	12.5
Agitation/ aggression	30.3	9.0	27.8	20	12.3	35.0	20.0
Depression/ dysphoria	32.3	20.5	32.4	38.3	23.9	21.7	32.5
Anxiety	21.5	8.9	35.2	25.0	20.4	23.3	20.0
Euphoria/ elation	3.1	9.5	4.6	5.0	6.4	8.3	10.0
Apathy/ indifference	35.9	50.3	53.7	53.3	21.7	56.7	25.0
Disinhibition	12.7	n.a.	12.0	16.7	1.3	8.3	10.0
Irritability/ lability	27.0	28.8	26.9	23.3	16.9	31.7	27.5
Aberrant motor behavior	16.0	12.8	16.7	10.0	12.1	31.7	7.5
Nighttime behavior	27.4	42.0	22.2	38.3	19.8	n.a.	17.5
Appetite/eating change	19.6	n.a.	30.6	23.3	11.8	n.a.	42.5

[a]BPSD were assessed using interviews and observations instead of Neuropsychiatric Inventory.
n.a. = not available

As illustrated in Table 7.1, population-based prevalence of BPSD in persons with dementia was dissimilar in the studies conducted in the United States (Lyketsos et al., 2002), United Kingdom (Savva et al., 2009), Spain (Fernández Martínez et al., 2008), Brazil (Tatsch et al., 2006), China (Xie et al., 2004), Japan (Ikeda et al., 2004), and Nigeria (Baiyewu et al., 2003). Probably the most remarkable difference was the frequency of apathetic symptoms in China and Nigeria compared to other countries. This difference may be explained by the fact that apathy is generally under-recognized, especially in the elderly who have limited roles in society.

BPSD in people of African descent living in Nigeria, Jamaica and the United States. One of the major transcultural studies of dementia involved a comparison of a Nigerian community (the Yoruba people living in Ibadan, Nigeria), a Jamaican community (in Kingston, Jamaica), and an African American community (living in Indianapolis, Indiana, United States) (Hendrie et al., 1996). Differences in the prevalence and levels of tolerance of BPSD in each have been described. Ibadan is a major Nigerian city of more than one million people; however, despite its

urban setting, the Yoruba community functions much like a village. The Jamaican population lives in a poor suburb of Kingston, and the African American population lives in a moderate-size city of approximately one million people.

Data regarding the prevalence of BPSD in the different communities were gathered from caregiver reports. The findings are presented in Table 7.2. It should be noted that these data are not corrected for age and severity of dementia among populations, and so direct comparisons among the groups are difficult. Dementia was most severe in the Jamaican sample (previously identified dementia patients attending a medical clinic) and least severe in the Nigerian sample (patients with dementia identified as part of a community study). The comparison showed that:

- African American and Jamaican patients were less likely than Nigerians to complete tasks related to personal care (functional ability) and more likely to become lost in the community.
- Caregivers of African American patients were more likely to report changes in personality—whether this result reflects a real difference in the number of patients with personality changes or a difference in the level of tolerance to such symptoms is not clear.
- Nigerian caregivers were clearly more concerned than their counterparts in the United States and Jamaica by their demented relatives becoming involved in situations they regarded as embarrassing.
- Neither Nigerian nor Jamaican caregivers reported depression associated with dementia as a significant symptom.

Table 7.2: Prevalence (by percent) of selected BPSD and functional deficits in the United States, Jamaica, and Nigeria. Reprinted with permission from Hendrie et al., 1996.

BPSD and Functional Deficits	Indianapolis USA (n = 50)	Kingston Jamaica (n = 18)	Ibadan Nigeria (n = 28)
Personal care			
Feeds self	57	64	86
Dresses self	42	28	75
Personal hygiene	42	28	75
Lost in community	22	50	15
Personality Changes			
Any change*	64	29	37
Stubborn or obstinate	72	50	26
Irritable or angry	52	33	19
Inappropriate behavior in public	17	19	26
Psychiatric symptoms			
Depression	14	6	4
Delusions	21	18	4
Hallucinations	4	22	4

*Reflects the clinician's opinion about whether the change significantly affected caregiving. The percentage in this category may be lower than that for the other subcategories.

Neuropsychiatric symptoms in MCI. Table 7.3 summarizes the population-based prevalence of neuropsychiatric symptoms in individuals with MCI. The commonest symptoms in MCI are depression, nighttime behavior, apathy, anxiety, and irritability. However, symptoms such as delusions, hallucinations, euphoria, disinhibition, and aberrant motor behaviors are relatively infrequent in MCI. Generally there are no remarkable differences across studies in the United States (Lyketsos et al., 2002; Geda et al., 2008), Brazil (Tatsch et al., 2006), Hong Kong (Chan et al., 2010) and Australia (Brodaty et al., 2012).

Table 7.3: Population-based prevalence (%) of neuropsychiatric symptoms in persons with MCI

	US Lyketsos et al., 2002	US Geda et al., 2008	Brazil Tatsch et al., 2006	Hong Kong Chan et al., 2010	Australia Brodaty et al., 2012
Symptoms in NPI	(n = 320)	(n = 319)	(n = 25)	(n = 338)	(n = 319)
Delusions	3.1	3.4	0.0	2.4	0.0
Hallucinations	1.3	0.6	0.0	0.9	0.3
Agitation/aggression	11.3	9.1	8.0	5.1	4.7
Depression/dysphoria	20.1	27.0	16.0	14.6	14.7
Anxiety	9.9	14.1	24.0	12.5	5.0
Euphoria/elation	0.6	1.3	0.0	0.6	1.6
Apathy/indifference	14.7	18.5	12.0	15.2	4.7
Disinhibition	3.1	4.7	0.0	1.8	2.5
Irritability/lability	14.7	19.4	12.0	8.0	6.3
Aberrant motor behavior	3.8	1.3	0.0	0.9	1.9
Nighttime behavior	13.8	18.3	24.0	16.1	7.9
Appetite/eating change	10.4	10.7	4.0	2.1	6.0

Approaches to assessment

Evaluation of behavioral disorders in older patients with dementia poses some specific problems when working in different cultural settings. It is important to note the following critical factors when making comparisons across cultures:

- Awareness of the significance of BPSD
- Level of expertise in assessment of BPSD
- Tolerance of specific behavioral and psychological symptoms
- Cultural appropriateness of rating scales

In many countries dementia and BPSD are perceived as a consequence of aging. As a result, caregivers may not even seek assessment of the symptoms unless these symptoms are deemed severe. It is important to note, however, that some countries highlighted in this module have

made a concerted effort to promote the awareness of dementia over the last few years. For example, as Alzheimer's organizations are becoming more active in many areas of the world the awareness of dementia is heightened, and caregivers are finding outlets to discuss dementia. In immigrant countries such as Australia, Canada, the United States, and the United Kingdom, dementia awareness in minority ethnic groups may be lower than the rest of the population. For example, Italian, Greek and Chinese Australians had poor dementia literacy in comparison with third-generation Australians, and there were also differences among the three ethnic groups (Low et al., 2010).

The tolerance of specific BPSD also differs across cultures. Although wandering may be considered an important focus in the management of dementia in the United States, it was not considered a problem in India until recently. Incontinence, however, has been noted in the literature to be of concern, because there is a high expectation of a certain level of personal hygiene in India (Chandra, 1996). A study comparing frontotemporal dementia (FTD) in the United States, Greece, and Turkey found that the frontal variant of FTD was diagnosed at an earlier age and had reported earlier symptom onset in the United States than in Greece or Turkey. Furthermore, neuropsychological measures indicate that at diagnosis, FTD patients in the United States were less impaired than patients in Greece and Turkey. Patients with FTD in Greece and Turkey were diagnosed later in the disease, presumably because their behavioral symptoms were not easily detected by the medical system in these countries (Papatriantafyllou et al., 2009).

Rating scales are an important means in assessing BPSD. Yet, if cross-cultural comparisons are to be made, these rating scales must be compatible across cultures. Most rating scales involve observations of symptoms by key informants, usually spouses. This element is probably a reasonable way to proceed within one culture or one defined population, because informants' views about what constitute acceptable behavior or disruptive symptoms are likely to be somewhat similar. This similarity may not hold across cultures, however, where tolerance of behaviors and understanding and expectations of the elderly may vary widely. To ensure validity in the assessment of BPSD, rating scales need to include some measurement of informant personality characteristics including tolerance of disruptive behavior and views on the role of the elderly.

› Rating scales need to be translated into local languages. Further, the scales should be 'harmonized'—the instruments must be consistent with the cultural, linguistic, and educational norms of the subject population.

Prior to the development of local language versions of rating scales, the clinical terms included in the scales should be clearly defined. For example, the definition of agitation used in the CMAI is somewhat different from that in Japan where physically abusive behaviors are usually not included in agitation. In Japan, agitation means behaviors with restlessness and irritable mood.

Rating scales that can be applied with validity in different cultures have been developed. For example, the Composite International Diagnostic Interview (CIDI), a World Health Organization (WHO)-sponsored international epidemiologic interview, and an expansion of the Diagnostic Interview Schedule (DIS), has now been tested in worldwide field trials.

There are now reliable screening instruments to identify dementia based upon cognitive performance. Some of these, like the Hindi Mental State Exam (HMSE) and the Cognitive Abilities Screening Instrument (CASI), have been used successfully in cross-cultural studies. The Rowland Universal Dementia Assessment Scale (RUDAS) is an Australian screening instrument designed to be language- and culture-fair with promising psychometric properties (Rowland et al., 2006); however, it needs further validation across a range of cultural and ethnic groups, in different settings (general practice, acute hospitals, community service providers), and in measuring change.

One assessment scale, the Community Screening Instrument for Dementia (CSID) has been developed to include both cognitive testing and informant data about performance in everyday living. This instrument has now been used with good sensitivity and specificity in the Cree (Native American), African American, Chinese, and Yoruba (Nigerian) populations.

Clinical assessment instruments based upon translations of the Consortium to Establish a Registry in Alzheimer's disease (CERAD) neuropsychological battery, the Geriatric Mental Status (GMS), and the Cambridge Examination for Mental Disorders of the Elderly (CAMDEX) are also available. There are now several internationally used rating scales available in Asian countries (Homma et al., 2000). The NPI has been used to assess BPSD in the United States, Taiwan, Japan, and Italy. More recently, the NPI has been used in patients with dementia from Yoruba, Nigeria, after being translated, back translated, and harmonized into Yoruba (Baiyewu et al., 2003).

In its pilot study, the 10/66 Dementia Research Group made an attempt to develop a one-stage screening procedure for dementia in the community (Prince et al., 2003). They interviewed 2,885 persons aged 60 and older in 25 centers in India, China and South East Asia, Latin America and the Caribbean, and Africa; 729 people with dementia and three groups free of dementia; 702 with depression, 694 with high education, and 760 with low education. Experienced local clinicians diagnosed dementia (DSM-IV dementia and Clinical Dementia Rating mild or moderate) and depression (Montgomery Asberg Depression Rating Scale 18 or over). The Geriatric Mental State, the Community Screening Instrument for Dementia, and the modified CERAD 10-word list-learning tasks were then administered by an interviewer, masked to case status.

Each measure independently predicted dementia diagnosis. In a split-half procedure, an algorithm derived from all three performed better than any of them individually; applied to the other half of the sample, it identified 94% of dementia cases with false positive rates of 15%, 3%, and 6% in the depression, high education, and low education groups. The algorithm developed and tested by the 10/66 Dementia Research Group provides a sound basis for culture and education-fair dementia diagnosis in clinical and population-based research, supported by translations of its constituent measures into many languages, covering the majority of the peoples of the developing world (Prince et al., 2003).

When conducting cross-cultural comparative studies, there is no doubt that rating scales employed in the study should be harmonized from the view point of different ethnic backgrounds, as stated earlier. However, one of the more sensitive problems for most health professionals is how to choose an appropriate rating scale for the study or their daily activities in the community or facilities.

Shah et al., (2005) reviewed the instruments for measuring BPSD across different cultures and found that most measurement instruments have mainly been developed with conventional translation and back-translation techniques and subsequent evaluation of psychometric properties. Many rating scales have been translated and validated in other languages as documented in Table 7.4, which was adapted from Shah et al., (2005). In addition, the BEHAVE-AD has been used in India (Shaji et al., 2003) and the Neuropsychiatric Inventory (NPI) has been used in a Yoruba version in Nigeria (Baiyewu et al., 2003) and translated to Italian (Binetti et al., 1998). There are French versions of the Cornell Scale for Depression in Dementia (CSDD) and the Dementia Mood Assessment Scale (DMAS) (Camus et al., 1995) and a Chinese version of the Rating Scale for Aggression in the Elderly (RAGE) (Lam et al., 1997).

Table 7.4: Available language versions of BPSD measurement instruments

Instruments	Chinese	Japanese	Korean	Dutch	Spanish
BEHAVE-AD (Reisberg et al., 1987)	Lam et al., 2001	Asada et al., 1999	Suh et al., 2001 Suh and Park, 2001		Boada et al., 2006
NPI (Cummings et al., 1994) NPI-NH (Wood et al., 2000)	Fuh et al., 2001 Leung et al., 2001 Xie et al., 2004 Ma et al., 2010 (NPI-Q)	Hirono et al., 1997	Choi et al., 2000	Kat et al., (2002)	Boada et al., 2005
Revised Memory and Behavior Checklist (Teri et al., 1992)	Fuh et al., 1999				Harwood et al., 2001
Cohen-Mansfield Agitation Inventory (CMAI) (Cohen-Mansfield, 1986)	Choy et al., 2001	Schreiner, 2001	Suh, 2004	de Jonghe and Kat (1996)	
Cornell Scale for Depression in Dementia (Alexopoulos et al., 1988)		Schreiner and Morimoto, 2002	Shah et al., 2004		

Approaches to management

Reactions to BPSD and subsequent management approaches vary across different communities depending upon:

- Size and location of the community
- Availability of caregivers, and presence or absence of extended family
- Availability of healthcare services
- Availability of nursing homes

- Role and expectations of older people
- Concepts of dementia and deviant behavior
- Tolerance of BPSD in the community

In the study from Nigeria and Jamaica (Hendrie et al., 1996), data on the most troublesome symptoms reported by caregivers and most likely treatments were obtained from the study investigators who were also involved in providing healthcare to these elderly populations. Table 7.5 summarizes these findings.

Table 7.5: Treatment of BPSD in Jamaica and Nigeria. Adapted with permission from Hendrie et al., 1996

	Kingston, Jamaica	Ibadan, Nigeria
Recognized	Yes	Yes
Treatment available	Yes	Partially
Treatment sought	Yes	Seldom
More troublesome symptoms	Agitation	Agitation
	Wandering	Violence
	Violence	Delusions
	Sleeplessness	Hallucinations
Type of treatment	Pharmacotherapy and milieu therapy	Little direct treatment

Treatment depends largely on psychosocial and demographic factors, as has been noted earlier. In both Jamaican and Nigerian societies, the elderly are held in high regard and considered repositories of knowledge; thus, a considerable degree of tolerance towards BPSD is seen. Nigerians have a saying that, in old age, people become children again, despite their wisdom.

Early cognitive symptoms and BPSD are often misinterpreted by caregivers. In Jamaica, decreased cognitive function is often misunderstood by relatives and reported as 'difficult' behavior. Repeated question-asking is seen as 'attention-seeking'—a finding reported in a number of studies of caregiver perceptions in European and American populations. In Nigeria, caregivers often do not report symptoms such as hallucinations and delusions in their relatives with dementia for fear of a diagnosis of mental illness—something that carries considerable stigma in Yoruba culture.

Nursing home care is available for patients with dementia, with and without severe BPSD, in many countries. However, most patients with dementia reside at home with their families. In the United States, Caucasians utilize more nursing home beds compared to African Americans. In Turkey, patients with dementia reside mostly in their homes, although care in a specialized unit is reserved for those patients with severe BPSD. In Ibadan, Nigeria, there are no nursing homes for older patients with dementia, and consequently, all patients with dementia are managed at home by family members. Individuals with dementia are only brought to the hospital for concomitant illnesses such as fevers or pneumonia, and direct treatment of BPSD at home is unusual, although occasionally phenothiazines are prescribed.

In contrast, Jamaicans have access to primary care and specialist physicians, and treatment approaches are similar to those in the United States. There is little non-physician, community-based support. Treatment for the behavioral aspects of BPSD is primarily with milieu therapy, although pharmacotherapy is also used.

Research methodological considerations

Researchers must be careful about making assumptions about the prevalence or presentation of BPSD across cultures as well as the management and treatment of BPSD, due to a number of methodological factors (Jeste and Finkel, 2000; Cohen and Magai, 1999; Valle, 1994). Some specific examples include the following:

- It is important to note the comparability (or lack thereof) of the populations studied. Many studies are of convenience samples in nursing homes or outpatient clinics. Often, little information is provided about dementia severity, type of dementia, or methods of assessment and whatever information is provided might not be clearly defined.
- Many studies of BPSD do not provide a racial composition of the population studied or test for racial differences (Cohen and Magai, 1999).
- Much of the literature available from various countries is through studies with small sample sizes. More data from large representative samples are needed for useful comparisons.

BPSD in minority elders in the United States

The presence of Alzheimer's disease (AD) and other dementing disorders in different ethnic groups in the United States is well documented. However, the characteristics of dementing disorders, such as the presence of BPSD, remain largely unexplored in these groups. This situation is quite troublesome, in light of the diverse aging population.

Nearly 44 million people age 65 or older resided in the United States in 2013, representing about 13.9% of the population (CIA World Factbook, 2013). By 2060, the population aged 65 years and over is projected to more than double to 92 million (United States Census Bureau, 2012). The "oldest old," representing those people aged 85 and older, is the fastest growing segment of the elderly population. Representing approximately 5.7 million people in 2008 (2% of the U.S. population), it is projected that this group will increase to 18 million (4.3% US population) by 2060.

As the older population continues to grow, diseases such as dementia have a devastating impact on the older people and society. In 2012, 5.4 million Americans suffered from dementia (Alzheimer's Association, 2012). The growing number of patients with dementia has both public health and economic consequences. Despite underreporting, Alzheimer's disease is the sixth leading cause of death each year in the United States (Alzheimer's Association, 2012). Additionally, the annual cost of AD to society is approximately $200 billion (Alzheimer's Association, 2012).

As the United States witnesses an explosion of the elderly population, there will be a marked increase in the diversity of this population. This growth is of concern, because dementing disorders have been found to be high or higher in African Americans and Hispanics than in Caucasians (Tang et al., 1998). Hispanic Americans will be the fastest growing group and are

projected to increase from 17.8% of the US population in 2015 to 30.6% in 2060; African Americans from 13.2% in 2015 to 14.7% in 2060; Asian Americans from 5.3% in 2015 to 8.2% in 2060; and those reporting two or more races from 2.6% to 6.4% (US Census Bureau, 2012).

Yet, there is little scientific literature on dementia as it relates to ethnic minority elders. This lack is due mostly to the underrepresentation of minority elders in research (Morse et al., 1995; Lovato et al., 1997; Mouton et al., 1997; Stoy et al., 1995; Coleman et al., 1997; Moody et al., 1995; Arean and Gallagher-Thompson, 1996; Hall, 1999; Sinclair et al., 2000). For example, as part of the Genetics, Response and Cognitive Enhancers (GRACE) Conference, the data sets from Alzheimer's trials, including the National Institute on Aging (NIA)'s Alzheimer's Disease Cooperative Study (ADCS), and Phase II and III clinical trials for acetylcholinesterase inhibitors (galantamine, sabeluzole, and rivastigmine), were examined. Minorities represented only 3.6% (420) of the combined number of subjects enrolled in all studies (N = 11,537) (Sano, 2000).

Prevalence and presentation of BPSD in minority elders

Numerous studies have evaluated the prevalence and nature of BPSD in the United States (for example, see Cohen-Mansfield, 2009; Steinberg et al., 2008; Jeste and Finkel, 2000; Chen et al., 2000; Chung and Cummings, 2000). The reported prevalence of BPSD varies in AD literature as a result of a number of factors, including methodological variability, differences of inclusion and exclusion criteria, and selection bias in the referral population (Chung and Cummings, 2000). Further, much of the literature is limited by methodological concerns, including the inclusion of heterogeneous groups of dementia patients and small sample sizes. Studies that have evaluated the prevalence and presentation of BPSD across racial and ethnic groups in the United States have not been methodologically rigorous. Nevertheless, studies evaluating BPSD across racial and ethnic groups in the United States are presented in this module in order to highlight potential racial and ethnic differences and illustrate specific methodological issues.

Racial differences in neuropsychiatric symptoms were examined in 240 dementia outpatients (78% women) attending the Brooklyn Alzheimer's Disease Assistance Center of the State University of New York from 1992–1995 (Cohen & Magai, 1999). Sixty-eight percent of the cohort were African American (n = 164), and 32% were Caucasian (n = 76). Of the African American cohort, 63% were born in the United States and 37% were African Caribbean. Patients were diagnosed with dementia according to DMS-III-R criteria, resulting in a cohort with 70% AD; 17% with multi-infarct dementia; and 14% exhibiting features of AD and some mixed features. The authors specifically investigated psychoses, agitation, and depression in this group utilizing BEHAVE-AD.

Depressive affect was noted to be significantly higher in Caucasians than in African Americans. These findings are consistent with data showing fewer depressive symptoms among black nursing home residents (Walker et al., 1995). Psychoses and activity disturbance were noted to be significantly higher in African Americans, compared to Caucasians. These findings are consistent with other published literature (Cohen and Carlin, 1993; Cohen et al., 1996). After multivariate analysis, depressive affect and psychoses remained significant. No significant differences in symptoms were noted between United States-born African Americans and African Caribbeans. Differences were found between African Americans and Caucasians most likely due to racial differences in types of symptoms precipitating evaluation. The lack of significant differences between United States-born African Americans and African Caribbeans suggest that differences between African Americans and Caucasians may have biological or genetic etiology.

Limitations of this study included a nonrandom relatively small convenience sample of heterogeneous dementia patients brought to the center for evaluation. The racial differences may be, then, reflections of symptom perception and caregiver tolerance. Additionally, the authors suggest that African Caribbeans' presentation to the evaluation center may be due to acculturation. The authors note the possibility of different levels of symptomatology among African Caribbeans with dementia who have not received evaluation and treatment in the community setting, in comparison to African Caribbeans with dementia seeking evaluation and treatment.

A second study explored the stage-specific prevalence of behavioral symptoms in a multiethnic community sample of 125 outpatients diagnosed with either probable (n = 108) or possible (n = 17) Alzheimer's disease at the University of Washington Alzheimer's Disease Research Center (ADRC) (Chen et al., 2000), The study population included 38 African Americans, 63 Asian Americans/Pacific Islanders, 17 Hispanics, and seven native African Americans/Alaskan natives. A large number of the study population was non-English speaking immigrants, and 75% were women. Patients were diagnosed with dementia using the DSM-IV criteria for Alzheimer's disease and NINCDS/ADRDA. Behavioral symptoms were evaluated utilizing BEHAVE-AD. No significant differences were found in the severity of dementia among the ethnic groups. Hispanics were noted to have a significantly higher total behavioral symptom score compared to African Americans, who reported a lower overall prevalence of behavioral symptoms compared to the other ethnic groups and specifically had significantly reduced depressive, anxiety, and sleep symptoms compared to Asians and Hispanics.

Apart from possible concerns of the validity of the BEHAVE-AD (or any other behavioral scale for that matter) in a multiethnic population, the main limitations of this study were the convenience sampling and small sample sizes of the ethnic groups represented, thus limiting investigation of ethnic differences.

Two studies by the same research group, one a nursing home sample and the other a community sample post-discharge from a geriatric psychiatry unit, assessed for the presence and characteristics of agitation in African American and Caucasian patients with DSM-III dementia (Mintzer et al., 1996). The Cohen-Mansfield definition of *agitation* (i.e., inappropriate behavior unrelated to unmet needs or confusion per se) was used. Agitation was categorized according to the following three factors identified on the Cohen-Mansfield Agitation Inventory (CMAI):

- Aggressive behavior (e.g., hitting, kicking, pushing, scratching, tearing things, cursing or verbal aggression, grabbing, biting, spitting)
- Physically nonaggressive behavior (e.g., pacing, inappropriate dressing or undressing, repetitious sentences or questions, trying to get to a different place, handling things inappropriately, general restlessness, repetitious mannerisms)
- Verbally agitated behavior (e.g., complaining, constant requests for attention, negativism, repetitious sentences or questions, screaming)

An evaluation of 104 agitated patients with dementia was conducted in the nursing home study. The skilled-nursing-home patients were recruited from 12 centers as part of a multicenter clinical trial. There were 93 Caucasians and 11 African Americans. Of the Caucasian group, 62% were women. The African American group, however, had 73% men, who had a significantly

higher prevalence of aggressive behavior than Caucasians. Caucasians had a slightly higher prevalence of physically nonaggressive behaviors and verbally agitated behaviors compared with African Americans, but the differences were not statistically significant.

The community sample of 110 agitated patients with dementia post-discharge from a geriatric psychiatry unit had 86 Caucasians and 24 African Americans. The study population included 40 men. In the home setting, Caucasians exhibited significantly more verbally agitated behaviors than African Americans, although the overall level of agitation was not significantly different between the two ethnic groups. No significant differences in the prevalence of aggressive and physically nonaggressive behaviors were found between African Americans and Caucasians. Although African American patients had a higher prevalence of aggressive agitated behavior in nursing homes than did Caucasians, these differences were not elucidated in the community-based sample. Overall, the authors concluded that differences in agitated behavior appear to depend more on the setting than on the patient's race.

The limitations of these two studies included the small sample sizes, lack of control for dementia type and severity, and the higher proportion of males in the African American group.

A cross-sectional, case control study carried out at the Neuropsychiatry Service outpatient clinic at the Johns Hopkins School of Medicine, studied the relationship between isolated hallucinosis and race in AD (Bassiony et al., 2002). The participants were 237 community-residing patients with probable AD according to NINCDS/ADRDA criteria. Nine patients with isolated hallucinosis were compared to a control group of 228 patients who had neither delusions nor hallucinations. There was a significant association between hallucinations and race in patients with AD. Before adjustment for other variables, being African American conferred a 5.5-fold increased risk for isolated hallucinosis compared to being Caucasian. After adjustment for multiple other variables, this risk increased further to 27.2-fold. The limitations with this study included the small sample size and outpatient setting.

Assessment of dementia and BPSD. The actual assessment of dementia must be made before BPSD can be appropriately assessed. As stated earlier, a major goal is to develop culturally accurate measures that can be utilized in all ethnic populations (Sano, 2000). Clinicians and researchers must be aware that in the United States, ethnic groups differ from each other by language, communication, and quality of education—all of which can contribute to misdiagnosis (Manly, 2002; Espino and Lewis, 1998).

A number of studies in the United States have reported a significantly higher risk of developing Alzheimer's disease in African Americans and Hispanics than in Caucasians, even after correcting for years of education (Sano, 2000). Do these reports represent an increased prevalence of dementia or inaccurate assessments based on educational and/or literacy level? Manly et al., 2000, caution that the quality of education differs among countries but also within each country (Sano, 2000; Manly et al., 2000; Manly et al., 1999.) As such, matching ethnic groups on the basis of their years of education may be based on an inappropriate assumption that the quality of education is comparable (Manly, 2000). Another factor regarding the assessment of dementia is the caregiver-patient relationship, because many scales and assessments require information from the caregiver (Sano, 2000). Cultural differences have been noted in caregivers. For example, caregivers tend to be spouses for Caucasian patients, although for African American and Hispanic patients, caregivers tend to be children or

siblings. In the future, the effect of caregiver relationships on outcome measures will need to be explored. A systematic review and meta-analysis of ethnic differences in minority ethnic (ME) people with dementia in western countries found that minority ethnic people were more cognitively impaired and Hispanic people reported a longer duration of memory loss than non-ME people at the time of referral to diagnostic dementia services in the United States. These differences remained after controlling for premorbid level of education (Cooper et al., 2010).

Approaches to management. Methodologically rigorous data is lacking in the evaluation of cultural differences in the management of BPSD in the United States. Racial and ethnic differences could be responsible for differences in drug metabolism, side-effect profile, and treatment (Tang et al., 1998; Chang et al., 1991; Jann et al., 1989). Differences in anti-dementia medication use between non-Hispanic white and minority community-dwelling Medicare beneficiaries with dementia were investigated using multivariate analysis for anti-dementia medication use by race/ethnicity for 1,120 beneficiaries with dementia from years 2001 through 2003 of the Medicare Current Beneficiary Survey (Zuckerman et al., 2008). After adjusting for demographics, socioeconomics, health care access and utilization, comorbidities, and service year, the authors found that anti-dementia medication use was approximately 30% higher among non-Hispanic whites compared to other racial/ethnic groups. For individual racial/ethnic groups, prevalence disparities remained significant for non-Hispanic blacks and non-Hispanic others but were attenuated for Hispanics. Scientifically sound data is needed to evaluate the treatment of BPSD across racial and ethnic groups in the United States.

BPSD are common precipitants of nursing home admissions in the United States and a source of caregiver stress (Madhusoodanan, 2001; Chung and Cummings, 2000). Data suggest that minorities utilize nursing home care services less than non-minorities (Espino and Lewis, 1998; Walker et al., 1995; Valle, 1994). For example, data suggest that African American elderly utilize nursing homes at 50%–75% the rate of Caucasians (Walker et al, 1995).

BPSD in the Middle East

BPSD in Turkey

Studying BPSD across cultures allows the identification of similarities and differences that may be useful to determine the best approaches to management of these symptoms. The total population of Turkey was more than 80 million in 2013, with life expectancy of 73 years (male = 71 years; female = 75 years). Those 65 years old and older represented 6.6% of the total population (CIA World Factbook, 2013).

The concept of dementia is generally not considered a medical problem by the elderly Turkish population. A population-based, cross-sectional study of 859 people without dementia, aged 70 years or older, living in an urban area in Istanbul found that dementia was considered normal by the majority of respondents. Age and education did not influence this attitude, although women were significantly less inclined to consider dementia and its associated problems as normal (Sahin et al., 2006). Dementia prevalence in Turkey has been examined in a series of studies. In Middle Anatolia, the overall prevalence of dementia in 3,100 people aged 55 years and older was 8.4%, ranging from 2.2% among those aged 55–59 years to 5.3% among those aged 60–64 years, and to 30.4% among those aged 75 or older. Vascular dementia was the most common type (51.1%), followed by Alzheimer's dementia (48.8%). Significant risk factors for dementia

were being female, low education, age, living in a rural area, and a family history of dementia (Arslantas et al., 2009). In Istanbul, the prevalence of dementia in 1,019 people aged 70 years and older was 20% (Gurvit et al., 2008). A third study in the low socioeconomic region of Izmir found a dementia prevalence of 22.9% in 204 persons aged 65 years and older (Keskinoglu et al., 2006).

Assessment and frequency of BPSD. Turkish family practitioners, residents in psychiatry and neurology, and even psychiatrists and neurologists do not, in general, have sufficient experience to evaluate and treat BPSD (Eker et al., 2000). The Istanbul University, Cerrahpasa Medical School, Department of Geriatric Psychiatry has a memory outpatient clinic associated with the department. Since 1993, patients with AD have been referred to the outpatient clinic. One of the research objectives is to study the outpatient clinic population in order to examine behavioral and psychological symptoms in Turkish Alzheimer's patients. In a study on BPSD, presented at the 2002 World Psychiatric Association Congress in Yokohama, Japan, 190 patients with probable DSM-IV AD, admitted (consecutively) to the memory outpatient clinic, were assessed. The Turkish version of the MMSE for educated and uneducated patients was used (Gungen et al., 1999). Specific behavioral symptoms were systematically assessed by using the Behavioral Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD) (Reisberg et al., 1987). The study demonstrated that BPSD were found very frequently, in 91.5% of AD cases. The BPSD occurred most frequently in Stage 6 (severe dementia). The most frequently occurring symptoms in Turkish AD patients were purposeless activity, the delusion that "people are stealing things," wandering, tearfulness, and fear of being left alone.

More recently 217 patients with AD were evaluated from 18 referral centers across Turkey using a web-based dementia data registry (Yener et al., 2009). The MMSE and the NPI were used to evaluate the global cognitive function, and assessment of neuropsychiatric symptoms, respectively. The highest NPI scores were seen in patients with severe AD. The mean composite scores for apathy, anxiety, and depression were the highest. The prevalence of any behavioral symptom was 86%. There was no difference in the behavioral domain between the groups or between the referral centers. Moderate correlation was found between the severity of AD and the total NPI score. The caregivers' NPI distress scores varied among the regional referral centers.

In Turkey, patients in later stages of Alzheimer's disease, (i.e., GDS stages 5 and 6) are seen by neurologists and psychiatrists in outpatient clinics. Specialists interested in BPSD take the history and conduct physical, psychiatric, and neurological examinations. The DSM-IV and NINCDS-ADRDA are widely used. The Turkish version of the MMSE is the most widely used brief cognitive screening test; only a minority of Turkish psychiatrists and neurologists use the GDS and BEHAVE-AD.

Turkish family members are more likely to report behavioral and psychological symptoms rather than memory problems in their parents or relatives. Caregivers may underreport BPSD because they fear their relatives are mentally ill. On the other hand, their desire is not to relinquish their caregiver role or religious values. The Turkish culture has traditionally emphasized paternal authority and family loyalty, and children are typically expected to care for their parents who have dementia. Relatives who are caregivers of AD patients with BPSD do not want to place their charges in nursing homes. On the other hand, Turkey does not provide good quality services for AD patients (Eker, 1995). Patients with BPSD are usually placed in general

psychiatry departments and are treated by general psychiatrists who often lack sufficient knowledge of mental disorders in old age. There is a drastic shortage of centers that can provide care for patients with dementia and BPSD. In Turkey, patients with dementia are mostly cared for by their spouses or the eldest daughter in their homes. They are only admitted to a specialist unit when BPSD are severe. No specialized geriatric psychiatry consultation services are available for elderly people in the institutional care system in Turkey (Cankurtaran et al., 2006).

BPSD in Iran

While the elderly population is growing in Iran, aged health care and in particular mental health care is still in its infancy. There is no systematic screening and care program for dementing persons and behavioral problems of dementia are not regarded within the health program of the elderly. There is a shortage of centers providing care for patients with dementia and their disturbing behaviors. In developing countries such as Iran, there is still no systematized aged care program for dementia and its psychiatric manifestations.

Currently, patients complaining about memory problems are seen individually by general neurologists and psychiatrists. While they follow standardized diagnostic criteria, such as DSM to detect cognitive disorders like dementia, most are less familiar with challenging behaviors occurring in various stages of dementia. In addition to that, there are no consistent tools and approaches to BPSD. For this reason, the characteristics and management of BPSD in dementing patients remain strongly unexplored in Iran.

There is little research investigating the epidemiology and care of BPSD in Iran. Those few research and clinical projects are typically conducted by specialized university affiliated centers. Additionally, the Iran Alzheimer Association's educative and care program for dementing patients and their families are limited to a few areas of the capital, Tehran.

In Iran, like other developing countries, family members, particularly the spouse, are the main caregivers for the person with dementia. Most care occurs in the family home. The problems worsen when they move the family member with dementia from home to home. Over recent years the traditional family pattern, in which extended family of the same generation live together in large simple houses, has changed. Care for disabled senior families is limited to a few family caregivers in a limited housing space.

Results of an interventional study examining the role of family education on family caregivers have been promising. In this study, an eight-week educative program for caregivers has influenced both general health of caregivers and neuropsychiatric symptoms of patients. The most challenging behavior was night time behaviors. Sociodemographic variables, such as income and residential status, predicted more behavioral problems and subsequent burden to the caregivers (Javadpour et al., 2009).

In an empirical study on 50 consecutive older people with dementia referred to the psychogeriatric clinic of Shiraz University of Medical Sciences, the most problematic behaviors as measured by the Neuropsychiatry Inventory (NPI) were night time behaviors (55.2%) and aberrant motor behavior (51.7%). Delusions (44.8%), hallucinations (27.6%) and agitation (27.6%) were also common problems (Javadpour et al., unpublished study). The prevalence and severity of symptoms was correlated to dementia severity and the level of activities of daily living.

BPSD in Asia

BPSD in India

India is the largest democratic and culturally diversified nation. Rapid demographic changes are taking place due to better education, health facilities and increases in life expectancy.

Historical background. Historically, India has been a rural, agrarian society. A joint-family system has traditionally prevailed with several generations, and often multiple families from each generation, living together. In a system with many people living together, most of whom were able-bodied and working, the vulnerable were easily cared for, and this situation significantly lessened the burden of care. Things have changed in recent years, and the joint-family system is under stress. The emerging pattern is the following:

- Multiple families of the same generation are no longer living together
- The substantial burden of caring for frail or sick elderly is falling on only one or two caregivers
- Substantial, prolonged stress on individual caregivers
- Animosity against both the elderly and other family members who do not share in the caregiving

Cognitive decline with age is well recognized in ancient Indian culture. Around 800 BC, a term 'Smriti Bhransh' was described in the Ayurvedic literature implying 'loss of memory,' and a treatment for this condition was described. A term currently used in the Indian language to describe cognitive impairment translates literally as 'turned 60.' This term is used to describe patients who begin to exhibit signs and symptoms of cognitive decline, whatever their actual age. Because this phrase has been part of the language for centuries, it indicates that cognitive impairment was considered to be a part of aging, not a disease. In some parts of the southern state of Kerala, a term *Chinnan* is used to denote dementia-like conditions (Shaji et al., 2002). The symptoms, considered to be indicative of affliction with *Chinnan*, include inappropriate behavior, childish behavior, and incontinence, apart from failing memory. Again, this condition is considered part of the aging process rather than a disease during old age.

Demography of India. According to the 2011 Census, the total population of India as of March 1, 2011 was 1.21 billion. The percentage of elderly population (over 60 years of age) has gone up from 5.3% to 5.7% during the period1971 to 1981 and 6.0% to 8.0% respectively during the period 1991 to 2011. Male-Female differences in the age distribution of population are negligible except in the over 60 age-group and the 65+ age-group, where the percentage of female is 0.7% more than male. India is a "Graying Nation" by the United Nations standards (i.e., > 7% of total population). Currently the elderly population is greater than 90 million and this is expected to double by the year 2031. Two-thirds of the elderly population live in rural areas.

Economic conditions and social security for older people. The Indian aged population is currently the second largest in the world after China. The socio-economic condition of this group is a cause of concern, as most of them end up living below the poverty line due to inefficient and inadequate social security (Rajan, 2004). Social security schemes are available mainly for those retiring from the organized sector. Nearly 90% retiring from the non-organized sector with low wages, job insecurity and with lack of legal rights have no financial security. National Old Age Pension schemes provide nominal monthly pension of approximately

150–250 (US$3–5) to destitute persons above age of 65. Nearly 70% of all elderly are economically dependent on others, usually their children. Even those with pensions find their economic status lowered after retirement. Public investment in health care provision has not kept pace with population growth and the demand for basic health care (Prakash, 1999).

Impact on family. For generations, elderly people have been cared for by the traditional joint family system under which extended members of family live together—parents, children, children's spouses and their offspring. Usually the oldest male member is the head in this system that would look after the elderly. With urbanization and economic development, India has witnessed a breakup of traditional joint family into more nuclear-like families (Sinha, 1993).

Globalization and marginalization. Globalization and economic development over the last three decades has had negative impact on the well-being and welfare of the elderly. Migration of younger generations from rural to urban areas and trans-national migration has resulted in elderly being left to fend for themselves. With empowerment of women, more women are entering the work force, tending to reduce both their availability of care giving and willingness to take on this additional role. In India, Venkoba Rao has coined an acronym to describe this growing social phenomena P.I.C.A. (Parents in India, Children Abroad). Consumerism has permeated and changed the fabric of contemporary Indian society. As a result, this group is marginalized further with great risk for neglect, abuse and exploitation (Pais, 2006).

Impact of "Graying Nation" on health issues. Decline in mortality rate in the elderly population has created a high incidence of morbidity. A key finding from the Global Burden of Disease (GBD) report is that chronic non-communicable diseases are rapidly becoming the dominant causes of ill-health (WHO, 2008). Co-morbidity such as hypertension, strokes, metabolic disorders, dyslipidemia, chronic obstructive pulmonary disease and arthritis, along with usual age-related cataracts and hearing loss is on the rise in India. The GBD report indicates that dementia is one of the main causes of disability in later life. The World Alzheimer's Report (2009) highlights the importance of co-morbidity in the causation of disability and dependence.

Dementia prevalence, costs of care and services. The Alzheimer's and Related Disorders Society of India (ARDSI) produced *The Dementia India Report 2010* in which it estimated that in 2010 there were 3.69 million people with dementia in India and that this number was projected to increase to 14.32 million by 2050 (ARDSI, 2010). It was estimated the total societal costs of dementia for India would range between US$9.4 billion to US$13.7 billion, depending on the quantum of informal care (1.6 hours per day or 3.7 hours per day respectively). Direct costs were estimated to be US$6.1 billion (Wimo et al., 2010). India has few dementia specific facilities, with only ten dementia day care centers, six dementia-specific residential care facilities, six domiciliary care services and 100 memory clinics (ARDSI, 2010).

BPSD and burden of care. The I0/66 Dementia Research Group studied the care arrangements for dementia patients. Information on 87 patients from India showed that most caregivers were female children of the people with dementia, living with the people with dementia in extended family households. More than half of households included children. However, despite the traditional apparatus of family care, levels of caregiver strain were at least as high as in the developed world. Many family members had cut back on work hours to be caregivers, but they still faced the additional expense of paid caregivers and health services. Findings of the

study suggest that older people in India, like other developing countries, are indivisible from their younger family members. The high levels of family strain identified in this study feed into the cycle of disadvantage and should thus be a concern for policymakers (The 10/66 Research Group, 2004).

Nature and prevalence of BPSD. Based on reports from centers engaged in dementia research, the prevalence of BPSD in India may be higher than the prevalence of BPSD found in other parts of the world. The 10/66 study examined BPSD in four centers in India (Goa, Chennai, Bangalore, and Thrissur) and in 14 centers in Latin America, three Chinese centers, and one in Africa (10/66 Dementia Research Group, 2004). Overall, the 87 Indian people with dementia were rated as having the highest rates of BPSD. Wandering, agitation, and sleep disturbances were particularly common in India.

The Thrissur Center of the 10/66 Dementia Research Group assessed BPSD in a sample of 29 patients meeting the DSM-IV diagnosis of dementia, 14 with Alzheimer's disease, ten with vascular dementia, four with Lewy body dementia (DLB), and one 'other dementia' (Shaji et al., 2009). BPSD was measured with the BEHAVE-AD (see Table 7.6 for details). Patients with AD and DLB together had significantly higher total scores on BEHAVE-AD than did patients with vascular dementia; in particular, activity disturbances and delusional thinking were more common in AD and DLB.

BPSD symptoms cause severe stress on the coresident caregivers, who receive no support or guidance from the existing health care delivery system. In a qualitative study from Thrissur (Shaji et al., 2003), caregivers described BPSD and incontinence as the most distressing and difficult-to-manage symptoms. Dementia caregivers from Goa and Chennai spent significantly longer time providing care than did caregivers of depressed persons and controls (Dias et al., 2004). Emotional and economic strain was notably higher in the dementia caregivers.

Table 7.6: BPSD in Thrissur district, Kerala, India (adapted from Shaji et al., 2009)

BEHAVE–AD Items	People with dementia N = 29 (by percentage)
One or more BPSD	97
Paranoid and delusional ideation	66
Hallucinations	41
Activity disturbances	66
Aggressiveness	52
Diurnal rhythm disturbances	45
Affective disturbances	45
Anxiety and phobias	24

Approaches to management. The prevailing low level of public awareness of dementia in India has many implications. It reduces the chances of correct identification and management of BPSD in the community. BPSD are frequently misinterpreted by relatives as deliberate misbehavior by a patient. BPSD are sometimes misinterpreted by others as evidence of poor quality of care provided by the family. Allegations of this kind add to the misery of the caregiver and frequently result in interpersonal problems.

Since elderly patients with AD (or other types of dementia) are not often brought to a physician's attention, many BPSD go untreated. Even for those BPSD for which adequate treatments are available, it is hard to find a physician skilled in their diagnoses and treatment. There are no support groups to help family members, and consequently, both patients and their families can suffer.

Given the prospect of the increase in the number of old people affected by dementia in the developing world, we need to develop strategies that will assist families caring for persons with dementia at home. The development of simple, culturally acceptable, non-pharmacological interventions for the management of BPSD in the community would be an important step in this direction. Once the feasibility and cost effectiveness of such interventions are established, the interventions could provide an important ingredient of community-based dementia care services in developing countries. Informing and educating family members and giving them continued support and guidance in managing BPSD at home has the potential for wide application in developing countries.

The Indian network of the multicenter 10/66 Dementia Research Group has developed brief community-based caregiver education and training interventions administered by multipurpose health workers (MPHWs) (Prince and Trebilco, 2005). The health and social welfare systems of several developing countries utilize the services of community-based health workers. Workers who have achieved a basic standard of education receive additional training in simple health care programs. They are generally assigned to a catchment area. They get to know all of the families in their local area and visit their homes principally to monitor maternal and child health and development. MPHWs are, in many developing regions, the only generally available outreach arm of health care services because primary care teams often do not venture outside of their clinics. The training package for MPHWs includes at least three components: (1) general information about dementia, 2) training regarding detection of dementia in the community, and, (3) training in the implementation of various interventions. Management of BPSD, especially non-pharmacological approaches, is given due emphasis in this intervention. Because many caregivers have low literacy levels, special educational aids and teaching materials would be provided. Such educational material is developed locally and adapted to the cultural and linguistic differences.

There are changes occurring in India too. The Alzheimer's and Related Disorders Society of India (ARDSI), with 18 chapters all over India, has to some extent succeeded in increasing the level of awareness about dementia. The plight of the families who look after relatives with dementia at home is being recognized and discussed. Specialized dementia care services that focus on the management of BPSD are likely to come up in many general hospitals that are usually located in the urban areas. Primarily, this focus is due to increasing demand for such services from the educated sections of the society.

Barriers to dementia care in India. The following barriers to dementia care have been identified:

- Lack of awareness and low health seeking behavior due to social stigma, dependency, financial restraints and ageism
- Unlikely to accept he/she has dementia because the condition is seen as accelerated ageing process
- A diagnosis is unlikely to be believed or its impact understood
- Special needs of dementia patient are not understood or respected widely enough
- Old age homes neither a popular nor feasible option
- Bias, ageism and poor awareness within medical fraternity
- Inadequate and discriminatory financing of mental health services for the elderly
- Lack of policy initiatives and implementations
- Lack of funds for dementia services, research and training
- There is no psychogeriatric curriculum and training in the undergraduate and post graduate courses
- Acute national shortage of medical and social service professionals who have training and expertise in geriatric mental health care

Dementia care services in India. Services exclusively for people with dementia in India are mostly provided by registered non-profit organizations. They are funded primarily by donations and public contributions apart from the charges collected from those who utilize the services. ARDSI, Helpage India, Dignity Foundation, Nightingales Medical Trust, Dementia Society of Goa, Sangath and Silver Innings Foundation are some of the providers. Services include day care centers (10), residential care facilities (6), domiciliary care services (6), memory clinics (100), dementia help lines (10) and support groups (exact data not available).

The Ministry of Social Justice and Empowerment, which is the nodal Ministry for the purpose of the Welfare of the Elderly, created the Maintenance and Welfare of Parents and Senior Citizens Act 2007. It was enacted in December 2007 to ensure need based maintenance for parents and senior citizens and their welfare and provides for:

- Maintenance of parents/senior citizens by children/ relatives made obligatory and justiciable through Tribunals
- Revocation of transfer of property by senior citizens in case of negligence by relatives
- Penal provision for abandonment of senior citizens
- Establishment of old age homes for indigent senior citizens
- Adequate medical facilities and security for senior citizens

The Act has to be brought into force by individual State Government. As of 2010, the Act had been notified by 22 States and all Union Territories.

The ARDSI Dementia India Report 2010 made the following policy recommendations:

- Make dementia a national priority
- Increase funding for dementia research
- Increase awareness about dementia
- Improve dementia identification and care skills

- Develop community support
- Guarantee caregiver support packages
- Develop comprehensive dementia care models
- Develop new national policies and legislation for people with dementia

There are concerns that India is facing an impending public health crisis. Perhaps the only way to move forwards with limited resources is through the empowerment of older people. This can be achieved through "advocacy, research, involvement of voluntary agencies, training different levels of gerontological workers, catalyzing the community, awareness building, organizing older persons themselves and networking with international agencies" (Prakash, 1999).

BPSD in China, Hong Kong SAR and Taiwan

Prevalence and presentation. Alzheimer's disease is the most common cause of dementia in China, and many patients with AD manifest BPSD. Until recently, most research has focused on the neurobiological aspects of dementia and cognitive impairment, while BPSD have been relatively neglected. In the past few years, several studies have been conducted to examine the prevalence of neuropsychiatric symptoms in persons with AD and in individuals with MCI in clinic settings and community-dwelling populations in mainland China (Zhang et al., 2012), Hong Kong SAR (Chow et al., 2002; Chan et al., 2010b), and Taiwan (Liu et al., 1995, 1999; Tsai et al., 1997; Hwang et al., 2000, 1997, 1996; Chow et al., 2002). The prevalence findings are summarized in Tables 7.7 and 7.8.

Table 7.7: Prevalence (%) of neuropsychiatric symptoms in persons with AD and in individuals with MCI in Chinese patients.

	AD					MCI	
Symptoms in NPI	Beijing (n = 129)	Taipei (n = 86)	Kaohsiung (n = 144)	Hong Kong (n = 31)	Beijing (n = 373)	Beijing (n = 38)	Hong Kong (n = 338)
Research setting	clinic	clinic	clinic	clinic	multisite clinics	clinic	community
Delusions	39.5	31.5	40.3	58.1	11.0	10.5	2.4
Hallucinations	31.0	24.7	19.3	22.6	10.7	2.6	0.9
Agitation/ aggression	55.0	46.1	40.3	61.3	12.3	13.2	5.1
Depression/ dysphoria	33.3	49.4	43.7	46.7	23.9	28.9	14.6
Anxiety	30.2	39.3	37.8	58.1	20.4	26.3	12.5
Euphoria/elation	4.7	7.8	11.8	25.8	6.4	0.0	0.6
Apathy/ indifference	86.0	47.2	38.9	35.5	21.7	39.5	15.2
Disinhibition	19.4	19.1	35.4	25.8	1.3	2.6	1.8
Irritability/lability	63.6	51.7	44.4	63.3	16.9	44.7	8.0

	AD					MCI	
Symptoms in NPI	Beijing (n = 129)	Taipei (n = 86)	Kaohsiung (n = 144)	Hong Kong (n = 31)	Beijing (n = 373)	Beijing (n = 38)	Hong Kong (n = 338)
Aberrant motor behavior	48.1	37.1	40.6	61.3	12.1	5.3	0.9
Nighttime behavior	26.4	36.0	34.7	53.6	19.8	26.3	16.1
Appetite/eating change	6.2	29.2	29.2	53.6	11.8	5.3	2.1

Table 7.8: Prevalence of neuropsychiatric symptoms (%) in persons with dementia in Taiwan (Liu, 1999, 1995; Tsai, 1997; Hwang, 2000, 1997, 1996).

BPSD	Study in Psychiatry (Tsai, 1997; Hwang, 2000; 1997; 1996) (%)	Study in Neurology (Liu, 1999) (%)
Depressive symptoms Major depression Minor depression	—	22.0 5.0 11.3
Anxiety	—	35.3
Delusions	62.9	27.2
Delusion of theft	55.6	27.2
Persecutory delusion	24.1	28.0
Delusion of infidelity	15.8–16.7	3.4
Delusion of abandonment	9.3	2.2
Misidentification of someone in the house	22	2.2
Misidentification of people	11.1	3.4
Misidentification of TV	9.3	—
Misidentification of mirror image	7.4	—
Misidentification—house is not patient's home	16.7	16.5
Hallucination	25.9	—
Visual hallucination	14.8	19.5
Auditory hallucination	16.7	11.6
Tactile hallucination	—	0.7
Olfactory hallucination	—	0.7
Hyperphagia	30.8–36.0	—
Pica	7.7	—
Verbal aggression	—	21.4

BPSD	Study in Psychiatry (Tsai, 1997; Hwang, 2000; 1997; 1996) (%)	Study in Neurology (Liu, 1999) (%)
Violence	54.7–57.4	10.3
Hoarding	22.6	—
Getting lost	45.3	25.8
Repetitive phenomena	56.0–62.7	26.4
Sleep disturbance	61.3	23.4
Inappropriate sexual behavior	10.7	—

A number of these symptoms (wandering, hyperphagia, and sleep disturbance) were associated with the severity of cognitive impairment (Hwang et al., 1997). Studies in Hong Kong also revealed that BPSD are highly prevalent. Some symptoms are stage specific—most behavioral problems peak in the moderate stage and attenuate as dementia progresses. In a recent study conducted in a memory clinic in Beijing (Zhang et al., 2011), the occurrence of BPSD increases with the severity of AD. Three clusters of neuropsychiatric symptoms were mainly presented as measured with NPI, including psychosis and hyperactivity, and frontal and mood symptoms. The cluster scores of psychosis and hyperactivity, and frontal symptoms were significantly greater in severe AD compared to mild and moderate AD, but the mood symptoms did not change dramatically among three groups. Stepwise regression analysis showed that the total score of NPI correlated with the score of memory domain as measured with ADAS-Cog, and ADL score.

Approaches to management. Awareness of dementia among the general public is generally low in China, but it is emerging as an important public health issue (Chiu, Yu and Lam, 2010). The Practice Guideline of Dementia recommended the algorithm proposed by QoLDEM group to manage people with dementia (Chiu and Chiu, 2006), including three major components:

- Pharmacological management: Cognitive enhancers have been proposed as the first-line drug for dementia. Psychotropics, specifically referred to antipsychotics, antidepressants, mood stabilizers, and benzodiazepines, may be used for neuropsychiatric symptoms upon clinical benefit-risk evaluation.
- Non-pharmacological intervention: Clinicians, caregivers, and nursing staff are encouraged to use non-pharmacological intervention as the first choice for the management of BPSD.
- Caregiver support: Caregiver support groups have been organized, serving as the basis for health education, caregiving consultation, and a platform for sharing caregiving experiences. Also Alzheimer Associations in mainland China, Hong Kong SAR, and Taiwan have contributed greatly to improve the caregivers' coping skills to manage the behavioral symptoms of persons with dementia.

The past few years have seen an increased interest in examining the effectiveness of non-pharmacological management of BPSD in Chinese communities (e.g. individualized functional training program in treating affective symptoms in persons with dementia (Lam et al., 2010)). Researchers have also looked into the pharmacological strategies for BPSD in the Chinese. One interesting finding is that studies in Hong Kong did not detect significant increases in mortality

or cerebrovascular events in persons with dementia who were on antipsychotic medications (Chan et al., 2010a; Chan et al., 2011). It warrants further investigation in this area in other ethnic groups.

BPSD in South Korea

South Korea in 2013. Korean people are ethnically homogenous. Total population is 50 million. All Koreans are covered by the Nation Health Insurance Scheme, implemented in 1977. Proportion of elderly people age 65 and over is 12.3%. The number of people with dementia is estimated at 540,000. The long-term care insurance scheme was implemented in 2008 to provide home care, community care, and residential care for disabled elderly people with dementia and stroke. Life expectancy at birth is 79.6 years (male 76.5 years, female 82.9 years). The literacy rate is 98%.

Prevalence of BPSD in South Korea. Two studies using dementia cohorts in a geriatric hospital and a nursing home are introduced. The first study (Suh, 2004) was conducted in a nursing home with a total of 257 people with AD (n = 133) or vascular dementia (VaD) (n = 124) using the Cohen-Mansfield Agitation Inventory (CMAI). Eighty-three percent of the subjects with dementia manifested one or more agitated behaviors at least once a week. Verbally agitated behaviors were the type of agitation in which the highest percentage of subjects with dementia were engaged (67.3%), followed by 61.5% in physically non-aggressive behaviors, 38.5% in physically-aggressive behaviors, and 26.8% in hiding/hoarding behaviors. The most frequent agitated behaviors were cursing or verbal aggression (37.7%), screaming (37.7%), complaining (36.2%), negativism (30.7%), repetitive sentences or questions (30.4%), general restlessness (30.4%), and pacing and/or aimless wandering (28%). The percentage of subjects with dementia manifesting the four syndromal factors according to CDR stages in AD and VaD were shown in Figure 7.1. Prevalence rates of physically aggressive behaviors and verbally agitated behaviors in both AD and VaD group showed a linear upward trend as one progressed from one CDR stage to the next. Verbally agitated behaviors in VaD group were higher than those in AD group in CDR stage 2 and stage 3. Prevalence rates of physically non-aggressive behaviors and hiding/hoarding behaviors were higher in AD group.

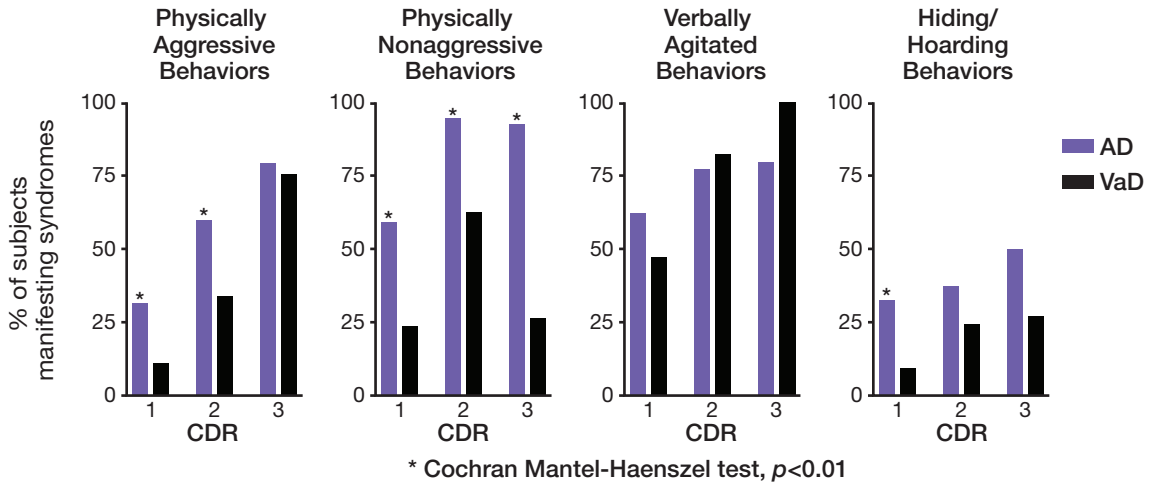


Figure 7.1: Prevalence of agitated behaviors of the CMAI-K at each Clinical Dementia Rating Scale (CDR) stage in Alzheimer's disease(AD) and vascular dementia (VaD)

The second study (Suh and Park, 2001) was conducted in a geriatric hospital with a total of 112 patients with AD using the BEHAVE-AD. The most frequent BPSD were depressed mood (47.6%), day/night disturbance (41.9%), agitation (41.0%), purposeless activity (39.4%), verbal aggressiveness (38.1%), tearfulness (36.2%), and anxiety and fear of being left alone (35.2%).

Awareness of dementia including BPSD. Many Korean people often regard dementia as a normal part of aging. Since 2008, when the long-term care insurance scheme was implemented, awareness of the significance of dementia and BPSD has been greatly raised. Before 2008, when there was no public assistance for dementia care, caregivers, general practitioners and even psychiatrists and neurologists had not made a concerted effort to find symptoms and signs of dementia. Thanks to long-term care (LTC) insurance, caregivers can reduce the burden of caring for dementia if they officially report symptoms of dementia, including BPSD, and can get approval for long-term care. Even media, doctor organizations and Alzheimer's associations continued campaigns to raise awareness of dementia. In 2009, the President of the Korean government declared a war against dementia.

Assessment of dementia. Rating scales have been translated into the Korean language and harmonized with the Korean population. Some rating scales for BPSD such as the CMAI, BEHAVE-AD and NPI have been validated and widely used in Korea. Further, the Korean versions of clinical assessment instruments such as the Consortium to Establish a Registry in Alzheimer's disease (CERAD) neuropsychological battery, the Geriatric Mental Status (GMS), and the Cambridge Examination for Mental Disorders of the Elderly (CAMDEX), the Composite International Diagnostic Interview (CIDI), and the Diagnostic Interview Schedule (DIS) are also available.

It is widely accepted that the initial identification of likely cases of dementia is an important function of primary care. It is widely suggested that formal diagnosis should be done by specialists. Neurologists and psychiatrists were most frequently diagnosing and managing dementia. Primary care physicians, geriatricians and nurse practitioners were less likely to be involved in diagnosis. Memory clinics are providing assessment, diagnosis and management of dementia, while dementia care is mostly provided by social services and long-term care scheme.

Management of dementia. Initiation of anti-dementia drug prescription should be carried out mostly by dementia experts. There appear to be relatively long delays separating a patient's initial diagnosis of dementia and the start of treatment. Slow initiation of treatment in newly diagnosed patients might be attributed to the pessimism about dementia as an incurable disease and to the unwillingness of patients and their families to receive treatment. All available anti-dementia drugs (i.e., donepezil, rivastigmine, galantamine, memantine) have been used as first-line drugs. Donepezil is always ranked as a first-line drug and most commonly prescribed. Vitamin E and ginkgo biloba are used for combination therapy.

The LTC insurance scheme provides dementia services at home, community and institutions with co-payment by care recipients. In addition, Korea has introduced small group homes of 6–10 residents, who are supported by staff around the clock, as an intermediate level of care between home and institutional care. Group home living provides an alternative to traditional institutionalization/residential care when there is a lack of informal or formal community support.

Challenges. It is expected that the LTC system can reduce the deficit in health insurance for health expenditure for the elderly. In Korea, 92% of long-term care beneficiaries suffer from chronic diseases, and 74.2% of them utilize medical services. In spite of entering into the LTC system, the need for disease management of these beneficiaries is not diminished. One of the challenges of the present health and LTC insurance program is how to meet the complex medical needs of those residing in LTC facilities or using community LTC services.

BPSD in Japan

In July 2013, Japan Ministry of Health, Labor, and Welfare announced the average life span of the Japanese in the year 2012 was 86.41 years for females and 79.94 years for males. The average life span of the Japanese female had been the longest in the world for 26 consecutive years until 2010, when it became second to Hong Kong in 2011, and then returned to the longest in 2012 by increasing 0.51 years compared with that of 2011. The average life span of Japanese males was ranked first in the world by increasing 0.50 years compared with that of the previous year.

In the years 1891–1898, the Japanese life span was only 44.3 years for females and 42.8 years for males, which became slightly shortened to 43.20 for females and 42.06 for males in 1921–1925 due to the Spanish influenza and loss of lives by the Kanto Earthquake in 1923. Before World War II, the average life span of the Japanese never exceeded 50 years. In 1947, the average life span of the Japanese was 53.96 for females and 50.06 for males, and it has shown rapid increase, especially in the period of 1954–1973, which coincided with rapid economic growth of Japan, reaching the longest life span, 83.18 years, which is expected to increase in the coming years.

Society aging. In the year 1936, the proportion of elderly people in Japan, age 65 years and above, was low (4.7%), and stable until the 1950s. Since then, it has shown a steep increase, exceeding 7% in 1970, 14% in 1995, and 20% in 2007. The Japanese total population was at its highest in 2007. The proportion of older people in the population, however, will keep increasing until the year 2050 when it is estimated to reach over 40% of the total population, following the second generation of the baby boomers (born in 1947–1949) attaining the age of 65. During the same period, the people in the productive age group (15–64 years old) will keep decreasing. At the present time, the productive age group is 65% of the total population, implying 2.5 people in the productive age group support one older person. In the near future, however, one person of productive age will support the life of one older person. Another feature of Japan is the significant increase in the ratio of the 'old old', 75 years or above. Now the 'old old' ratio is 10%, which will be increased to 22% by 2050 (Japanese Ministry of Health, Welfare & Labor, 2012).

Rapid transition from aging to aged society. When we compare the speed of the transition from an aging society (7% elderly) to an aged society (14% elderly), most European countries spent more than 50 years in this transition. France spent 115 years, United States 71 years, and Italy 61 years in transitioning from an aging society to aged society, while Japan transited in only 24 years (Takeda, 2004). Too rapid transition in a society will cause strains and frictions in social systems because the society itself will move forward before the social system becomes adapted to the change and people in the society become used to it. The Japanese Government is prepared for this type of social strain and in 2000 implemented Long-Term Care Insurance and the Adult Guardian Law.

BPSD. The Japanese Psychogeriatric Society collaborated in introducing the second edition of the IPA Educational Pack (2003) to Japanese professionals by producing a Japanese translation, which was published in 2005 (Fig. 7.2). The third edition, the Complete Guide to BPSD (2011) was also published in the Japanese language in 2013 (Fig.7.3).

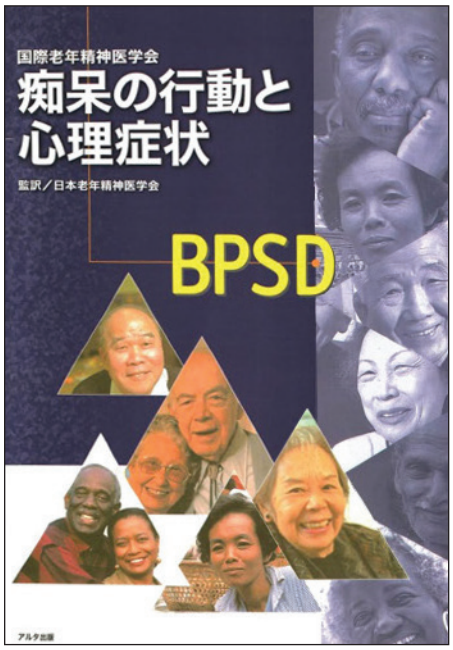


Figure 7.2 Japanese translation of Second Edition

Figure 7.3 Japanese translation of Third Edition

BPSD can be understood as the reflection of the friction between the person with dementia and other people caused by their incomplete recognition of the outside world. The key message is for clinicians to understand the background reason of various types of BPSD and try to resolve this difficult situation of the person with dementia and caregivers. Caregivers or family members should not think that BPSD is the problem of only the person with dementia, but we should think about how to resolve the situation caused by the friction between the person with dementia and the environment, paying more respect to the person's autonomy. We should find ways to help people with dementia keep functioning in society by reducing BPSD.

Japan is a leader in the world in terms of society aging and we think Japan is expected to create a new society in which people with dementia can live happily and safely, paying more attention to their needs so that this can be achieved for as long as possible.

Management of BPSD. A recent survey conducted in Japan showed that many family doctors prescribe antipsychotics to dementia patients, but only 19% of them prescribe antipsychotics after informed consent from the family of the patients (Japanese Ministry of Health, Welfare & Labor, 2013). Some family doctors prescribe antipsychotics to patients with types of BPSD which are known to have a poor response to antipsychotics such as talkativeness, pica, overeating, wandering, or resistance to care. Considering these facts, the Japanese Government has issued the statement that easy use of antipsychotics to people with dementia should be discouraged. In the statement, family doctors are advised to try to manage BPSD by modulating

environmental factors or by non-pharmacological means before using antipsychotics. Antipsychotics use for people with BPSD should be minimized. The following should be observed by family doctors:

- No antipsychotics have been approved for the treatment of BPSD because no data are available about the usefulness of antipsychotics for BPSD in Japanese patients. On the contrary, there are data which show antipsychotic use may increase risk of falls and bone fractures in people with dementia.
- Use of antipsychotics should be restricted to moderate to severe BPSD, such as aggression, excitement, or psychotic features and when there is no other choice to control BPSD.
- After the initiation of antipsychotics, the clinicians are expected to evaluate the necessity of continued use by close observation and discontinue them when there is no further benefit.
- Use antipsychotics in combination with non-pharmacological interventions.
- Try to avoid polypharmacy.
- Avoid antipsychotics which have higher risk of extrapyramidal side effects or tardive dyskinesia.
- Explain to the family members in detail the possibility of adverse side effects, such as falls, orthostatic hypotension, over sedation in addition to the increased risk of sudden death and cerebrovascular events and obtain consent.
- When there are signs of adverse effects, such as gait disturbance, dysphagia, dysarthria, rigidity, tremor, orthostatic hypotension, oversedation, reduce the dose or stop the use of antipsychotics as soon as possible.

Government policy to improve care for dementia patients. In September 2012, the Japanese Government announced a five-year policy plan to promote dementia care, in which the shift from late management to early intervention and management was strongly recommended, based on the understanding that the previous policy was mainly focused on post event management and crisis management due to BPSD. The Government is now advocating that early intervention and even preventive measures are more important and cost-effective in dementia care. The Government policy recommended:

- Standard care path for dementia care should be formalized, and be used in reimbursement of medical and care costs for dementia.
- Special teams for early identification and intervention of dementia patients should be implemented.
- The number of medical centers should be increased where early diagnosis of dementia can be made to 500 centers by year 2017.
- The number of family doctors who see dementia patients should be increased to 50,000 by 2017.
- The number of specialists for dementia should be increased to 4,000 by year 2017.
- Every town or city should have the specialized team for dementia care support.
- The number of social workers specialized for dementia should be increased to 700 by 2017.
- Education to the public should be promoted to increase the number of citizen dementia care supporters to 5,000,000 by 2017.

Conclusions. We are born alike as babies and accumulate our own experience along our life. When we enter old age, we show a great variety of reactions depending on our psychological and social experiences. The biological variance is large enough in old age, but the psychological and social variance makes us even more different. We should keep in mind that older people show wide variance due to psychological and social factors in addition to biological factors.

Dementia is a disease in which social life capacity is impaired due to gradual impairment in memory or cognitive function. People with dementia gradually lose social function, which makes it difficult for them to maintain adequate relationships with other people in society. As dementia progresses, personal life capacity such as meal preparation, bathing and toileting, will also be lost. But the biological life capacity such as respiration, circulation and body temperature will be mostly maintained. In other words, loss of social function is the core symptom of dementia, and psychological and social factors should be considered when we are facing BPSD. People with dementia are so different, just like healthy old people, and we clinicians are expected to differentiate the BPSD of each patient.

BPSD in Latin America

Population aging is a process that is especially accelerated in some parts of the world. Latin America has to confront population "graying" in the context of an emerging economy. Countries such as Brazil, Argentina, Uruguay, and Mexico face the aging of their populations. In other countries, including Haiti, Bolivia, and Guatemala, population aging will be delayed by continued high birth rates. In the 2009 World Alzheimer Report, it was estimated that there were 51.9 million people age 60 years and older living in Latin America (Alzheimer's Disease International, 2009).

Studies by the 10/66 Dementia Research Group, including seven sites from five Latin American countries (Peru, Cuba, Dominican Republic, Mexico, and Venezuela), have shown that the prevalence of dementia in this region is perhaps the highest in the world at 9.5% of the population age 65 years and older, according to 10/66 estimates, and 4.2% using DSM-IV criteria, with the discrepancy due to underreporting of cognitive decline and social/occupational impairment by relatives (Ferri and Prince, 2009). The 10/66 Dementia Research Group reported on BPSD in 387 Latin American people with dementia and compared them with Chinese, Indian, and African participants. Latin American participants had intermediate rates of BPSD but the highest rate of vocal disturbances (37%) and depressive syndromes (51%), although phobic neuroses and manic/hypomanic psychoses were only found in Latin American countries (The 10/66 Dementia Research Group, 2004).

BPSD in Argentina

Argentina is populated by a mixture of different ethnic cultures; however, unlike other Latin American countries, most Argentineans (97%) are of central- and west-European descent. The second largest ethnic group is the mestizos, a fusion of European immigrants and native aborigines, followed by the native aborigines who live in special reserves. The northern and western parts of Argentina are populated by a greater proportion of natives and mestizos living in rural areas; the center and the southeast are populated by European descendants, for the most part.

Argentina has one of the largest elderly populations in Latin America, with 11.3% of the population age 65 years and older (4.8 million) and a life expectancy at birth of 77 years (CIA World Fact Book, 2013). It is a highly urbanized society with 92% of the population living in cities, and about 15 million people living in the greater Buenos Aires region (CIA World Fact Book, 2013). The adult illiteracy rate is 2.8% for the population over 15 years old but higher in the elderly. However, a high percentage of persons older than 60 years are functionally illiterate, with fewer than four years of schooling. The low literacy rate of this group makes it difficult to assess the cognitive abilities of these people. Clinicians must adapt assessment instruments that cope with not only to the patients' language and culture but also to their educational levels.

It is estimated that there were nearly 322,000 people with dementia in Argentina in 2009 (Wimo et al., 2010). The total annual estimated cost was about US$4.6 billion per year if informal costs are just based on ADL support and more than US$7 billion each year if IADL support is included (Wimo et al., 2010). With projected increases in the number of persons at risk for developing AD in Latin America, the economic impact of the disease in the future will be highly significant. Most senior citizens live at home with their families; approximately 15% are institutionalized in nursing homes. This arrangement may result partly from the tradition of extended families, but it also evolves from the high cost of nursing home care.

Frequency of BPSD. In Argentina, the Neuropsychiatric Inventory and the BEHAVE-AD are the most common tools used to assess BPSD. One study of BPSD in 72 patients with AD found a prevalence of 87.5% using the Neuropsychiatric Inventory NPI-Q (Pollero et al., 2004; Kaufer et al., 2000). The most frequent symptoms were apathy, irritability, depression, and anxiety. Symptoms were predominantly found in moderate and severe dementia apart from depression and anxiety that were more common in mild-moderate dementia. A study of 258 patients with dementia from a memory clinic in Buenos Aires reported that over 44% had psychotic symptoms and 59% had depressive symptoms at least weekly (Machnicki et al., 2009).

BPSD and caregiver burden. The relationship between the caregivers' feelings of burden and the cognitive, behavioral, and functional impairment of patients with dementia has been investigated in an Argentinean study of 85 patients with probable AD (Mangone et al., 1993). BPSD and caregiver burden were assessed using the Functional Dementia Scale in the Blessed Dementia Scale and an adapted version of the Zarit Burden Interview, respectively. The study showed that caregiver reports of patients exhibiting BPSD were the best predictors of burden on the part of the caregivers. Aggressiveness, pacing, moaning, or shouting were among the items on the Functional Dementia Scale that were identified as independent predictors of caregiver burden. A more recent study found that behavioral, cognitive and functional factors contributed to caregiver burden in a memory clinic sample in Buenos Aires (Machnicki et al., 2009).

Approaches to management. Treatment depends on psychosocial and demographic factors; there are differences between the principal cities (such as Buenos Aires, Cordoba, Rosario, Mendoza) and the smaller cities or rural areas. For example, caregivers in the principal cities are more likely to be burdened by pacing or wandering than those in the provinces where most patients live in houses with room enough to pace and without the danger of becoming lost. Illiterate caregivers, most of whom are mestizos or natives living in smaller cities and rural areas, are more tolerant of BPSD and seek treatment only when behavioral problems become

overwhelming. These caregivers are convinced they are obliged to care for their relatives and are likely to keep others from knowing the difficulty of their caregiving situation. They also rely on prayer and their faith to handle problems related to caregiver burden (Mangone, 2000).

General practitioners consider cognitive symptoms and BPSD to be part of the normal aging process, and they do not perform a meticulous diagnosis. Specialists (neurologists, psychiatrists, and geriatricians), are unevenly distributed in the country, most of them located within large towns. There is a shortage of specialists in small towns and in the rural areas. The facilities needed for accurate diagnosis are scarce, except within Buenos Aires and a few other large provincial cities. Few young physicians are properly trained in dementia diagnosis and treatment during their medical residencies, and there are few specialists trained in dementia. In the past decade the role of memory clinics in dementia diagnosis has increased. These are mainly located in the private sector and are mostly run by neurologists (Bagnati et al., 2013).

There is evidence that admission to residential care in Buenos Aires is skewed towards social reasons with barriers for the admission of people with dementia (Lloyd-Sherlock and Redondo, 2009).

The pharmacological treatment approaches are similar to those in the United States. There are support groups (Association against Alzheimer's disease and Related Disorders of Argentina—ALMA) to help family members with more than 20 located around the country.

BPSD in Mexico

Background. Mexican society is a mixture of different cultures. Most Mexicans (60%) are descendants of the Spanish and native fusions. However, within its vast territory, more than 60 different native languages are still spoken, each one with its own particular culture and beliefs.

Demographically, Mexico is rapidly changing into a country where the children and the young no longer dominate the age structure. The population of over 116 million has 8 million (6.9%) people age 65 years and over (CIA World Factbook, 2013). The growth of the older population is expected to increase almost threefold in the next 20 years, with its concomitant burden to the economy and service delivery for the aged. In 2009 it was estimated that there were more than 485,000 people with dementia in Mexico (Wimo et al., 2010) and, according to the 10/66 Dementia Research Group, the prevalence of dementia in people 65 years and older was 8.6% in urban areas and 8.5% in rural areas (Ferri and Prince, 2009). It is conceivable that vascular dementia and mixed dementias are more common due to the fact that risk factors for vascular disease, in general, are poorly tackled in the realm of Mexican general health systems.

In 2001, the Mexican Ministry of Health developed a national plan under the guidance and direction of the new government. The health of the elderly and those who will develop dementia were the top priorities. The intent to develop a national action plan for dementia was announced in 2012 and is the first in the Spanish-speaking world.

BPSD prevalence and caregiver burden. In recent years several studies have quantified aspects of BPSD in Mexico. Data from the 10/66 project involving 180 cases diagnosed with dementia from a population-based cross-sectional study of 2,003 older adults living in rural and urban areas of low- to medium-income in Mexico used the abbreviated version of the Neuropsychiatric Inventory (NPI-Q) to measure BPSD. Depression (47.8%), sleep disorders (37.2%) and

irritability (34.4%) were the most prevalent and increased with dementia severity. Anxiety, depression and sleep disorders were associated with mild/moderate caregivers stress levels (Acosta-Castillo et al., 2012). Fewer BPSD were reported from rural areas (Rodriguez-Agudelo et al., 2011). A multicenter study from Mexico City reported that caregiver burden as measured by the Spanish Caregiver Burden Screen was associated with dysexecutive syndrome and sleep disorders as well as caregiver depression (Rosas-Carrasco et al., 2013).

BPSD in Brazil

According to United Nations (UN) estimates for 2005, Brazil was considered as belonging to the group of ten countries with the largest population of people aged 60 years or more, and estimates indicate that Brazil, in 2050, will be one of the six countries that have more than 10 million over 80 years old. Among developing nations, Brazil has the highest percentage increase of the elderly population worldwide, with the group above 60 years-old increasing by about 23 times from 1950 to 2050, while its population as a whole is expected to grow about 4.5 times during this period (UNO, 2002).

Since 2002, several research studies have described the prevalence of dementia in the population over 65 years old in Brazil. The first one reported that in older subjects living in Catanduva, in the state of São Paulo, dementia prevalence was 7.1% (Herrera Jr et al., 2002). In another study (Bottino et al., 2008), the estimated prevalence of dementia found in São Paulo city was 12.9% in the population over 60 years, figures equal to or higher than the prevalence rates of dementia found in developed countries (Lopes et al., 2007).

In parallel with the interest in dementia, the BPSD or neuropsychiatric symptoms in dementia have been studied more intensively in the last few years. On a PUBMED search using the keywords BPSD or neuropsychiatric symptoms, dementia and Brazil, 32 original articles and reviews were found since January1999 to June 2013.

BPSD prevalence and measurement. Following reports of BPSD prevalence in outpatient samples, the first account of these symptoms on a representative sample with Alzheimer's disease (AD) or Cognitive Impaired Not Demented (CIND) was published by Tatsch et al. (2006). The authors reported that 60 patients with AD, 25 CIND, and 78 healthy elderly subjects were evaluated. Of this sample, 78.3% of patients with AD had one or more neuropsychiatric symptoms, with apathy (53.3%), depression (38.3%), sleep alterations (38.3%), and anxiety (25%) the most prevalent disturbances in AD subjects. In the CIND group, the most frequent neuropsychiatric symptoms were anxiety and sleep alterations (both with 24%) followed by depression (16%), while the total NPI scores were significantly different between the three groups. Apathy was the only symptom that was significantly different between the groups divided according to the CDR, being more frequent in subjects with moderate to severe dementia. The authors concluded that neuropsychiatric symptoms seem to be as common in patients living in a developing country as they are in dementing patients from the developed world, suggesting that cultural factors play a minor role in the emergence of these symptoms, at least in a country like Brazil (Tatsch et al., 2006).

Another significant contribution to the field was the publication from Camozzatto et al. (2008), which reported the psychometric properties of the Brazilian Portuguese version of the Neuropsychiatric Inventory (NPI), in a sample of 36 Alzheimer's disease (AD) outpatients from southern Brazil. The Brazilian version of the NPI showed good inter-rater, test-retest reliability, and internal consistency. Apathy provided higher NPI scores of total severity and distress.

In another research line, Stella et al. (2009) presented an account of 50 patients with idiopathic Parkinson's disease (PD) and their caregivers seen consecutively at the Movement Disorder Outpatient Clinic at the Hospital of State University of Campinas. The authors found that patients with PD and dementia presented the highest NPI scores, followed by patients with PD and depression. Caregivers' burden was found to be proportional to the degree of patients' symptomatology. Patients with dementia presented more severe motor impairment and lower functionality, with psychotic symptoms, agitation, aberrant motor behaviors and sleep disturbances higher in the dementia group.

BPSD treatment. Regarding BPSD treatment, interesting reports have investigated the efficacy of non-pharmacologic interventions to reduce the neuropsychiatric symptoms of AD patients and caregivers' burden. For instance, a controlled trial to evaluate the effects of a motor intervention program on the neuropsychiatric symptoms was performed on community patients from two university centers specializing in physical exercise for the elderly (Stella et al., 2011). Thirty-two AD patients were divided in two groups: the motor intervention and the control groups. Aerobic exercises (flexibility, strength, and agility) and functional balance exercises were conducted over six months for 60 minutes, three times per week. Patients from the intervention presented a significant reduction in neuropsychiatric conditions when compared to controls. The burden and stress of caregivers responsible for patients who participated in the intervention significantly decreased when compared to caregivers responsible for controls. The authors concluded that aerobic exercise was associated with a reduction in the neuropsychiatric symptoms and contributed to attenuate the caregivers' burden, but the researchers were not blinded to the patient's intervention status, which constituted a limitation of the study.

In another paper, a multidisciplinary rehabilitation program on cognition, quality of life, and neuropsychiatry symptoms was applied to 25 patients with mild AD and their caregivers. They were included in a 12-week stimulation and psychoeducational program and compared to 16 AD patients in waiting lists. Group sessions were provided by a multi-professional team and included memory training, computer-assisted cognitive stimulation, expressive activities (painting, verbal expression, writing), physiotherapy, and physical training administered twice a week. Measurements of global cognitive function and performance on attention tasks indicated that patients in the experimental group remained stable, whereas controls displayed mild but significant worsening. The intervention was associated with reduced depressive symptoms for patients and caregivers and decreased neuropsychiatric symptoms in AD subjects (Viola et al., 2011).

Finally, forty dementia family caregivers were enrolled in a Cognitive-Behavioral Therapy (CBT) program intervention across eight weekly sessions (Fialho et al., 2012). At the end of the program, family caregivers reported fewer neuropsychiatric symptoms among patients and an

improvement in patients' quality of life. In addition, caregivers changed their coping strategies, whereas a significant decrease was observed in their anxiety levels. These studies stressed the importance of considering structured non-pharmacological interventions for patients with dementia and their caregivers to reduce BPSD symptoms and caregivers burden.

Conclusions. The BPSD field in Brazil is moving forward, departing from the initial reports of prevalence of symptoms to more recent studies focusing on the neurobiology and non-pharmacological treatment of these symptoms. The education of clinicians to correctly identify and manage these symptoms is a fundamental task to improve the care of dementia patients with BPSD and their caregivers in Brazil.

BPSD in Africa

This section will mainly focus on BPSD in Nigeria. However in Africa there are high rates of HIV-associated dementia in HIV positive patients ranging from 14% in Malawi (Patel et al., 2010) to 31% in Uganda (Wong et al, 2007). Thus, patients with dementia are also likely to have a shorter life expectancy.

BPSD in Nigeria

Baiyewu et al. (2003) examined 40 people with dementia residing in Nigeria using the NPI and found that changes in eating behavior, mood, and irritability/lability were the most prevalent BPSD (see Table 7.1). There had been other studies on BPSD or other behavior symptoms in Nigeria using the NPI as well. Baiyewu et al. (2012) reported BPSD in subjects whose diagnosis remained stable as normal or CIND/MCI over a period of three years in the Indianapolis-Ibadan Community based dementia study. In that study, patients diagnosed with dementia, CIND/MCI and normal cognition in 2001, were administered the NPI at a mean period of 17 months after assessment. Those with diagnoses of MCI and normal were reassessed in 2004, and then those with stable diagnosis of CIND/MCI or normal cognition were included in analysis. Major findings were that frequency of depression was higher in CIND/MCI and dementia compared with normal cognition, but severity and distress impairment increased from normal cognition through CIND/MCI to dementia. Caregivers of patients with dementia rated depression, apathy and hallucination as more severe in dementia compare with MCI and normal cognition. Only hallucination was significantly more distressful in dementia compare with MCI and normal cognition. Hallucinations were recorded only in subjects with dementia.

Caregivers were predominantly females (about 70%) with an average age of 40, while participants with dementia were also predominantly females (about 80%) averaging 80 years old. Both MMSE and Blessed Dementia Scale correlated with NPI severity and distress. Although 62% of participants with normal cognition had behavior symptoms, these were neither severe nor distressful and probably due to physical illness conditions like blindness and arthritis. Authors opined that it is necessary to consider starting intervention for BPSD from the stage of CIND/MCI since it appears that significant symptoms exist at this stage (Baiyewu et al., 2012).

A related study by Ojagbemi et al. (2013), also using NPI, rated behavior symptoms in 50 idiopathic Parkinson's disease patients and compared that with 50 age and gender matched controls who had a diagnosis of essential hypertension, but had controlled BP. Main findings

were that behavior symptoms were more prevalent, more severe and caregivers of Parkinson's disease patients expressed more distress than caregivers of patients with hypertension. Delusions, hallucinations, agitation, apathy irritability and appetite change were significantly more frequent. Irritability, appetite change and total severity NPI scores were significantly more severe; while significant distress was recorded with delusions, hallucinations, agitation, depression, apathy, appetite change and total NPI distress score. Mean age of Parkinson's disease patient was 65 years and about 75% of them had some schooling. Seventy four percent of patients with Parkinson's disease had at least one behavior symptom compared with 64% of controls. Slightly more than half of the caregivers for Parkinson's disease were males and were about 40 years old; about 50% had university or college education.

As part of the Indianapolis-Ibadan dementia project, a caregiver support group led by a physician and nurse was established and was very well received by caregivers. Observers have been impressed with the level of understanding of the disease process displayed by the caregivers after simple educational presentations. As in Western countries, the major focus of the meetings is on managing the aberrant behaviors associated with AD, including behavioral disturbances.

Donepezil is now available in Nigeria, but it is very expensive, and it is difficult to convey to families in which improvements are limited and might take months to achieve. Caregivers are often looking for a permanent cure. It is not unusual for psychotropics and hypnotics to be used inappropriately with unacceptable drowsiness and other side effects (Uwakwe, 2010).

There are now formal treatment modalities in some centers in Nigeria. At the University College Hospital Ibadan, a geriatric psychiatric clinic runs once a week and patients have full diagnostic work up including appropriate laboratory tests and neuropsychological tests. Treatment consists of pharmacological and non-pharmacological modalities. Caregivers are counseled on how to handle legal issues, driving and administration of properties of patients who can no longer administer them. Psychoeducation is carried out on how to handle behavior disturbances. Information is also given on the course and prognosis of the illness. We apply rational use of anti-dementia and antipsychotic drugs. Our treatment approach is multidisciplinary consisting of physicians, nurses and social workers. A general observation is that follow-up appointments are not kept for long, probably because we do not meet the caregivers' expectation of permanent cure or because of deterioration that sets in later. Even though there are currently few nursing homes, most patients are still cared for by family and in one unpublished survey it was observed that caregivers who have to leave or cut down on work to take care of their relatives are often burdened. Most families also have to pay out-of-pocket as health insurance coverage is poor and in some cases unavailable.

References and recommended reading

Aspects of BPSD likely to vary across cultures

Alexopoulos, G.S., Abrahams, R.C., Young, R.C., Shamoian, C.A. Cornell Scale for depression in dementia. *Biological Psychiatry* 1988; 23: 271–284.

Asada, T., Homma, A., Kimura, M., Uno, M. Reliability of a Japanese version of BEHAVE-AD. *Japanese Journal of Geriatric Psychiatry* 1999; 825–834.

Baiyewu, O., Smith-Gamble, V., Akinbiyi, A., et al. Behavioral and caregiver reaction of dementia as measured by the Neuropsychiatric Inventory in Nigerian community residents. *International Psychogeriatrics* 2003; 15: 399–409.

Binetti, G., Mega, M.S., Magni, E., et al. Behavioural disorders in Alzheimer's disease: A transcultural perspective. *Archives of Neurology* 1998; 55: 539–544.

Boada, M., Tarraga, L., Modinos, G., Lopez, O. L., Cummings, J. L. Neuropsychiatric Inventory —Nursing Home version (NPI-NH): Spanish validation. *Neurologia* 2005; 20(10): 665–673.

Boada, M., Tarraga, L., Modinos, G., Diego, S., Reisberg, B. Behavioral pathology in Alzheimer's disease Rating Scale (BEHAVE-AD): Spanish validation. *Neurologia* 2006; 21(1): 19–25.

Brodaty, H., Heffernan, M., Kochan, N., Draper, B., Trollor, J., Reppermund, S., Slavin, M., Sachdev, P. Neuropsychiatric symptoms in a population of older people with and without cognitive impairment. *Journal of Alzheimer's Disease* 2012; 31: 411–420.

Camus, V., Schmitt, L., Ousset, P. J., Micas, M. Depression and dementia: Contribution to the French validation of 2 depression scales: the Cornell Scale for Depression in Dementia and the Dementia Mood Assessment Scale. *Encephale* 1995; 21(3): 201–208.

Chan, W.C., Lam, L.C.W., Tam, C.W.C., et al. Prevalence of neuropsychiatric symptoms in Chinese older persons with mild cognitive impairment—a population-based study. *Am J Geriatr Psychiatry* 2010; 18(10): 948–954.

Chandra,V. Cross-cultural perspectives: India. *International Psychogeriatrics* 1996; 8 (Suppl 3): 479–481.

Choi, S.H., Na, D.L., Kwon, H.M., et al. The Korean version of the Neuropsychiatric Inventory: A scoring tool for neuropsychiatric disturbance in dementia patients. *Journal of Korean Medical Science* 2000; 15(6), 609–615.

Choy, C.N., P, Lam, L.C.W., Chan, W.C., Li, S.W., Chiu, H.F.K. Agitation in Chinese Elderly: Validation of the Chinese version of the Cohen-Mansfield Agitation Inventory. *International Psychogeriatrics* 2001; 13, 325–335.

Cohen, C., Magai, C. Racial differences in neuropsychiatric symptoms among dementia outpatients. *American Journal of Geriatric Psychiatry* 1999; 7: 57–63.

Cohen-Mansfield, J. Agitated behavior in the elderly II. Preliminary results in the cognitively deteriorated. *Journal of the American Geriatrics Society* 1986; 34: 722–727.

Cummings, J.L., Mega, M., Gray, K., et al. The Neuropsychiatric inventory: Comprehensive assessment of psychopathology in dementia. *Neurology* 1994; 44: 2308–2314.

de Jonghe, J.F., Kat, M.G. Factor structure and validity of the Dutch version of the Cohen-Mansfield Agitation Inventory (CMAI-D). *Journal of the American Geriatrics Society* 1996; 44(7): 88–89.

Fernández Martínez, M., Castro Flores, J., Pérez de las Heras, S. Prevalence of neuropsychiatric symptoms in elderly patients with dementia in Mungialde County (Basque Country, Spain). *Dementia and Geriatric Cognitive Disorders* 2008; 25:103–108.

Fuh, J.L., Liu, C.Y., Mega, M.S., Wang, S.J., Cummings, J. Behavioural disorders and caregivers' reaction in Taiwanese patients with Alzheimer's disease. *International Psychogeriatrics* 2001; 13: 121–128.

Fuh, J.L., Liu, C.Y., Wang, S.J., Wang, H.C., Liu, H.C. Revised memory and behaviour checklist in Taiwanese patients with Alzheimer's disease. *International Psychogeriatrics* 1999; 11: 181–189.

Geda, Y.E., Roberts, R.O., Knopman, D.S., et al. Prevalence of Neuropsychiatric symptoms in mild cognitive impairment and normal cognitive aging. *Archives of General Psychiatry* 2008; 65: 1193–1198.

Harwood, D.G., Barker, W.W., Ownby, R.L., Bravo, M., Aguero, H., Duara, R. The Behaviour Problems Checklist-Spanish: a preliminary study of a new scale for the assessment of depressive symptoms and disruptive behaviour in Hispanic patients with dementia. *International Psychogeriatrics* 2001; 13: 23–35.

Hendrie, H., Baiyewu, O., Edemire, D., Prince, C. Cross-cultural perspectives: Caribbean, native American and Yoruba. *International Psychogeriatrics* 1996; 8 (Suppl 3): 483–486.

Hirono, S., Mori, E., Ikejiri, Y., Imamura, T., Shimomura, T. A Japanese version of Neuropsychiatric Inventory: Utility of the assessment for psychiatric symptoms in dementia. *Brain Nerve* 1997; 49: 266–271.

Homma, A., Woo, J., Chiu, H., Hoek, K. Behavioral and psychological symptoms of dementia in Japan and the Asian Pacific region. *International Psychogeriatrics* 2000; 12 (Suppl 1): 419–422.

Ikeda, M., Fukuhara, R., Shigenobu, K., et al. Dementia associated mental and behavioural disturbances in elderly people in the community: findings from the first Nakayama study. *Journal of Neurology, Neurosurgery & Psychiatry* 2004; 75: 146–148.

Jeste, D., Finkel, S. Psychosis of Alzheimer's disease and related dementias: Diagnostic criteria for a distinct syndrome. *American Journal of Geriatric Psychiatry* 2000; 8(1): 29–34.

Kat, M.G., de Jonghe, J.F., Aalten, P. et al. Neuropsychiatric symptoms of dementia: Psychometric aspects of the Dutch Neuropsychiatric Inventory (NPI). *Tijdschr Gerontol Geriatr* 2002; 33: 150–155.

Lam, L.C.W., Chiu, H.F.K., Ng, J. Aggressive behaviour in the Chinese elderly–validation of the Chinese version of the rating scale for aggressive behaviour in the elderly (RAGE) in hospital and nursing home settings. *International Journal of Geriatric Psychiatry* 1997; 12: 678–681.

Lam, L.C.W., Tang, W.K., Leung, V., Chiu, H.F.K. Behavioural profile of Alzheimer's disease in Chinese elderly—a validation study of the Chinese version of the Alzheimer's disease behavioural pathology rating scale. *International Journal of Geriatric Psychiatry* 2001; 16: 368–373.

Leung,V.P.Y., Lam, L.C.W., Chiu, H.F.,K, Cummings, J.L., Chen, Q.L. Validation study of the Chinese version of the neuropsychiatric inventory (CNPI). *International Journal of Geriatric Psychiatry* 2001; 16: 789–793.

Low, L.F., Anstey, K.J., Lackersteen, S.M., et al. Recognition, attitudes and causal beliefs regarding dementia in Italian, Greek and Chinese Australians. *Dementia and Geriatric Cognitive Disorders* 2010; 30: 499–508.

Lyketsos, C.G., Lopez, O., Jones, B., et al. Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment. *JAMA* 2002; 288: 1475–1483.

Ma, W., Wang, H., Cummings, J., Yu, X. Reliability and validity of Chinese version of Neuropsychiatric Inventory-Questionnaire in patients with Alzheimer's disease. *Chinese Mental Health Journal* 2010

Papatriantafyllou, J.D., Viskontas, I.V., Papageorgiou, S.G., et al. Difficulties in detecting behavioral symptoms of frontotemporal lobar degeneration across cultures. *Alzheimer's Disease & Associated Disorders* 2009; 23(1): 77–81.

Prince, M., Acosta, D., Chiu, H., Scazufca, M., Varghese, M. 10/66 Dementia Research Group. Dementia diagnosis in developing countries: A cross-cultural validation study. *Lancet* 2003; 361(9361): 909–917.

Reisberg, B., Borenstein, J., Salob, S., Ferris, S. Behavioral symptoms in Alzheimer's disease: Phenomenology and treatment. *Journal of Clinical Psychiatry* 1987; 48 (Suppl): 9–15.

Rowland, J.T., Basic, D., Storey, J.E., Conforti, D.A. The Rowland Universal Dementia Assessment Scale (RUDAS) and the Folstein MMSE in a multicultural cohort of elderly persons. *International Psychogeriatrics* 2006; 18: 111–120.

Savva, G.M., Zaccai, J., Matthews, F.E., et al. Prevalence, correlates and course of behavioural and psychological symptoms of dementia in the population. *British Journal of Psychiatry*, 2009; 194: 212–219.

Schreiner, A.S. Aggressive behaviours among demented nursing home residents in Japan. *International Journal of Geriatric Psychiatry* 2001; 16: 209–215.

Schreiner, A.S., Morimoto, T. Factor structure of the Cornell Scale for Depression in Dementia among Japanese poststroke patients. *International Journal of Geriatric Psychiatry* 2002; 17: 715–722.

Shah, A., Dalvi, M., Thompson, T. Behavioral and psychological signs and symptoms of dementia across cultures: current status and the future. *International Journal of Geriatric Psychiatry* 2005; 20: 1187–1195.

Shah, A.K., Ellanchenny, N., Suh, G. A comparative study of behavioural and psychological symptoms of dementia in patients with Alzheimer's disease and vascular dementia referred to psychogeriatric services in Korea and the United Kingdom. *International Psychogeriatrics* 2004; 16: 219–236.

Shaji, K., Smitha, P., Lal, K., Prince, M. Caregivers of patients with Alzheimer's disease: A qualitative study from the Indian 10/66 dementia research network. *International Journal of Geriatric Psychiatry* 2003; 18(1): 1–6.

Suh, G.K. Agitated behaviours among the institutionalised elderly with dementia: Validation of the Korean version of the Cohen-Mansfield agitation inventory. *International Journal of Geriatric Psychiatry* 2004; 19: 378–385.

Suh, G.H., Park, J.H. The Behaviour Pathology in Alzheimer's Disease Rating Scale, Korean Version (BEHAVE-AD-K): factor structure among Alzheimer's disease inpatients. *Journal of the Korean Geriatric Society* 2001; 5: 86–91.

Suh, G.H., Son, H.G., Shin, H., et al. Reliability and analysis of symptom category scores of the Behaviour Pathology in Alzheimer's Disease Rating Scale, Korean Version (BEHAVE-AD-K). *Journal of the Korean Geriatric Society* 2001; 5: 50–57.

Tatsch, M. F., de Campos Bottino, C.M., Azevedo, D., et al. Neuropsychiatric symptoms in Alzheimer disease and cognitively impaired, nondemented elderly from a community-based sample in Brazil: prevalence and relationship with dementia severity. *American Journal of Geriatric Psychiatry* 2006; 14: 438–445.

Teri, L., Truaz, P., Logsdon, R., et al. Assessment of behavioral problems in dementia: The Revised Memory and Behavior Problems Checklist. *Psychological Aging* 1992; 7: 622–631.

The 10/66 Dementia Research Group. Behavioral and psychological symptoms of dementia in developing countries. *International Psychogeriatrics* 2004; 16(4): 441–459.

Valle, R. Culture-fair behavioral symptom differential assessment and intervention in dementing illness. *Alzheimer Disease and Associated Disorders* 1994; 8 (Suppl 3): 21–45.

Wood, S., Cummings, J., Hsu, M. et al. The use of the neuropsychiatric inventory in nursing home residents. Characterization and measurement. *American Journal of Geriatric Psychiatry* 2000; 8: 75–83.

Xie, H., Wang, L., Yu, X., et al. Neuropsychiatric symptoms in dementia and elderly people in the community: results from the Beijing Dementia Cooperative Study. *Chinese Journal of Epidemiology* 2004; 25: 829–832.

BPSD in minority elders in the United States

Alzheimer's Association. *Alzheimer's Disease Facts and Figures* 2012.

Arean, P., Gallagher-Thompson, D. Issues and recommendations for the recruitment and retention of older ethnic minority adults in clinical research. *Journal of Consulting and Clinical Psychology* 1996; 67: 875–880.

Bassiony, M.M., Warren, A., Rosenblatt, A., et al. Isolated hallucinosis in Alzheimer's disease is associated with African American race. *International Journal of Geriatric Psychiatry* 2002; 17(3): 205–210.

Chang, W., Jann, M., Hwu, H., et al. Ethnic comparison of haloperidol and reduced haloperidol plasma levels: Taiwan Chinese versus American non-Chinese. *Journal of the Formosan Medical Association* 1991; 90: 572–578.

Chen, J., Borson, S., Scanlan, J. Stage-specific prevalence of behavioral symptoms in Alzheimer's disease in a multi-ethnic community sample. *American Journal of Geriatric Psychiatry* 2000; 8(2): 123–133.

Chung, J., Cummings, J. Neurobehavioral and neuropsychiatric symptoms in Alzheimer's disease. *Neurological Clinics* 2000; 18(4): 829–846.

CIA—The World Factbook. Accessed 6 December 2013
www.cia.gov/library/publications/the-world-factbook/geos/xx.html

Cohen, C., Carlin, L. Racial differences in clinical and social variables among patients evaluated in a dementia assessment center. *Journal of the National Medical Association* 1993; 85: 379–384.

Cohen, C., Magai, C. Racial differences in neuropsychiatric symptoms among dementia outpatients. *American Journal of Geriatric Psychiatry* 1999; 7: 57–63.

Cohen, C., Weston, R., Hyland, K. Mood psychoses, and agitation among Afro-American, Afro-Caribbean, and Caucasian dementia patients: Final report. *New York State Dept. of Health* 1996.

Cohen-Mansfield, J. Agitated behavior in persons with dementia: The relationship between type of behavior, its frequency, and its disruptiveness. *Journal of Psychiatric Research* 2009; 43: 64–69.

Coleman, E., Tyll, L., LaCroix, A., et al. Recruiting African American older adults for a community-based health promotion intervention: Which strategies are effective? *American Journal of Preventative Medicine* 1997; 13: 51–56.

Cooper, C., Tandy, A.R., Balamurali, T.B., Livingston, G. A systematic review and meta-analysis of ethnic differences in use of dementia treatment, care, and research. *American Journal of Geriatric Psychiatry* 2010; 18(3): 193–203.

Espino, D., Lewis, R. Dementia in older minority populations. *American Journal of Geriatric Psychiatry* 1998; 6: S19–S25.

Hall, W. Representation of blacks, women and the very elderly in 28 major randomized clinical trials. *Ethnicity and Disease* 1999; 3: 333–340.

Jann, M., Chang, W., Davis, C., et al. Haloperidol and reduced haloperidol plasma levels in Chinese vs. non-Chinese psychiatric patients. *Psychiatry Research* 1989; 30(1): 45–52.

Jeste, D., Finkel, S. Psychosis of Alzheimer's disease and related dementias: Diagnostic criteria for a distinct syndrome. *American Journal of Geriatric Psychiatry* 2000; 8(1): 29–34.

Lovato, L., Hill, K., Hertert, S., et al. Recruitment for controlled clinical trials: Literature summary and annotated bibliography. *Controlled Clinical Trials* 1997; 18: 328–357.

Manly, J. Reading level attenuates differences in neuropsychological test performance between African Americans and white elders. *Journal of the International Neuropsychological Society* 2002; 8(3): 341–348.

Manly, J., Jacobs, D., Mayeux, R. Alzheimer disease among different ethnic and racial groups. In R.D. Terry, R. Katzman, K.L. Bick, S.S. Sisodia (Eds.), *Alzheimer Disease* 1999 (pp. 117–132). Philadelphia, PA: Lippincott Williams & Wilkins.

Madhusoodanan, S. Antipsychotic treatment of behavioral and psychological symptoms in dementia in geropsychiatric patients. *American Journal of Geriatric Psychiatry* 2001; 9(3): 283–288.

Manly, J., Jacobs, D., Touradji, P., et al. Are ethnic group differences in neuropsychological test performance explained by reading level? A preliminary analysis. *Journal of the International Neuropsychological Society* 2000; 6: 245.

Mintzer, J., Nietert, P., Costa, K., Waid, L. Cross-cultural perspectives: Agitation in demented patients in the United States. *International Psychogeriatrics* 1996; (Suppl 3): 487–490.

Moody, L., Gregory, S., Bocanegra, T., Vasey, F. Factors influencing post-menopausal African American women participation in a clinical trial. *Journal of the American Academy of Nurse Practitioners* 1995; 7: 483–488.

Morse, E., Simon, Besch, C., Walker, J. Issues of recruitment, retention, and compliance in community-based clinical trials with traditionally underserved populations. *Applied Nursing Research* 1995; 8: 8–14.

Mouton, C., Harris, S., Rovi, S., et al. Barriers to black women's participation in cancer clinical trials. *Journal of the National Medical Association* 1997; 89: 721–727.

Sano, M. *Clinical outcome measures and ethnicity in AD.* GRACE Conference (Genetics, Response, and Cognitive Enhancers: Implications for Alzheimer's disease, Bethesda, Maryland, United States, December 2–3, 2000.

Sinclair, S., Hayes-Reams, P., Myers, H., Allen, W., Hawes-Dawson, J., Kington, R. Recruiting African Americans for health studies: Lessons from the Drew-RAND Center on Health and Aging. *Journal of Mental Health And Aging* 2000; 6: 39–51.

Steinberg, M., Shao, H., Zandi, P. et al. Point and 5-year period prevalence of neuropsychiatric symptoms in dementia: The Cache County study. *International Journal of Geriatric Psychiatry* 2008; 23: 170–177.

Stoy, D., Curtis, C., Dameworth, K., et al. The successful recruitment of elderly black subjects in a clinical trial: the CRISP experience. Cholesterol Reduction in Seniors Program. *Journal of the National Medical Association* 1995; 87: 280–287.

Tang, M., Stern, Y., Marder, K., et al. The APOE-e4 allele and the risk of Alzheimer's disease among African Americans, whites, and Hispanics. *JAMA* 1998; 279: 751–755.

US Census Bureau. 2012 Population Projections 2015–2060. Accessed 5 December 2013 www.census.gov/population/projections/data/national/2012/summarytables.html

Walker, S., Borson, S., Katon, W., et al. Differential clinical characteristics of older black and white nursing home residents. *American Journal of Geriatric Psychiatry* 1995; 3(3): 229–238.

Zuckerman, I.H., Ryder, P.T., Simoni-Wastila, L. et al. Racial and ethnic disparities in the treatment of dementia among Medicare beneficiaries. *Journals of Gerontology Series B-Psychological Sciences & Social Science* 2008; 63(5): S328–S333.

BPSD in Turkey

Arslantas, D., Ozbabalik, D., Metintas, S. et al. Prevalence of dementia and associated risk factors in Middle Anatolia, Turkey. *Journal of Clinical Neuroscience* 2009; 16(11): 1455–1459.

Cankurtaran, E.S., Kutluer, I., Senturk, M., et al. Psychiatric consultations for nursing home residents: A perspective from Turkey and the implications for comparable countries. *International Psychogeriatrics* 2008; 20(4): 752–763.

CIA—The World Factbook. Accessed 6 December 2013 www.cia.gov/library/publications/the-world-factbook/geos/xx.html

Eker, E. Services for elderly care in Turkey. Presented at the Seventh Congress of the International Psychogeriatric Association, Sydney, Australia, 1995.

Eker, E., Ertan, T. Behavioral and psychological symptoms of dementia in Eastern and Southeastern Europe and the Middle East. *International Psychogeriatrics* 2000; 12 (Suppl1): 409–413.

Gungen, C., Ertan, T., Eker, E., et al. The standardized Mini Mental State Examination in Turkish. In: Ninth Congress of the IPA, 15–20 August, Vancouver, Canada, 1999.

Gurvit, H., Emre, M., Tinaz, S., et al. The prevalence of dementia in an urban Turkish population. *American Journal of Alzheimer's Disease & Other Dementias* 2008; 23(1): 67–76.

Keskinoglu, P., Giray, H., Picakciefe, M., et al. The prevalence and risk factors of dementia in the elderly population in a low socio-economic region of Izmir, Turkey. *Archives of Gerontology & Geriatrics* 2006; 43(1): 93–100.

Reisberg, B., Borenstein, J., Salob, S., Ferris, S. Behavioral symptoms in Alzheimer's disease: Phenomenology and treatment. *Journal of Clinical Psychiatry* 1987; 48 (Suppl): 9–15.

Sahin, H.A., Gurvit, I.H., Emre, M., et al. The attitude of elderly lay people towards the symptoms of dementia. *International Psychogeriatrics* 2006; 18(2): 251–258.

Yener, G.G., Turkuaz Alzheimer Working (TAC) Group. The neuropsychiatric inventory scores change across the mini mental state examination ranges in patients with Alzheimer's disease: A multicenter study in Turkey. *Cognitive & Behavioral Neurology* 2009; 22(4): 264–269.

BPSD in Iran

Javadpour, A., Ahmadzadeh, L., Bahredar, M.J. An educative support group for female family caregivers: impact on caregivers' psychological distress and patient's neuropsychiatry symptoms. *International Journal of Geriatric Psychiatry* 2009; 24(5): 469–471.

BPSD in India

Alzheimer's and Related Disorders Society of India. The Dementia India Report: Prevalence, impacts, costs and services for Dementia. *ARDSI*, New Delhi, India, 2010.

Alzheimer's Disease International World Alzheimer's Report 2009; Prince, M. & Jackson, J. (Eds.).

Dias, A., Samuel, R., Patel, V. et al. The impact associated with caring for a person with dementia: a report from the 10/66 Dementia Research Group's Indian Network. *International Journal of Geriatric Psychiatry* 2004; 19: 182–184.

India Census Report 2011, Office of the Registrar General & Census Commissioner, Government of India. Chapter 2, Population composition.

National Policies & Programmes for the Welfare of the Elderly 2011, Chapter 4, Situation Analysis of the Elderly in India. Central Statistics Office, Ministry of Statistics & Programme Implementation, Govt. of India

Pais, S. Globalization and its Impact on Families, 4th Viennese Conference on Mediation. Vienna, Austria, 2006

Prakash, I.J. Ageing in India, WHO, Geneva, 1999.

Prince, M., Trebilco, P. Mental health services for older people: A developing countries perspective. In B. Draper, P. Melding, & H. Brodaty (Eds.) *Psychogeriatric Service Delivery: An International Perspective* 2005 (pp. 33–54). New York: Oxford University Press.

Rajan S I, Chronic Poverty among the Elderly. Working paper 17, Chronic Poverty Research Centre, IIP, 2004.

Shaji, K., Arun, P., Lal, K., Prince, M. Revealing a hidden problem: An evaluation of a community dementia case-finding program from the Indian 10/66 Dementia Research Network. *International Journal of Geriatric Psychiatry* 2002; 17(2): 222–225.

Shaji, K.S., George, R.K., Prince, M.J., Jacob, K.S. Behavioral symptoms and caregiver burden in dementia. *Indian Journal of Psychiatry* 2009; 51(1): 45–49.

Shaji, K., Smitha, P., Lal, K., Prince, M. Caregivers of patients with Alzheimer's disease: A qualitative study from the Indian 10/66 dementia research network. *International Journal of Geriatric Psychiatry* 2003; 18(1): 1–6.

Sinha, R. Dynamics of change in the Modern Hindu Family. South Asia Books 1993.

The 10/66 Dementia Research Group. Behavioral and psychological symptoms of dementia in developing countries. *International Psychogeriatrics* 2004; 16(4): 441–459.

Wimo, A., Winblad, B., Jonsson, L. The worldwide societal costs of dementia: Estimates for 2009. *Alzheimer's & Dementia* 2010; 6: 98–103.

World Health Organization. The Global Burden of Disease: 2004 Update. WHO: Geneva, 2008.

BPSD in China, Hong Kong SAR and Taiwan

Chan, M.C., Chong, C.S., Wu, A.Y., Wong, K.C., Dunn, E.L., Tang, O.W., Chan, W.F. Antipsychotics and risk of cerebrovascular events in treatment of behavioural and psychological symptoms of dementia in Hong Kong: a hospital-based, retrospective, cohort study. *International Journal of Geriatric Psychiatry*, 2010a; 25(4): 362–370.

Chan, W.C., Lam, L.C.W., Tam, C.W.C., et al. Prevalence of neuropsychiatric symptoms in Chinese older persons with mild cognitive impairment—a population-based study. *American Journal of Geriatric Psychiatry* 2010b; 18(10): 948–954.

Chan, T.C., Luk, J.K., Shea, Y.F., Lau, K.H., Chan, F.H., Yu, G.K., Chu, L.W. Continuous use of antipsychotics and its association with mortality and hospitalization in institutionalized Chinese older adults: an 18-month prospective cohort study. *International Psychogeriatrics* 2011; 23(10): 1640–1648.

Chiu, E., Chiu, H.F.K. Dementia care in Asia-Second Consensus Statement on Quality Services. *International Psychogeriatrics* 2006; 18: 176.

Chiu, H.F.K., Yu, X., Lam, L.C.W. Dementia strategy in China and Hong Kong. *International Journal of Geriatric Psychiatry* 2010; 25: 905–907.

Chow, T.W., Liu, C.K., Fuh, J.L., et al. Neuropsychiatric symptoms of Alzheimer's disease differ in Chinese and American patients. *International Journal of Geriatric Psychiatry* 2002; 17: 22–28.

Hwang, J.P., Tsai, S.J., Yang, C.H., et al. Repetitive phenomena in dementia. *The International Journal of Psychiatry in Medicine* 2000; 30: 165–171.

Hwang, J., Yang, C., Tsai, S., Liu, K. Behavioral disturbances in psychiatric inpatients with dementia of the Alzheimer's type in Taiwan. *International Journal of Geriatric Psychiatry* 1997; 12: 902–906.

Hwang, J., Yang, C., Tsai, S., Liu, K. Psychotic symptoms in psychiatric inpatients with dementia of the Alzheimer and vascular type. *Chinese Medical Journal* 1996; 58: 35–39.

Lam, L.C.W., Lui, V.W.C., Luk, D.N.Y., Chau, R., So, C., Poon, V. et al. Effectiveness of an individualized functional training program on affective disturbances and functional skills in mild and moderate dementia—A randomized control trial. *International Journal of Geriatric Psychiatry* 2010; 25: 133–141.

Liu, C., Fuh, J., Teng, E., et al. Depressive disorders in Chinese patients with Alzheimer's disease. *Acta Psychiatrica Scandinavica* 1999; 100: 451–455.

Liu, H.C., Lin, K.N., Tang, E.L., et al. Prevalence and subtypes of dementia in Taiwan: A community survey of 5297 individuals. *Journal of the American Geriatrics Society* 1995; 43: 144–149.

Tsai, S., Hwang, J., Yang, C., Liu, K. Delusional jealousy in dementia. *The Journal of Clinical Psychiatry* 1997; 58: 492–494.

Zhang, M.Y., Wang, H.L., Li, T., Yu, X. Characteristics of neuropsychiatric symptoms among individuals with Alzheimer's disease in a memory clinic setting. *Chinese Mental Health Journal* 2011; 25(4): 259–264.

Zhang, M., Wang, H., Li, T., Yu, X. Prevalence of neuropsychiatric symptoms across the declining memory continuum: an observational study in a memory clinic setting. *Dementia and Geriatric Cognitive Disorders Extra* 2012; 2(2): 200–208.

BPSD in South Korea

Suh, G.K. Agitated behaviours among the institutionalised elderly with dementia: Validation of the Korean version of the Cohen-Mansfield agitation inventory. *International Journal of Geriatric Psychiatry* 2004; 19: 378–385.

Suh, G.H., Park, J.H. The Behaviour Pathology in Alzheimer's Disease Rating Scale, Korean Version (BEHAVE-AD-K): factor structure among Alzheimer's disease inpatients. *Journal of the Korean Geriatric Society* 2001; 5: 86–91.

BPSD in Japan

Japanese Ministry of Health, Welfare, and Labor. White Paper on Society Aging 2012.

Japanese Ministry of Health, Welfare, and Labor. Guideline for Antipsychotics use against BPSD 2013. www.mhlw.go.jp/stf/houdou/2r98520000036k0c-att/2r98520000036k1t.pdf

Takeda, M. Role of psychiatrists in long-term care for the aged. *Journal of Psychiatry and Neurology* 2004; 106(1): 53–55.

BPSD in Latin America

Alzheimer's Disease International. World Alzheimer's Report 2009; Prince, M. & Jackson, J. (Eds.).

Ferri, C.P., Prince, M. 10/66 Dementia Research Group: Recently published data for seven Latin America sites. *International Psychogeriatrics* 2009; 22: 158–159.

The 10/66 Dementia Research Group. Behavioral and psychological symptoms of dementia in developing countries. *International Psychogeriatrics* 2004; 16(4): 441–459.

BPSD in Argentina

Bagnati, P.M., Kremer, J.L., Taragano, F.E., Allegri, R.F. Argentina In de Waal, H., Lyketsos, C., Ames, D., O'Brien, J. *Designing and Delivering Dementia Services* 2013 John Wiley & Sons, p. 142

CIA—The World Factbook. Accessed 6 December 2013 www.cia.gov/library/publications/the-world-factbook/geos/xx.html

Kaufer, D., Cummings, J., Ketchel, P., Smith, D., et al. Validation of the NPI-Q a Brief Clinical Form of the Neuropsychiatric Inventory. *Journal of Neuropsychiatry & Clinical Neurosciences* 2000; 12(2): 233–239.

Lloyd-Sherlock, P. , Redondo, N. Institutional Care for Older People in Developing Countries: The Case of Buenos Aires, Argentina. *Journal of Population Ageing* 2009; 2: 41–56

Machnicki, G., Allegri, R.F., Dillon, C., Serrano, C.M., Taragano, F.E. Cognitive, functional and behavioral factors associated with the burden of caring for geriatric patients with cognitive impairment or depression: evidence from a South American sample. *International Journal of Geriatric Psychiatry* 2009; 24: 382–389.

Mangone, C., Bueno, A., Allegri, R., Arizaga, R., Nitrini, R., et al. Behavioral and Psychological Symptoms of Dementia in Latin America. *International Psychogeriatrics* 2000; 12 (Suppl 1): 415–418.

Mangone, C., Sanguinetti, R., Baumann, P., et al. Implications of feelings of burden on caregiver perception of the patient's functional status. *Dementia* 1993; 4: 287–293.

Pollero, A., Gimenez, M., Allegri, R.F., Taragano, F.E. Behavioral symptoms in Alzheimer disease. *Vertex* 2004; 15: 5–9.

Wimo, A., Winblad, B., Jonsson, L. The worldwide societal costs of dementia: Estimates for 2009. *Alzheimer's & Dementia* 2010; 6: 98–103.

BPSD in Mexico

Acosta-Castillo, G.I., Sosa, A.L., Orozco, R., Borges, G. Neuropsychiatric symptoms in older adults with dementia and their relationship to disease severity. *Rev Invest Clin* Jul–Aug 2012; 64(4): 354–363.

CIA—The World Factbook. Accessed 6 December 2013 www.cia.gov/library/publications/the-world-factbook/geos/xx.html

Ferri, C.P., Prince, M. 10/66 Dementia Research Group: Recently published data for seven Latin America sites. *International Psychogeriatrics* 2009; 22: 158–159.

Rodríguez-Agudelo, Y., Solís-Vivanco, R., Acosta-Castillo, I., García-Ramírez, N., Rojas-de-la-Torre, G., Sosa, A.L. Neuropsychiatric symptoms in older adults with and without dementia in urban and rural regions. Results of the 10/66 Dementia Research Group in Mexico. *Rev Invest Clin* Jul–Aug 2011; 63(4): 382–390.

Rosas-Carrasco, O., Guerra-Silla, M., Torres-Arreola, L., García-Peña, C., Escamilla-Jiménez, C., González-González, C. Caregiver burden of Mexican dementia patients: The role of dysexecutive syndrome, sleep disorders, schooling and caregiver depression. *Geriatrics & Gerontology International* 2013; DOI: 10.1111/ggi.12072

Wimo, A., Winblad, B., Jonsson, L. The worldwide societal costs of dementia: Estimates for 2009. *Alzheimer's & Dementia* 2010; 6: 98–103.

BPSD in Brazil

Bottino, C.M., Azevedo, D. Jr., Tatsch, M., et al. Estimate of dementia prevalence in a community sample from São Paulo, Brazil. *Dementia and Geriatric Cognitive Disorders* 2008; 26: 291–299.

Camozzato, A.L., Kochhann, R., Simeoni, C., et al. Reliability of the Brazilian Portuguese version of the Neuropsychiatric Inventory (NPI) for patients with Alzheimer's disease and their caregivers. *International Psychogeriatrics* 2008; 20(2): 383–393.

Fialho, P.P., Köenig, A.M., Santos, M.D., et al. Positive effects of a cognitive-behavioral intervention program for family caregivers of demented elderly. *Archives of Neuro-Psychiatry* 2012; 70(10): 786–792.

Herrera, Jr., E., Caramelli, P., Silveira, A.S., et al. Epidemiologic survey of dementia in a community-dwelling Brazilian population. *Alzheimer Disease and Associated Disorders* 2002; 16: 103–108.

Lopes, M.A., Hototian, S.R., Reis, G.C., et al. Systematic review of dementia prevalence 1994 to 2000. *Dementia & Neuropsychologia* 2007; 1: 230–240.

Stella, F., Banzato, C.E., Quagliato, E.M., et al. Psychopathological features in patients with Parkinson's disease and related caregivers' burden. *International Journal of Geriatric Psychiatry* 2009; 24(10): 1158–1165.

Stella, F., Canonici, A.P., Gobbi, S., et al. Attenuation of neuropsychiatric symptoms and caregiver burden in Alzheimer's disease by motor intervention: a controlled trial. *Clinics* 2011 (Sao Paulo); 66(8): 1353–1360.

Tatsch, M.F., Bottino, C.M., Azevedo, D., et al. Neuropsychiatric symptoms in Alzheimer disease and cognitively impaired, nondemented elderly from a community-based sample in Brazil: prevalence and relationship with dementia severity. *American Journal of Geriatric Psychiatry* 2006; 14: 438–445.

Viola, L.F., Nunes, P.V., Yassuda, M.S., et al. Effects of a multidisciplinary cognitive rehabilitation program for patients with mild Alzheimer's disease. *Clinics* 2011 (Sao Paulo); 66(8): 1395–1400.

United Nations Department of Economic and Social Affairs. World Population Ageing 1950–2050 (2002).

BPSD in Africa

Baiyewu, O., Smith-Gamble, V., Akinbiyi, A., et al. Behavioral and caregiver reaction of dementia as measured by the Neuropsychiatric Inventory in Nigerian community residents. *International Psychogeriatrics* 2003; 15: 399–409.

Baiyewu, O., Unverzagt, F.W., Ogunniyi, A., Smith-Gamble, V., Gureje, O., Lane, K.A., Goa, S., Hall, K.S., Hendrie, H.C. Behavioral symptoms in community dwelling elderly Nigerians with dementia, mild cognitive impairment and normal cognition. *International Journal of Geriatric Psychiatry* 2012; 27(9) 931–939.

Ojagbemi, A.A., Akinyemi, R.O., Baiyewu, O. Neuropsychiatric symptoms in Nigerian patients with Parkinson disease. *Acta Neurologica Scandinavica* 2013; 128(1): 9–16.

Patel, V.N., Mungwira, R.G., Tarumbiswa, T.F., Heikinheimo, T., van Oosterhout, J.J. High prevalence of suspected HIV-associated dementia in adult Malawian HIV patients. *International Journal of STD & AIDS* 2010; 21(5): 356–358.

Uwakwe, R. Nigeria. In E.S. Krishnamoorthy, M.J. Prince, & J.L. Cummings (Eds.). *Dementia: A Global Approach* (pp. 127–130). Cambridge: Cambridge University Press 2010.

Wong, M.H., Robertson, K., Nakasujja, N., et al. Frequency of and risk factors for HIV dementia in an HIV clinic in sub-Saharan Africa. *Neurology* 2007; 68(5): 350–355.

INTERNATIONAL PSYCHOGERIATRIC ASSOCIATION

www.ipa-online.org

MODULE 8

Long-term care (LTC)

The IPA Complete Guides to Behavioral and Psychological Symptoms of Dementia

BPSD

Specialists Guide

Specialists • Primary Care Physicians • Nurses

MODULE 8: Long-term care (LTC)

Contents

Key messages	**8.2**
Introduction	**8.3**
Principles of good care	**8.3**
Environmental design	**8.4**
Screening and behavioral assessment	**8.4**
Useful steps to take in assessment	8.5
Resources to access and evaluate assessment tools	8.6
Non-pharmacological interventions	**8.7**
Training programs for long-term care staff	8.7
Individualized assessment and care plans	8.8
Psychosocial activities	8.8
Exercise programs	8.8
Music therapy	8.8
Sensory stimulation	8.9
Conclusions	8.9
Pharmacological interventions	**8.9**
Atypical antipsychotics	8.9
Antidepressants	8.10
Anticonvulsants	8.10
Cognitive enhancers	8.10
Other medications	8.10
Conclusions	8.11
Optimizing the use of psychotropic medications	**8.11**
Strategies for optimization/discontinuation	8.12
Recommendations	8.13
Role of the interdisciplinary team	**8.15**
Differences between multidisciplinary and interdisciplinary teams	8.16
Disciplines and how they contribute to interdisciplinary treatment of BPSD	8.16
Models of mental health care	8.18
Education and training	**8.19**
Evidence for best practice	8.20
Guidelines	**8.20**
References and recommended reading	**8.22**

Key messages

- Behavioral and psychological symptoms of dementia (BPSD) are very common in Long-Term Care (LTC) facilities. They include aggression, agitation, depression, anxiety, delusions and hallucinations, pacing, screaming, wandering and apathy. Some of these cause great distress for the person, their family, caregivers and the staff.
- Comprehensive biopsychosocial assessment of BPSD is a necessary first step to ascertain causative factors and consider optimal interventions. Indeed, without preliminary assessment data, one cannot evaluate the effectiveness of an intervention.
- It is important to try to rule out worsening of a chronic medical or psychiatric disorder, a new medical condition, delirium, pain, constipation, substance abuse or withdrawal, hearing and vision problems and adverse effects of medications.
- Careful selection of appropriate assessment tools can help to craft and carry out empirically-based, person-centered care plans to help alleviate BPSD. Screening and assessment measures may require varying levels of training to administer and score correctly. Necessary training as well as appropriate follow-up is essential.
- The needs of persons with dementia and BPSD are often extensive, with complex etiologies and triggers. A range of pharmacological and non-pharmacological approaches are required.
- There is a substantial body of evidence in support of the use of psychosocial interventions for BPSD. These approaches are indicated as first-line management for all emotional and behavioral disturbances in individuals with dementia.
- Psychotropic drugs (antipsychotic drugs in particular) are often prescribed too often and for too long. Evidence has shown that psychotropic drugs can be safely discontinued in many cases.
- Education on drug efficacy and safety, increased psychosocial interventions and medication review are effective strategies to optimize psychotropic drug prescription in long-term care.
- Follow-up assessment is vital to determine whether interventions have been sufficient, whether further complications have arisen, or to determine whether the need for continued treatment (particularly with pharmacological interventions) is warranted.
- Interdisciplinary treatment teams have been shown to provide superior care in community and hospital-based aged care settings; research evidence is accumulating about their efficacy in long-term care settings. Interdisciplinary teams differ in structure and process to multidisciplinary treatment teams.
- A wide variety of disciplines may participate in an interdisciplinary care team. While the exact professional mix within teams may vary due to many factors (e.g. patient mix, funding constraints), key elements of interdisciplinary knowledge, communication, and respect remain.
- There is increasing evidence that geriatric mental health training and education can improve staff understanding of disease and treatment needs, improve job satisfaction and self-worth, reduce the potential for challenging behaviors and improve quality of life of older people living in long-term care.

Introduction

Behavioral and psychological symptoms of dementia (BPSD) are highly prevalent in long-term care (LTC) settings. Approximately 60% of older adults in LTC facilities have dementia and the prevalence of BPSD among individuals with dementia in LTC is as high as 90% in some studies, with a median prevalence of any behavior symptom of 78% (Seitz et al., 2010). Such symptoms cause significant loss of quality of life and present formidable challenges to the staff of LTC facilities charged with their care (Ballard et al., 2001). A detailed description of BPSD and their prevalence can be found in Module 2 (Clinical Issues). It is important to note that behavioral and mood symptoms can range from mild to very severe and that interventions for individuals and service planning must take this into account. The seven-tiered model of management for BPSD (Brodaty et al., 2003) is very helpful with regard to service planning.

Principles of good care

Long-term care facilities in different regions and countries include a variable mix of social, physical, clinical and mental health services (Brodsky et al., 2002; Brodsky et al., 2003; Wikler and Hirschfeld, 2002). The economic challenges of providing health care contribute to disparities within and across countries. And yet, despite differences in culture, resources and government policy among nations, a review of international consensus documents on human dignity, elder well-being and human rights as well as specific mental health practice guidelines, conducted under the auspices of the International Psychogeriatric Association Task Force on Mental Health Services in Long-Term Care Homes, revealed broad support for certain core principles (Gibson et al., 2010). These include that: (1) residential care should be situated within a continuum of services which are accessible on the basis of need; (2) there should be an explicit focus on quality of care in long-term care facilities; and (3) quality of life for the residents of these facilities should be a primary objective. The following observations taken from this search for principles of good care are of particular interest to the issue of BPSD in facility-based long term care:

- Much of the work on improving residential care has focused on aspects of basic physical care, such as decreasing pressure sores, countering weight loss, removing physical and chemical restraints, etc.
- Complex needs that must be addressed in a high quality care system include interactions among increased physical frailty, multiple chronic illnesses, cognitive decline and emotional distress.
- High quality mental health care in nursing homes is possible only where overall care is of high quality (American Geriatrics Society and American Association for Geriatric Psychiatry, 2003).
- The person-centered care movement, which originated in the context of caring for older people with dementia in the United Kingdom, is now influential in many parts of the world, including Australia, parts of Western Europe and North America (Dewing, 2004).
- Quality of care implies the ability to compromise and to balance the needs of all parties involved, including the recipient of care, family members and care providers (Sandberg et al., 2002).

- The stigma of LTC residency persists, to the detriment of those individuals who need this level of support in order to survive. Issues of stigma and discrimination are compounded for those individuals who are aging with a mental disorder (Graham et al., 2003).

Environmental design

In 2001, Marshall published an important statement on the design of environments for people with dementia. She recommended that facilities should be designed in such a way as to compensate for disability, maximize independence, reinforce personal identity, enhance self-esteem and confidence, demonstrate care for staff and welcome relatives and the local community (Marshall, 2001). Fleming and Purandare (2010) recently reviewed 57 studies and synthesized the evidence with respect to environmental design in LTC. They concluded that the empirical evidence supports the recommendations that long-term facilities for people with dementia should be designed and constructed with the following features in mind:

- Where it is necessary to provide for the safety and security of the residents by confining them within a secure perimeter, this should be achieved by means of unobtrusive security measures that maximize the feeling of control over the environment.
- Those parts of the facility which are accessible to the residents should contain a variety of spaces that provide the residents with differing ambience, size and function.
- Each resident should have the opportunity to have a single room and be allowed to personalize that room.
- Residents should be able to see the features that are most important to them from the location(s) where they spend most of their time.
- The levels of stimulation should be adjusted to minimize unhelpful stimulation and optimize helpful stimuli with the periodic availability of high levels of illumination.
- It is desirable that the facility should be small, have a homelike appearance, provide opportunities for engagement with the ordinary activities of daily living, and have an outside space that is accessible to the resident when accompanied by a member of staff.

Screening and behavioral assessment

A wide range of assessment tools may play a role in the successful management of BPSD within LTC settings. Psychological testing can be used to screen for the presence of BPSD. It can also ascertain the extent to which the frequency and severity of such symptoms distress the person with dementia or their caregivers. More formal assessment tools can assist in gathering information on a broader range of cognitive impairment or emotional distress that can help identify etiologies and suggest possible interventions. Targeted measures (e.g., for assessment of delirium) may form a critical component of the management of BPSD. In order to put into place effective strategies to manage BPSD, it is necessary to accurately measure the nature of the behaviors, their frequency and timing, and potential triggers and underlying causes. Just as important is the accurate documentation of the circumstances in which such behaviors do *not* occur. Measurement of the medical, psychological, social and environmental context of the unique individual with dementia is critical.

BPSD occur against a background of the resident's premorbid personality and their premorbid social and occupational functioning. Quite often, current behaviors can be understood in the light of these pre-existing personal characteristics. In addition, the type of dementia that they have is likely to have certain characteristic effects on their mental state and behavior. For instance, people with dementia of the Alzheimer's type (DAT) tend to exhibit stereotypic personality changes, including increased neuroticism (Robins, Wahlin and Byrne, 2010). Assessment of BPSD also needs to take into account the often transient nature of many symptoms (Aalten et al., 2005). Symptoms may vary across time of day and across staff members, and may change in response to the person's health status and environment. The utility of screening and assessment measures to augment clinical charting of BPSD is critical. Such measures can provide a standardized, objective record of what are often changeable behaviors and circumstances over time. This can allow for the most effective, empirically-based interventions to be enacted. The use of measures demonstrating sensitivity to change is important here.

LTC settings may be staffed and supported by a wide range of health care professionals, who may have varying degrees of familiarity with assessment instruments. Measurement issues such as standardized administration of measures, and the distinction between screening and diagnostic assessment may be unfamiliar to many staff members in such settings (Pachana et al., 2010). For example, screening often involves the use of cut scores, and more involved psychological assessment batteries make use of normative data to place an individual's scores within the context of relevant peer groups. In contrast, individual-centered (idiographic) approaches to assessment do not make use of such normative data. In addition, sensory and communication difficulties of residents may make meaningful assessment challenging.

Useful steps to take in assessment

Ideally, the treatment team should take some time to discuss *why* assessment of an individual is required. Is it to measure frequency and timing of the behavior? What are the levels of distress in the resident? Are there related consequences of behaviors (such as falls or care refusals)? Determining what questions need to be answered can help ascertain which tools will work best for the purpose.

Is assessment actually necessary? Has the reported problem reached the threshold for assessment and management? Trivial or transient problems might not need assessment. Sometimes an assessment is requested by a certain party when not all parties agree that it is needed.

Who "owns" the problem? Does the resident have the problem, does the staff have the problem or does the family have the problem? It is important to identify who has the problem, otherwise the assessment and management may be off target. Which problem should be assessed? The resident might have a number of interrelated problems. It is often impractical to assess them all. It is best to identify the one worst problem and focus on it. If there has been an acute change it is important to rule out a new medical condition or exacerbation of a chronic medical or psychiatric disorder.

Next, a discussion of *who* will administer the assessment, and to *whom*, should follow. Some assessments may require a referral (for example, to a psychologist) if staff deem this necessary. But a wide range of measures designed for use in nursing home contexts may be used by nursing staff. Having multiple assessors, if implemented well, can help mitigate against any biases of a single assessor.

Use of informants is often vital in gathering information about past behavior and preferences, as well as current insights into possible triggers for behaviors. However, caution is warranted as no one person can have wholly accurate knowledge of the person with dementia's internal state. For example, in a study by Chopra and colleagues (2008), the self-report of persons with mild cognitive impairment (MCI) or DAT, as reflected in a Mini-Mental State Examination (MMSE) mean score of 24 was compared with the reports of family members or close associates. Results in this study indicated significant disagreement on all items of the Geriatric Depression Scale (GDS-15), with the exception of the item pertaining to memory problems. Thus proxy reports, which are often essential when assessing persons with significant cognitive impairment, should be used with due care.

It is important also to distinguish between *screening* measures, which usually only give information about the possible presence of a symptom, and more fully developed *assessment* measures, which can provide diagnostic indications and more robust symptom and behavior levels and severity assessment. Screens are often designed to be administered by a wide range of health professionals, and are relatively straightforward to deliver, score and interpret. More complex assessment tools may provide vital information necessary to implement management strategies, but require administration, scoring and interpretation by specific professionals, including the use of normative data to gauge whether an individual's presentation is outside that expected. When measures are inappropriately treated as screens, harm may be done. For example, while MMSE scores may be interpreted using simple cut-off scores, such scores obtained without reference to age and education specific normative data (Crum et al., 1993) are highly misleading, as are interpretations stemming from them.

Finally, once interventions have been put into place, it is essential to ascertain their efficacy and determine when they are no longer needed. This is particularly true of pharmacological measures implemented to assist in behavior management. The woeful statistics on the number and duration of antipsychotic use in older adults in nursing home care speaks to the need to implement steps to gather data on when medication may no longer be required (Porsteinsson, Ryan, Ismail, and Tariot, 2003). This statistic also speaks to the need for greater use of non-pharmacological interventions for BPSD in LTC.

Resources to access and evaluate assessment tools

There are a variety of resources available on screening tools. These include reference texts, compilations of screening tests and individual reviews and analyses in the published literature (e.g., Burns et al., 2004; Neville and Byrne, 2001; Pachana et al., 2010; Snowden et al., 2003). Review articles on particular issues such as behavioral pain assessment tools (e.g., Zwakhalen et al., 2006) may be particularly useful.

If measures are required to be translated from the original language of publication, great care must be taken to ensure linguistic equivalence and adequate psychometric properties are established (Stewart, 2008). Metaphorical language may be difficult to get across in another cultural context, and factors such as varying levels of schooling or familiarity with testing in general may limit utility in new contexts. The World Health Organization has useful guidelines for appropriate practices to follow when translating a measure (World Health Organization, 2007).

Unfortunately, adequate research on the use and efficacy of screening tools and assessment measures in LTC lags behind clinical demands. More work on determining the clinical efficacy of screening instruments is required, particularly with respect to clinical outcomes, for example in terms of symptom reduction or delay in disease progression (Pachana et al., 2010). The development of more internationally applicable instruments specifically to assist with management of BPSD is particularly needed.

In day-to-day practice within nursing homes, care staff require adequate resources to be able to provide high-quality care to residents. This includes the provision by the facility of necessary assessment tools, the regular review and updating of said measures, and any attendant training that is necessary to use such tools appropriately. Policies on the assessment of residents within facilities should be developed with the input of staff and should be reviewed periodically.

- Using assessment tools appropriately in nursing facilities requires input from all levels of care providers as well as relatives of residents, with respect to decisions around use of such tools as well as collaborative cooperation in their administration and interpretation.
- Ultimately, the quality of data obtained with respect to BPSD is only as good as the tools used to measure their parameters. Particular care should be taken in the choice of test and its implementation for individuals for whom sensory impairments, communication issues or other unique contextual issues could bias the data obtained.
- Key decision points in the care of an individual with BPSD are when to test, how to assess, and what follow-up actions are required given the assessment data obtained. An important use of assessment is to determine not only the starting points and nature of interventions, but also when they are no longer required, or when they need to be altered to reflect changing circumstances.

Non-pharmacological interventions

This section of the module supplements Module 5, Non-pharmacological treatments, by providing a brief overview of non-pharmacological treatments for BPSD that are supported by evidence from randomized controlled clinical trials conducted in LTC settings. The categories of non-pharmacological interventions that are included in this overview are: training programs for LTC staff; individualized assessment and care planning; psychosocial activities; exercise; music therapy; and other forms of sensory stimulation.

Training programs for long-term care staff

Several studies have examined the effects of providing training to LTC staff on strategies to decrease BPSD in residents. The strategies that form the content of training vary in their specificity and comprehensiveness, and in some cases represent overarching care approaches. For example, the recent Caring for Aged Dementia Care Resident Study (CADRES) conducted in 15 LTC facilities in Australia evaluated the effects of two care approaches, dementia care mapping and patient-centered care, when compared to usual care for LTC residents with dementia. Eight months following the intervention both dementia care mapping and patient-centered care groups had significantly lower scores on agitation when compared to the usual care group who deteriorated during the study period (Chenoweth et al., 2009). The interventions did not show a significant difference on BPSD symptoms measured on the Neuropsychiatric Inventory (NPI).

Another study examining the effects of nurse training and coaching also demonstrated some benefit in some symptoms of agitation (McCallion et al., 1999).

Individualized assessment and care plans

Comprehensive evaluation of BPSD with individualized treatment planning has been evaluated in LTC residents. There is evidence that agitated behaviors can be reduced when care includes assessment of agitated behaviors and potential causes, followed by implementation of psychosocial activities that address the perceived causes and take into consideration the patient's background and interests (Cohen-Mansfield et al., 2007). Symptom management has also been demonstrated when care includes a review of BPSD symptoms and possible causes, along with adherence to guidelines for medication management and an activity program (Rovner et al., 1996).

Psychosocial activities

Psychosocial activity programming has been evaluated in a number of studies in LTC as a potential intervention for managing BPSD. Psychosocial activity programming includes regular participation in personally meaningful or enjoyable events, either on one's own or as a member of a group. Improvement in symptoms of BPSD was demonstrated in a small study that provided a one-to-one pleasant event activity that had been tailored to an individual's interests for 30 minutes, three times weekly (Lichtenberg et al., 2005). Another study found that participation in group-based validation therapy reduced agitation following three months of treatment when compared to usual care (Toseland et al., 1997).

Exercise programs

There is evidence to support the physical health benefits of exercise programs for older adults with dementia in LTC. In addition, several studies have evaluated the effects of exercise on BPSD symptoms, including agitation, aggression and negative affect. A program involving daytime exercise along with changes to nighttime nursing routines was compared to a nighttime intervention alone. A significant reduction in agitated behavior was observed in the group who received the daytime exercise intervention (Alessi et al., 1999). Physically aggressive behavior was reduced among residents who participated in exercise and physical activity rather than receiving usual care in another small study (Landi et al., 2004). A study that looked at residents' negative affect found that mood was improved by participation in an individualized exercise program, as compared to participation in a walking program or social conversation (Williams et al., 2007).

Music therapy

Two studies have demonstrated a beneficial effect for music on BPSD in LTC residents. Participation in a group music therapy intervention accompanied by movement was beneficial in reducing symptoms of agitation for the participating individuals as compared to those who received usual care (Sung et al., 2006). A second study of music therapy also found significant reductions in BPSD symptoms when music therapy participants were compared to residents whose caregivers received support sessions (Raglio et al., 2008).

Sensory stimulation

Sensory stimulation involving visual, tactile or olfactory senses has also been examined in LTC. Agitation was reduced with the use of aromatherapy using lemon balm when compared to administration of placebo oil (Ballard et al., 2002). Therapeutic touch consisting of gentle massage without aromatherapy has also been found to have some benefit for reducing agitation or aggressive behaviors (Woods et al., 2005; Hawranik et al., 2008).

Conclusions

There is a small body of evidence to support the use of several non-pharmacological interventions for reducing selected BPSD in LTC (notably agitation, aggression and negative affect). These interventions include training LTC staff in BPSD management, individualized assessment and treatment planning, exercise and a variety of pleasant psychosocial activities and sensory stimulation. Some of the more concrete or tangible interventions (exercise, psychosocial interventions and sensory stimulation) have been found to have an effect on BPSD while they are being administered, rather than over a longer term. There is certainly a need for interventions that can be used to reduce agitation and aggression and elevate mood in the moment, both as crisis management interventions and as a means of enhancing quality of life. More programmatic interventions (staff training, individualized assessment and care planning) may be expected to have a more generalized effect, changing the prevalence and intensity of BPSD within the LTC facility as a whole on an ongoing basis. There is need for greater understanding of the potential of approaches such as dementia care mapping and patient-centered care to change the culture of behavioral response in LTC overall. This is particularly critical as a focus for future research, since the availability of resources and staffing to support more piecemeal interventions may be more or less feasible in various LTC settings, and more or less efficacious in the long term.

Pharmacological interventions

This section of the module supplements Module 6, Pharmacological Treatments, by providing a brief overview of pharmacological treatments for BPSD that are supported by evidence from randomized controlled clinical trials conducted in LTC settings. Among all LTC residents, up to 40% of individuals receive antidepressants, 30% receive antipsychotics and 30% receive benzodiazepines (Conn et al., 1999; Pitkala et al., 2004; Seitz et al., 2009). Therefore, an understanding of the efficacy and indications for use of these medications in the LTC setting is of great importance, especially considering the increased risk for adverse events such as stroke, falls and death (Gill et al., 2007; Gill et al., 2005; Herrmann et al., 2004; Rochon et al., 2008; Schneider et al., 2005). The categories of pharmacological interventions that are included in this overview are: atypical antipsychotics, antidepressants, anticonvulsants, cholinesterase inhibitors and other medications. A review of pertinent negative studies in the literature will also be presented.

Atypical antipsychotics

The atypical antipsychotics are the most extensively studied pharmacological intervention for BPSD. There is good evidence from large scale randomized controlled trials conducted in LTC demonstrating efficacy for risperidone (Brodaty et al., 2003; Holmes et al., 2007; Katz et al.,

1999), olanzapine (De Deyn et al., 2004; Street et al., 2000) and aripiprazole (Mintzer et al., 2007) in the reduction of agitation and aggression in patients with AD. Daily doses of risperidone 1–2mg and olanzapine 5–10mg, and aripiprazole 5–10 mg are significantly better than placebo at reducing BPSD (De Deyn et al., 2004; Street et al., 2000; Mintzer et al., 2007). Aripiprazole 10mg daily has been shown to be significantly better than placebo in treating psychosis, though less is known of its effects on agitation and aggression (De Deyn et al., 2005). The antipsychotic quetiapine has been studied in two randomized controlled trials both of which did not demonstrate any significant benefit over placebo (Tariot et al., 2006; Zhong et al., 2007).

Antidepressants

While a number of studies have shown the use of antidepressants to manage depression in AD (Lyketsos et al., 2003; Magai et al., 2000) and some limited evidence for antidepressants in treating BPSD in community-based or hospitalized geriatric psychiatry populations (Seitz et al., 2011), there is limited evidence supporting the use of antidepressants for the management of BPSD in LTC. Currently, only one randomized controlled clinical trial investigating the use of the antidepressant, sertraline, for treatment of aggression and agitation specifically in LTC exists with efficacy similar for sertraline when compared to haloperidol (Gaber et al., 2001). More studies are needed to determine the efficacy of antidepressants for treating agitation and aggression.

Anticonvulsants

The use of anticonvulsants for the treatment of BPSD in LTC has included randomized controlled trials of carbamazepine (Tariot et al., 1998), valproic acid (Porsteinsson et al., 2001; Tariot et al., 2005) and oxcarbazepine (Sommer et al., 2009). Of these, only carbamazepine 300mg daily has been shown to be significantly better than placebo in reducing BPSD in AD (Tariot et al., 1998).

Cognitive enhancers

The cholinesterase inhibitors (ChEIs: donepezil, galantamine, and rivastigmine) and the *N*-methyl-D-aspartate (NMDA) receptor antagonist, memantine, have been examined as potential treatments for BPSD. Results suggest that the ChEIs have a slight effect in decreasing BPSD and caregiver burden in patients with mild to moderate AD living in the community (Cummings et al., 2006; Cummings et al., 2004; Herrmann et al., 2005; Mega et al., 1999; Trinh et al., 2003). However, there is no evidence to support a role for the use of ChEIs to treat BPSD in the LTC setting, perhaps because this is predominantly the moderate to severe spectrum of AD (Tariot et al., 2001). In a 24-week study of moderate to severe AD patients living in LTC, there was no significant change in BPSD in individuals taking donepezil vs. placebo as measured by the Neuropsychiatric Inventory (Tariot et al., 2001).

Other medications

There have been several randomized controlled clinical trials examining the use of non-conventional psychiatric medications for the treatment of BPSD in AD. Sex hormones have been targeted as potential moderators of agitation and aggression. One study has shown 100 mg daily of cyproterone, an antiandrogen, to be significantly more effective than haloperidol

in reducing general aggression in institutionalized AD patients, though the authors note that further studies are required to determine efficacy in patients with more severe BPSD (Huertas et al., 2007). Additionally, estrogen therapy (0.65–2.5mg daily) was shown to be significantly greater than placebo in improving aggressive behavior in a short-term study (Kyomen et al., 1999). This finding was not reproduced in a later study utilizing transdermal estrogen patches (50mcg–100mcg daily) (Hall et al., 2005), suggesting more research is required to determine the effectiveness of estrogen therapy in management of BPSD. Propanolol, a beta-adrenergic antagonist has been found to be significantly greater than placebo in reducing agitation/aggression and anxiety in patients with probable AD in LTC at doses of 30–120mg daily (Peskind et al., 2005). The authors note, however, that initiation of this treatment must be closely monitored for contraindications of beta-adrenergic antagonist therapy in a very frail population (Peskind et al., 2005). The antihypertensive, prazosin, was shown to be significantly greater than placebo in reducing BPSD in the LTC setting at doses of 1–6mg daily (Wang et al., 2009). This finding was based on a relatively small sample size at one facility, prompting further investigation of the positive result. Melatonin, a naturally occurring hormone with a known role in regulating circadian rhythm, has been studied as a possible treatment for BPSD in AD with poor results, showing no significant difference compared to placebo in studies conducted in LTC (Gehrman et al., 2009; Serfaty et al., 2002; Singer et al., 2003).

Conclusions

There are a number of studies of various pharmacological treatments for BPSD in LTC. Medications that have been shown to be significantly more effective than placebo in managing BPSD in the LTC setting are the antipsychotics risperidone, olanzapine, and aripiprazole and the anticonvulsant carbamazepine. Cyproterone, estrogen, prazosin and propranol have also demonstrated promising results in single studies but require further investigation.

It must be noted that use of these pharmacological interventions must be closely monitored in LTC due to the risk of severe adverse events such as increased risk of falls, stroke and death (Gill et al., 2007; Gill et al., 2005; Herrmann et al., 2004; Huybrechts et al., 2011; Rochon et al., 2008; Schneider et al., 2005), particularly with antipsychotics. Non-pharmacological interventions (Module 6) such as staff training, psychosocial therapy, music therapy and exercise should be employed whenever possible given availability of resources and severity of patient symptoms. It may be necessary to implement pharmacological treatments in specific cases, such as physical aggression, as the non-pharmacological interventions may have limited efficacy in this setting and may be difficult to utilize in acute situations where patient safety may be at risk.

Optimizing the use of psychotropic medications

In LTC homes, 65%–78% of the patients with dementia use at least one psychotropic drug (Pitkala et al., 2004; Kim and Whall, 2006; Lovheim et al., 2006; Selbaek et al., 2007; Zuidema et al., 2007). A majority of 83% of psychotropic drug use was chronic (Van Dijk et al., 2000). Recent data confirmed that 85% of antipsychotic drug users continue to use them for a 6-month period, and 12% for a period of two years (Wetzels et al., 2011). Psychotropic drug prescription is correlated with the degree of neuropsychiatric symptoms (Kim et al., 2006; Kamble et al., 2009; Nijk et al., 2009), environmental correlates, such as bed capacity of the

nursing home and physicians' drug prescription policy (Wood-Mitchell et al., 2008). Physicians are more likely to prescribe psychotropic drugs in patients with Neuropsychiatric Symptoms (NPS) in a situation where the staff is additionally distressed, and when staff apply pressure to the physician to prescribe drugs (Cornege-Blokland et al., 2010). Physicians themselves often consider the possible benefits of antipsychotics to outweigh the risk of side effects (Cornege-Blokland et al., 2010).

High rates of sustained psychotropic drug use, especially antipsychotics, suggest non-adherence to international guidelines. In general, antipsychotic drugs and benzodiazepines are prescribed too often and for too long. Although some psychotropic drugs might be overused, there may also be underuse in some cases. Notably antidepressants, that are recommended in cases of depression in dementia, have the risk of being underused, because depression is not always detected (Smalbrugge et al., 2006).

The high rates of psychotropic drug use, in relation to the limited efficacy and considerable side effects, warrant a growing awareness of medical doctors, professionals and bodies representing professionals to be cautious with psychotropic drug prescription (Banerjee, 2009). People with dementia should receive psychotropic medication only when they really need it (Salzman et al., 2008). Optimization of psychotropic drug prescription is vitally important. In cases where drugs are prescribed too often and too long, optimization means reduction of over prescription. In other situations optimization means detailed assessment of indication, dosage, duration and side effects of psychotropic drugs, assisted with techniques like medication review to assess the appropriateness of prescription.

Strategies for optimization/discontinuation

In general, when symptoms have subsided, some psychotropic drugs can be safely discontinued after a while. Supportive evidence exists that discontinuation of psychotropic drugs, i.e., antipsychotics (Ballard et al., 2004; Bridges-Parlet et al., 1997; van Reekum et al., 2002; Ruths et al., 2004; Thapa et al., 1994) and anxiolytics is possible for most individuals without increase of NPS. In a recent randomized controlled withdrawal study (Dart-AD study—Ballard et al., 2009), in 165 long-term care patients, no differences were found between the antipsychotic-continuation group compared to the withdrawal group, but mortality rates were lower in the latter group. In a subgroup of patients with high-level of neuropsychiatric symptoms (NPI score > 14), withdrawal was accompanied by an increase/relapse of neuropsychiatric symptoms, suggesting that antipsychotics should only be prescribed in severe cases.

Three strategies had been found to facilitate discontinuation of psychotropic drugs: education on efficacy and safety, medication review and enhanced psychosocial care (sometimes carried out in combination).

Education

In five out of seven randomized controlled trials, education on effects and adverse events of psychotropic drugs by pharmacists to physicians and nurses is effective in reduction of psychotropics in general (Avorn et al., 1992), antipsychotics (Fossey et al., 2006), hypnotics (Eide et al., 2001) and more, specifically in reduction of the percentage of inappropriate psychotropic drug prescription (Crotty et al., 2004). However, in two other studies education

did not have any effect on psychotropic (Hagen et al., 2005), antipsychotic (Ray et al., 1993; Hagen et al., 2005) or benzodiazepine (Hagen et al., 2005) drug prescription.

Medication review

Medication review can be used to decrease psychotropic drug prescription or to optimize psychotropic drug therapy. Medication review, using the expertise of a pharmacist, has been shown to increase physicians' and nurses' knowledge and awareness of medication (Verrue et al., 2009). In Australia, drug review—multidisciplinary case conferences by pharmacists, geriatrics, general practitioners (GP) and residential care staff on the quality of prescribing—has been shown to optimize drug prescription in patients with dementia or pain related medication problems in long-term care facilities (Westbury et al., 2010). In an Irish randomized controlled clinical trial in 22 nursing homes, particularly aimed at reduction of inappropriate prescription, a pharmacist drug review resulted in a significant, considerable and cost-effective decrease in inappropriate psychotropic drug use (Patterson et al., 2010).

In four out of the five randomized controlled trials aimed at reduction of the volume of psychotropic drug prescription, medication review appeared to be effective in the reduction of the number of antipsychotic drugs (Ray et al., 1993; Westbury et al., 2010; Roberts et al., 2001; Schmidt et al., 1998), hypnotic drugs (Schmidt et al., 1998), benzodiazepines (Westbury et al., 2010; Roberts et al., 2001), and antidepressants (Schmidt et al., 1998). It is interesting to note that in the largest study, of 1,600 nursing home residents with the most detailed interventions (Westbury et al., 2010), the effects are rather small, with only significant reduction of antipsychotics of 5% and no significant effect on benzodiazepine and antidepressant use. In only one large randomized controlled clinical trial in which medication review is carried out solely by the pharmacist (without any interaction with other care workers), did the prescription rates not change (Furniss et al., 2000).

Enhanced psychosocial care

In four out of four randomized controlled trials, enhanced psychosocial care was effective in reduction of psychotropic (Rovner et al., 1996; Kovach et al., 2006) or antipsychotic drugs (Fossey et al., 2006; Bird et al., 2007), with rather large reductions of 14–24%. The enhanced psychosocial care encompassed implementation of a dementia care program (Rovner et al., 1996), stepwise treatment of unmet needs (Kovach et al., 2006), a variety of patient-centered individualized psychosocial interventions, such as behavioral management techniques, person-centered care, reminiscence, involvement of family carers (Fossey et al., 2006). Studies in which these three strategies were combined (Fossey et al., 2006; Ray et al., 1993; Westbury et al., 2010; Roberts et al., 2001) seemed to do just as well in terms of a reduction of psychotropic drugs, but the number of studies is too small for comparison of effect sizes.

Recommendations

General considerations of psychotropic drug prescription and discontinuation:

- As proposed by several international guidelines, psychosocial interventions should be the first-line treatment, and psychotropic drugs should only be prescribed in very severe cases of aggression/psychosis in dementia or in delirium, and/or when an acute intervention (with behavior that causes immediate risk to patients or staff) is needed.

- Optimization of psychotropic drugs includes limited use, i.e. only in neuropsychiatric symptoms in which prescription is necessary, such as with severe symptoms where other non-pharmacological interventions has been tried and turned out to be unsuccessful.
- It is essential to obtain informed consent. In most cases this involves a substitute decision-maker. Requirements vary in different jurisdictions with written consent becoming a more frequent requirement or recommendation for some psychotropic medications.
- Choose the type of psychotropic drug with a valid indication and dosage.
- Monitor symptoms ideally utilizing assessment instruments and be vigilant for adverse events.
- Prescribe psychotropic drugs for a limited amount of time, in accordance with guidelines.

Drug review:

- Psychotropic drugs should be reviewed regularly. Ideally medication review should be carried out by a physician, pharmacist and nurse although this will depend on staff availability.
- Medication review should preferably include the full evaluation of medication appropriateness of each psychotropic drug, i.e., indication, effectiveness, dosage, directions, drug-drug interactions, drug-disease interactions, duplication, duration and expense.

Education regarding efficacy and safety:

- Education should be provided to staff by pharmacists, and other psychogeriatric experts such as old-age psychiatrists, elderly care physicians, and experienced general practitioners.
- Education should include knowledge transfer on the modest efficacy and considerable side effects of psychotropic drugs, and ways to assess efficacy and adverse events/side effects in an individual patient.
- In the broader context, professionals (general practitioners and other physicians working in long-term care facilities) should receive education to equip them for their role in the management of the complexity, co-morbidity and severity of mental and physical disorders in those residing in care homes. This should be available as part of continuing professional development (Banerjee et al., 2009).

Organization of long-term care (Banerjee et al., 2009):

- Local specialists (elderly care physicians, old age psychiatrists, geriatricians) should be available for outreach services that support primary care staff. This extension of service needs the capacity to work routinely in all facilities where there may be people with dementia. They may be aided by pharmacist input into homes to support or carry out regular drug reviews, including psychotropic drugs.
- Work to overcome financial and organizational barriers to implement non-pharmacological interventions in long-term care.
- Maximize use of qualified staff in long-term care facilities.

Role of the interdisciplinary team

A wide variety of health professionals have roles to play in providing optimum care to address BPSD within LTC settings. Ideally, these individuals function within a cohesive team to assess potential causes of behaviors and symptoms of concern and to provide continuously updated care plans, including potential interventions to lessen such behaviors and symptoms. No single individual or profession can bring the necessary wide diversity of knowledge and strategies to the unique issues raised particularly by BPSD. The needs of persons with dementia can be complex, evolve over time, and require novel approaches to care. Interdisciplinary teams are a key component in such care. LTC settings may be staffed by a wide range of health care professionals, often augmented by consulting health care professionals as well as community and volunteer workers. There is strong evidence from the broader field of geriatric medicine that there are unique advantages to care provided to older adults by cohesively functioning multidisciplinary or interdisciplinary teams. Such multidisciplinary models are particularly efficacious in treating older individuals with complex medical and/or psychiatric co-morbidities (e.g., Draper and Low, 2005; Grahn, Ekdahl and Borquist, 2000; Lidell and Fridlund, 1996; Rubenstein, Stuck, Sui and Weiland, 1991).

While most literature on multidisciplinary or interdisciplinary team functioning and efficacy is within the broader realm of geriatric medicine, a few studies highlight their benefits within LTC (e.g. Schmidt et al, 1998, 2002). Benefits include reduced use of antipsychotics and benzodiazepine hypnotics, more appropriate antidepressant medications and lower prevalence of BPSD. Effective interdisciplinary collaboration in a multidisciplinary team can be undermined by a variety of influences. These may include a lack of understanding of one another's roles, infringement at professional boundaries, limited communication and poorly coordinated work within the team (Zwarenstein, Goldman and Reeves, 2009). All members of the team need to be informed about the medical, emotional and social needs of the patients within the contexts of their families, communities and cultures. In turn the members of the team need to have knowledge of and respect for various discipline-based approaches, so as to maximize benefits to patients in their care.

It is also important to emphasize that strong and clear leadership is essential for effective interdisciplinary collaboration and teamwork (Reeves et al., 2010). The leadership role can be challenging including the need to deal with conflict at multiple levels. Reeves et al., (2010) outline the historical development of the professions, noting that each has separate professional responsibilities and different lines of management reporting. They describe the need for changing leadership within teams depending on the patient's needs. For example, medical leadership is appropriate when medical needs are paramount, but when the focus is on social care other team members may need to take the lead. Many qualities are necessary for successful leadership including the capacity to utilize a variety of leadership styles. One important characteristic is the capacity to explore team motives and beliefs in accomplishing a change or perceived vision of success (Oliver, 2006). Leaders must be able to critically appraise team processes and outcomes on the path to achieving shared goals. In the increasingly complex world of healthcare adequate training in leadership skills for senior staff is essential.

Differences between multidisciplinary and interdisciplinary teams

The terms *multidisciplinary* and *interdisciplinary* are often used interchangeably, but this is not the case as each type of team is distinct. Furthermore, research has shown each type of team to have differential impacts on patient care and outcomes. It is important to note that some teams utilize a mixed model which incorporates elements of both of these approaches.

In a *multidisciplinary* team, varieties of disciplines work in the same setting and provide care to the same patients, but each discipline operates with considerable independence. For example, each discipline may pursue their own assessment of the patient and generate a discipline-specific treatment plan, implemented and reviewed with little input from other team members. Team members may share information with each other, but there is no attempt to generate a common treatment plan or coordinate implementation of the plan more systematically. Multidisciplinary teams are hierarchically organized, with a designated team leader (commonly a physician). This individual is responsible for overseeing the team and its functioning. According to Zeiss (2003), in such multidisciplinary team settings, team members feel responsible only for the clinical work of their own discipline, while not sharing a more cohesive sense of shared responsibility both for patient care as well as the functioning and effectiveness of the team itself.

An *interdisciplinary* team is characterized by a much higher degree of collaboration in the care of patients. Team members work together across their various disciplines to devise, implement and evaluate a care plan for their patients. Knowledge of each discipline's unique skill sets and strengths as well as areas of overlapping competence are more fully realized on an interdisciplinary team. This in turn leads to improved understanding of the possible ways each member might contribute to individual aspects of patient care. Within interdisciplinary teams, leadership functions are shared among members and Zeiss (2003) stresses that there is an expectation that everyone will be committed to both the clinical content of the program as well as the team's method of working together. Such teams routinely will set aside time to review the process of team functioning, with a view to resolving issues between team members or with respect to conflicts in philosophy of care, before these erode the efficacy of the team and negatively impact care. Within such an interdisciplinary structure, all team members are assumed to be colleagues, and there is no hierarchical team organization. For a detailed review of interdisciplinary teams see Zeiss and Steffen (1998).

Disciplines and how they contribute to interdisciplinary treatment of BPSD

General Practitioners/Primary Care Physicians

General practice physicians provide primary care for acute and chronic illness across ages and genders, and although individual terms may vary, "general practitioner" and "primary care physician" are among the more common terms for such individuals. Within LTC settings such physicians are often the primary source of medical care. Within the Netherlands, medical care in nursing homes is provided by specially trained elderly care physicians, with specific competencies in psychogeriatrics, geriatric rehabilitation and palliative care (SOON 2010).

Geriatricians

Geriatricians specialize in treating individuals over age 65 and often act in a consulting role within LTC settings, although in some countries and contexts their role may be greater. In

the United States a set of Minimum Geriatric Competencies in eight content domains (which include cognitive and behavioral disorders, medication management, hospital care for older adults and palliative care) have been endorsed by such bodies as the American Geriatrics Society, and the American Medical Association (Leipzig et al., 2009).

Old Age Psychiatrists (Geriatric psychiatrists, psychogeriatricians)

Geriatric psychiatry involves treatment of disorders of affect, behavior, cognition and perception in older adults. The psychiatrist's medical training affords an appreciation of the mental health issues that may be associated with physical disorders as well as complications from surgical procedures, including delirium. Psychiatrists are also likely to look for drug interactions before suspecting a psychiatric etiology, and like geriatricians may be able to spot ways in which medication use can be more judicious (Jeste et al., 1999).

Nurses

Nursing practice incorporates the application of knowledge, skills and attitudes towards effecting improved care of persons with a wide range of illnesses within a broad range of settings, including LTC. Nurses often take responsibility for care management and on-going assessment, monitoring symptom presentation, responding to functional or medication issues, liaising with families and other professionals. There are a number of levels of recognized nursing practice spanning generalist and advanced as well as specialist areas of practice such as geriatric and mental health nursing.

Nursing assistants/Care workers

Nursing assistants/care workers generally work under the direction of a registered nurse and assist with patient care and activities of daily living. Historically they have had minimal training in aspects of both mental health and dementia, including BPSD.

Psychologists and Neuropsychologists

Clinical psychology is concerned with the assessment and treatment of mental illnesses, whereas neuropsychologists are particularly focused on cognitive and behavioral disturbance. Geropsychologists are specialists in aging mental health issues; in the United States, there is a specialist group of psychologists in long-term care (see links at the end of this module) and guidelines for psychological care are developing in many countries (e.g. Lichtenberg et al., 1998). With respect to BPSD, psychologists offer particular skills in conceptualizing prompts for such symptoms as well as devising care plans that include behavior management, communication, and environmental management as key strategies.

Social Workers/Welfare Officers

Social work competencies with older adults include case management (involving linking patients with services to meet their psychosocial needs), counseling and therapy, addressing family and social support concerns and advocacy. Issues such as financial abuse and working through of advanced care directives may be facilitated by social workers. Geriatric social workers are increasingly involved in program development within LTC settings (Leipzig, 2009).

Occupational Therapists

As a discipline, occupational therapy promotes health and addresses disability and illness through enabling people to perform meaningful activities or to work to resume former roles

and occupations. Within LTC settings, occupational therapists may focus on activities of daily living or self-care tasks such as feeding or dressing. Occupational therapists work with assistive devices to assist with such activities and can often offer expertise in modifying the LTC environment to facilitate independence.

Physical Therapists/Physiotherapists

Physical therapists or physiotherapists are concerned with physical illness or other conditions impairing movement and limiting the ability to perform activities of daily living. Optimizing physical functioning and maintaining safe mobility are key goals for physical therapists within LTC settings. Physical activity in LTC residents has the potential to impact positively on such concerns as falls risk (Nowalk et al., 2001) and pain management (Ferrell, 2004).

Music Therapists and Diversional Therapists

Music therapists are trained professionals who use all aspects of music, including its physical production, emotional sequelae and potential for social bonding, to help effect positive changes in mood and well-being.

Models of mental health care

Effective models of mental health service delivery to residents of long-term care facilities are needed to meet the growing number of individuals who will be cared for in such facilities in the coming decades. Bartels et al., (2002) report that multidisciplinary team models that emphasize the complementary contributions of different disciplines can greatly increase the efficacy of direct clinical consultation services to individual nursing home residents. The extant literature in general supports providing for the routine presence of qualified mental health clinicians in the nursing home. In addition, within such a multidisciplinary team context, the most effective mental health interventions are those that blend consultation with training and educational interventions for staff. Snowdon (2010) outlined six different models of mental health care provision:

- Consultative
- Consultation-liaison
- Nurse-centered
- Facility-based staffing
- Externally based multidisciplinary team
- Telepsychiatry services

Interprofessional collaboration approaches have been increasingly studied and have been the subject of several Cochrane reviews. Interprofessional collaboration approaches are characterized by interprofessional rounds, interprofessional meetings and externally facilitated audits of team functioning. Some method of reviewing functioning of the team itself, in addition to following clinical outcomes of the patient population served, is vital to effective team performance. IPC interventions can improve healthcare processes and outcomes, but further studies are needed to have a better understanding of the range of possible interventions afforded by such teams as well as their effectiveness, and in what circumstances these interventions may be most useful (Zwarenstein, Goldman and Reeves, 2009).

In the Netherlands, a well-structured and integrated model of an interdisciplinary treatment team operating within nursing homes has existed for some time. Comprised of specially trained elderly care physicians, nurses and psychologists, and with input from other disciplines, such teams have spearheaded both innovative care and empirical research on best practice models of care within nursing home settings, with BPSD as a strong focus (Hertogh, Deerenberg-Kessler and Ribbe, 1996).

Conclusions:

- An interdisciplinary team approach may improve treatment outcomes for a wide variety of presenting problems within LTC. Structured, empirically-based interventions for BPSD require interdisciplinary teams with particular interest and commitment to this type of care (Lawlor, 2002).
- Ultimately, the quality of such interventions is dependent on teams which have been able to work out a common set of objectives and approach to practice. Successful treatment relies on open communication and interplay between team process and competence in care provision.
- There is good evidence that interventions work best when tailored to people's interests and skills. For those with advanced dementia, this information must be sought from a family member.

Education and training

The recognition and treatment of mental illness in older people living in long-term care is challenged by the scarcity of trained staff working in this environment and the limited access to specialist health professionals such as old age psychiatrists, geropsychiatric nurse practitioners and neuropsychologists. Staff working in LTC are regularly challenged by residents who have BPSD. Staff education and training offers the opportunity to equip staff to appropriately manage treatment and care of older people living with mental illness in long-term care.

There is strong evidence that LTC settings are predominately staffed by relatively unskilled workers supervised by registered nurses. These registered nurses may or may not have professional qualifications in geriatric mental health. The LTC workforce often has limited training and therefore poor understanding of disease, assessment and treatment of older people with mental illness (Hsu et al., 2005). Therefore there is a reliance on specialist services such as old age psychiatrists, neuropsychologists, behavioral management services and geropsychiatric nurse practitioners coming into the LTC setting to provide mental health services.

Several countries have tried to promote geriatric mental health education and training through the production of freely available education and training materials (see *Canadian Coalition for Seniors' Mental Health,* 2006, and *Australian Government Dementia Training and Study Centers,* 2009). An important component of education and training programs is legislation that dictates curricula content and more importantly a legislative body that will approve the curricula (Hyer et al., 2010). An example of this is the National Council of Certified Dementia Practitioners that aims to promote national standards for comprehensive Alzheimer's and dementia education (http://www.nccdp.org).

Evidence for best practice

Many of the successful training programs focus on dementia education. There are limited examples of successful programs focusing on broader geriatric mental illness. A number of key features of effective geriatric mental health education and training in LTC include:

- To be meaningful curriculum content must be directly planned with the audience for which it is intended.
- Education and training should be directed towards the assessed learning needs of the audience.
- Education and training is directed towards the needs of the residents living in LTC.
- The education and training materials should be related and incorporate the philosophy of care being promoted within the LTC setting.
- Organizational leadership and support is essential for maintaining learning and transfer of knowledge into practice.
- Training should be conducted as a whole of facility approach.
- Qualified people who have expertise in working with older people with mental illness, including dementia, should conduct training.
- Training sessions should be held at times that suit the intended audience.
- Content should be packaged to facilitate interactive classes with short and regular sessions that can be readily repeated.
- Positive staff behavior change can be encouraged through activities such as online learning and tip sheets indicating essential features.
- A dedicated education and training resource person may increase sustainability of programs (Beeber et al., 2010; Kuske et al., 2007; McAiney et al., 2007; Rampatige et al., 2009; Visser et al., 2008).

For more extensive reading refer to Moyle et al. (2010). In conclusion, staff working in LTC may benefit from an education and training program on geriatric mental illness. There is good evidence that education and training programs that utilize key success features help to encourage change in practice. Effective education and training relies on the commitment of LTC administration to such programs, offering opportunities for staff to attend and to integrate new knowledge into practice.

Guidelines

Overarching principles that promote and support the mental health of all LTC residents include facility-wide commitment to:

- Individualized, person-centered care
- Respect for family ties
- A biopsychosocial care planning framework
- A culture of caring that prioritizes quality of life
- A social and physical environment that is responsive to changing needs
- A focus on early intervention and prevention as well as treatment

- Staff training and development as necessary to enable the provision of informed and competent care

(Canadian Coalition for Seniors' Mental Health, 2006).

Guidelines focused on the care of individuals with mental disorders in LTC have been developed in a number of countries (e.g. Canadian Coalition for Seniors' Mental Health, 2006; American Geriatrics Society/American Association for Geriatric Psychiatry, 2003; American Medical Directors Association, 2003). A series of useful evidence-based protocols have also been developed by the University of Iowa Gerontological Nursing Interventions Research Center (can be purchased via www.nursing.uiowa.edu/excellence/evidence-based-practice-guidelines). General guidelines for the care of individuals with dementia have also been developed in a number of countries including Australia, Canada and the United Kingdom.

Great efforts are made to produce these documents but ultimately the question is *are they being implemented?* National guidelines can be helpful but all implementation is really local in nature. The process of implementing best practices to improve quality of care is fraught with difficulty. Experts in knowledge translation are examining the processes required. Recently a Canadian group studied implementation in a LTC Home using a participatory action approach. Many of the outcomes were positive but some were unexpected, involving a change of culture on the units. These included the development of team huddles and the inclusion of personal support workers in team rounds (Sokoloff et al., 2012).

Caring for residents in LTC with BPSD and other mental disorders is often challenging. Concern about the quality of care around the globe led to the formation of an International Psychogeriatric Association (IPA) Task Force on Mental Health Services in Residential Care Homes (www.ipa-online.org). Discussions suggest that similar issues are relevant in almost all countries. These issues include inadequate staffing levels, lack of staff training regarding mental health issues, aging and poorly designed LTC homes, failure to identify and assess residents in a timely fashion, inappropriate use of psychotropic medications, and limited availability of mental health consultants. Although it may be difficult to implement all of the recommendations in this module or in guideline documents, given the challenges outlined above, each facility should strive to adopt as many as possible.

References and recommended reading

Introduction

Ballard, C., O'Brien, J., James, I., et al. Quality of life for people with dementia living in residential and nursing home care: the impact of performance on activities of daily living, behavioral and psychological symptoms, language skills, and psychotropic drugs. *International Psychogeriatrics*. 2001; **13**: 93–106.

Brodaty, H., Draper, B.M., Low, L.F. Behavioural and psychological symptoms of dementia: a seven-tiered model of service delivery. *Medical Journal of Australia*. 2003; **178**: 231–234.

Seitz, D., Purandare, N., Conn, D. Prevalence of psychiatric disorders among older adults in long-term care homes: a systematic review. *International Psychogeriatrics*. 2010; **22**: 1025–1039.

Principles of good care

American Geriatrics Society and American Association for Geriatric Psychiatry. Consensus statement on improving the quality of mental health care in U.S. nursing homes: management of depression and behavioral symptoms associated with dementia. *Journal of the American Geriatrics Society*. 2003; **51**: 1287–1298.

Brodsky, J., Habib, J., Hirschfeld, M. Long-Term Care in Developing Countries: Ten Case-Studies. World Health Organization. 2003; http://whqlibdoc.who.int/publications/2003/9241562498.pdf.

Brodsky, J., Habib, J., Siegel, B. Lessons for Long-Term Care Policy: The Cross-Cluster Initiative on Long-Term Care. World Health Organization. 2002; http://whqlibdoc.who.int/hq/2002/WHO_NMH7CCL_02.1.pdf.

Dewing, J. Concerns relating to the application of frameworks to promote person-centeredness in nursing with older people. *Journal of Clinical Nursing*. 2004; **13**: 39–44.

Gibson, M.C., Carter, M.W., Helmes, E., Edberg, A-K. Principles of good care for long term care facilities. *International Psychogeriatrics*. 2010; **22(7)**: 1072–1083.

Graham, N., et al. Reducing the stigma and discrimination against older people with mental disorders: a technical consensus statement. *International Journal of Geriatric Psychiatry*. 2003; **18**: 670–678.

Sandberg, J., Nolan, M.R., Lundh, U. "Entering a New World": empathic awareness as the key to positive family/staff relationships in care homes. *International Journal of Nursing Studies*. 2002; **39**: 507–515.

Wikler, D., Hirschfeld, M. Ethical Choices in Long-Term Care: What Does Justice Require? World Health Organization. 2002; www.who.int/mediacentre/news/notes/ethical_choices.pdf.

Environmental design

Fleming, R., Purandare, N. Long-term care for people with dementia: Environmental design guidelines. *International Psychogeriatrics*. 2010; **22**: 1084–1096.

Marshall, M. Environment: How it helps to see dementia as a disability. Care Homes and Dementia. *Journal of Dementia Care*. 2001; **6**: 15–17.

Screening and assessment

Aalten, P., de Vugt, M.E., Jaspers, N., Jolles, J., Verhey, F.R. The course of neuropsychiatric symptoms in dementia. Part I: findings from the two-year longitudinal Maasbed study. *International Journal of Geriatric Psychiatry*. 2005; **20**: 523–530.

Ballard, C., O'Brien, J., James, I., Mynt, P., Lana, M., Potkins, D., Reichelt, K., Lee, L., Swann, A., Fossey, J. Quality of life for people with dementia living in residential and nursing home care: The impact of performance on activities of daily living, behavioral and psychological symptoms, language skills, and psychotropic drugs. *International Psychogeriatrics*. 2001; **13**: 93–106.

Burns, A., Lawlor, B., Craig, S. *Assessment Scales in Old Age Psychiatry (2nd Edition)*. 2004; London, United Kingdom: Artin Dunitz.

Neville, C.C., Byrne, G.J.A. Behaviour rating scales for older people with dementia: Which is best for use by nurses? *Australasian Journal on Ageing*. 2001; **20**: 166–172.

Pachana, N.A., Helmes, E., Byrne, G.J.A., Edelstein, B.A., Konnert, C.A., Pot, A.M. Screening for mental disorders in residential aged care facilities. *International Psychogeriatrics*. 2010; **22(7)**: 1107–1120.

Porsteinsson, A.P., Ryan, J.M., Ismail, S., Tariot, P.N. Psychiatric assessment and treatment of nonpsychotic behavioral disturbance in dementia. *Handbook of Dementia: Psychological, Neurological and Psychiatric Perspectives*. 2003; Hoboken, New Jersey, United States: Wiley.

Robins Wahlin, T-B., Byrne, G.J. Personality changes in Alzheimer's disease: a systematic review. *International Journal of Geriatric Psychiatry*. 2011; **26**: 1019–1029.

Snowden, M., Sato, K., Roy-Byrne, P. Assessment and treatment of nursing home residents with depression or behavioural symptoms associated with dementia: A review of the literature. *Journal of the American Geriatrics Society*. 2003; **51(9)**: 1305–1317.

Stewart, S.M. Methods in cross-cultural psychopathology. *Handbook of Research Methods in Abnormal and Clinical Psychology*. 2008; Los Angeles, California, United States: Sage Publishing.

Process of translation and adaptation of instruments. World Health Organization. 2007; www. who.int/substance_abuse/research_tools/translation/en.

Zwakhalen, S.M.G., Hamers, J.P.H., Abu-Saad, H.H., Berger, M.P.F. Pain in elderly people with severe dementia: A systematic review of behavioural pain assessment tools. *BMC Geriatrics*. 2006; **6(3)**: 1471–2318.

Non-pharmacological interventions

Alessi, C.A., Yoon, E.J., Schnelle, J.F., Al-Samarrai, N.R., Cruise, P.A. A randomized trial of a combined physical activity and environmental intervention in nursing home residents: do sleep and agitation improve? *Journal of the American Geriatrics Society*. 1999; **47**: 784–791.

Ballard, C.G., O'Brien, J.T., Reichelt, K., Perry, E.K. Aromatherapy as a safe and effective treatment for the management of agitation in severe dementia: the results of a double-blind, placebo-controlled trial with Melissa. *Journal of Clinical Psychiatry*. 2002; **63**: 553–558.

Chenoweth, L., King, M.T., Jeon, Y.H., et al. Caring for Aged Dementia Care Resident Study (CADRES) of person-centered care, dementia-care mapping, and usual care in dementia: a cluster-randomised trial. *Lancet Neurology*. 2009; **8**: 317–325.

Cohen-Mansfield, J., Libin, A., Marx, M.S. Nonpharmacological treatment of agitation: a controlled trial of systematic individualized intervention. *The Journals of Gerontology: Series A*. 2007; **62**: 908–916.

Hawranik, P., Johnston, P., Deatrich, J. Therapeutic touch and agitation in individuals with Alzheimer's disease. *Western Journal of Nursing Research*. 2008; **30**: 417–434.

Landi, F., Russo, A., Bernabei, R. Physical activity and behavior in the elderly: a pilot study. *Archives of Gerontology and Geriatrics*. 2004; **Supplement (9)**: 235–241.

Lichtenberg, P.A., Kemp-Havican, J., MacNeill, S.E., Johnson, A.S. Pilot Study of Behavioral Treatment in Dementia Care Units. *The Gerontologist*. 2005; **45**: 406–410.

McCallion, P., Toseland, R.W., Lacey, D., Banks, S. Educating nursing assistants to communicate more effectively with nursing home residents with dementia. *Gerontologist*. 1999; **39**: 546–558.

Raglio, A., Bellelli, G., Traficante, D., et al. Efficacy of music therapy in the treatment of behavioral and psychiatric symptoms of dementia. *Alzheimer Disease and Associated Disorders*. 2008; **22(2)**: 158–162.

Rovner, B.W., Steele, C.D., Shmuely, Y., Folstein, M.F. A randomized trial of dementia care in nursing homes. *Journal of the American Geriatrics Society*. 1996; **44**: 7–13.

Sung, H-C., Chang, A.M., Abbey, J. The effects of preferred music on agitation of older people with dementia in Taiwan. *International Journal of Geriatric Psychiatry*. 2006; **21**: 999–1000.

Toseland, R.W., Diehl, M., Freeman, K., Manzanares, T., Naleppa, M., McCallion, P. The impact of validation group therapy on nursing home residents with dementia. *Journal of Applied Gerontology*. 1997; **16**: 31–50.

Williams, C.L., Tappen, R.M. Effect of exercise on mood in nursing home residents with Alzheimer's disease. *American Journal of Alzheimer's Disease and Other Dementias*. 2007; **22**: 389–397.

Woods, D.L., Craven, R.F., Whitney, J. The effect of therapeutic touch on behavioral symptoms of persons with dementia. *Alternative Therapies in Health and Medicine*. 2005; **11(1)**: 66–74.

Pharmacological interventions

Brodaty, H., Ames, D., Snowdon, J., Woodward, M., Kirwan, J., Clarnette, R., Lee, E., Lyons, B., Grossman, F. A randomized placebo-controlled trial of risperidone for the treatment of aggression, agitation, and psychosis of dementia. *Journal of Clinical Psychiatry*. 2003; **64**: 134–143.

Conn, D.K., Ferguson, I., Mandelman, K., Ward, C. Psychotropic drug utilization in long-term care facilities for the elderly in Ontario, Canada. *International Psychogeriatrics*. 1999; **11**: 223–233.

Cummings, J.L., McRae, T., Zhang, R. Effects of donepezil on neuropsychiatric symptoms in patients with dementia and severe behavioral disorders. *American Journal of Geriatric Psychiatry*. 2006; **14(7)**: 605–612.

Cummings, J.L., Schneider, L., Tariot, P.N., Kershaw, P.R., Yuan, W. Reduction of behavioral disturbances and caregiver distress by galantamine in patients with Alzheimer's disease. *American Journal of Psychiatry*. 2004; **161**: 532–538.

De Deyn, P., Jeste, D.V., Swanink, R., Kostic, D., Breder, C. Aripiprazole for the treatment of psychosis in patients with Alzheimer's disease: A randomized, placebo-controlled study. *Journal of Clinical Psychopharmacology*. 2005; **25(5)**: 463–467.

De Deyn, P., Carrasco, M.M., Deberdt, W., Jeandel, C., Hay, D.P., Feldman, P.D., Young, C.A., Lehman, D.L., Breier, A. Olanzapine versus placebo in the treatment of psychosis with or without associated behavioral disturbances in patients with Alzheimer's disease. *International Journal of Geriatric Psychiatry*. 2004; **19**: 115–126.

Gaber, S., Ronzoli, S., Bruno, A., Biagi, A. Sertraline versus small doses of haloperidol in the treatment of agitated behavior in patients with dementia. *Archives of Gerontology and Geriatrics*. 2001; **Supplement 33**: 159–162.

Gehrman, P.R., Connor, D.J., Martin, J.L., Shochat, T., Corey-Bloom, J., Ancoli-Israel, S. Melatonin fails to improve sleep or agitation in double-blind randomized placebo-controlled trial of institutionalized patients with Alzheimer disease. *American Journal of Geriatric Psychiatry*. 2009; **17**: 166–169.

Gill, S.S., Bronskill, S.E., Normand, S.L.T., Anderson, G.M., Sykora, K., Lam, K., Bell, C.M., Lee, P.E., Fischer, H.D., Herrmann, N., et al. Antipsychotic drug use and mortality in older adults with dementia. *Annals of Internal Medicine*. 2007; **146(11)**: 775–786.

Gill, S.S., Rochon, P.A., Herrmann, N., Lee, P.E., Sykora, K., Gunraj, N., Normand, S.L.T., Gurwitz, J.H., Marras, C., Wodchis, W.P., et al. Atypical antipsychotic drugs and risk of ischaemic stroke: Population based retrospective cohort study. *British Medical Journal*. 2005; **330(7489)**: 445–448.

Hall, K.A., Keks, N.A., O'Connor, D.W. Transdermal estrogen patches for aggressive behavior in male patients with dementia: a randomized, controlled trial. *International Psychogeriatrics*. 2005; **17**: 165–178.

Herrmann, N., Mamdani, M., Lanctot, K.L. Atypical antipsychotics and risk of cerebrovascular accidents. *American Journal of Psychiatry*. 2004; **161(6)**: 1113–1115.

Herrmann, N., Rabheru, K., Wang, J., Binder, C. Galantamine treatment of problematic behavior in Alzheimer disease: post-hoc analysis of pooled data from three large trials. *American Journal of Geriatric Psychiatry*. 2005; **13**: 527–534.

Holmes, C., Wilkinson, D., Dean, C., Clare, C., El-Okl, M., Hensford, C., Moghul, S. Risperidone and rivastigmine and agitated behaviour in severe Alzheimer's disease: a randomised double-blind placebo controlled study. *International Journal of Geriatric Psychiatry*. 2007; **22**: 380–381.

Huertas, D., Lopez-Ibor Alino, J.J., Molina, J.D., Chamorro, L., Balanza, J., Jimenez, M.P., Hornillos, M. Antiaggressive effect of cyproterone versus haloperidol in Alzheimer's disease: A randomized double-blind pilot study. *Journal of Clinical Psychiatry*. 2007; **68(3)**: 439–444.

Huybrechts, K.F., Rothman, K.J., Silliman, R.A., Brookhart, M.A., Schneeweiss, S. Risk of death and hospital admission for major medical events after initiation of psychotropic medications in older adults admitted to nursing homes. *Canadian Medical Association Journal*. 2011; **183**: E411–E419.

Katz, I.R., Jeste, D.V., Mintzer, J.E., Clyde, C., Napolitano, J., Brecher, M. Comparison of risperidone and placebo for psychosis and behavioral disturbances associated with dementia: A randomized, double-blind trial. *Journal of Clinical Psychiatry*. 1999; **60(2)**: 107–115.

Kyomen, H.H., Satlin, A., Hennen, J., Wei, J.Y. Estrogen therapy and aggressive behavior in elderly patients with moderate-to-severe dementia: results from a short-term, randomized, double-blind trial. *American Journal of Geriatric Psychiatry*. 1999; **7**: 339–348.

Lyketsos, C.G., DelCampo, L., Steinberg, M., Miles, Q., Steele, C.D., Munro, C., Baker, A.S., Sheppard, J-M.E., Frangakis, C., Brandt, J., et al. Treating depression in Alzheimer disease: efficacy and safety of sertraline therapy, and the benefits of depression reduction: the DIADS. *Archives of General Psychiatry*. 2003; **60**: 737–746.

Magai, C., Kennedy, G., Cohen, C.I., Gomberg, D. A controlled clinical trial of sertraline in the treatment of depression in nursing home patients with late-stage Alzheimer's disease. *American Journal of Geriatric Psychiatry*. 2000; **8**: 66–74.

Mega, M.S., Mastennan, D.M., O'Connor, S.M., Barclay, T.R., Cummings, J.L. The spectrum of behavioral responses to cholinesterase inhibitor therapy in Alzheimer disease. *Archives of Neurology*. 1999; **56(11)**: 1388–1393.

Mintzer, J.E., Tune, L.E., Breder, C.D., Swanink, R., Marcus, R.N., McQuade, R.D., Forbes, A. Aripiprazole for the treatment of psychoses in institutionalized patients with Alzheimer dementia: a multicenter, randomized, double-blind, placebo-controlled assessment of three fixed doses. *American Journal of Geriatric Psychiatry*. 2007; **15**: 918–931.

Peskind, E.R., Tsuang, D.W., Bonner, L.T., Pascualy, M., Riekse, R.G., Snowden, M.B., Thomas, R., Raskind, M.A. Propranolol for Disruptive Behaviors in Nursing Home Residents With Probable or Possible Alzheimer Disease: A Placebo-Controlled Study. *Alzheimer Disease and Associated Disorders*. 2005; **19**: 23–28.

Pitkala, K.H., Laurila, J., Strandberg, T., Tilvis, R. Behavioral symptoms and the administration of psychotropic drugs to aged patients with dementia in nursing homes and in acute geriatric wards. *International Psychogeriatrics*. 2004; **16**: 61–74.

Porsteinsson, A.P., Tariot, P.N., Erb, R., Cox, C., Smith, E., Jakimovich, L., Noviasky, J., Kowalski, N., Holt, C.J., Irvine, C. Placebo-controlled study of divalproex sodium for agitation in dementia. *American Journal of Geriatric Psychiatry*. 2001; **9**: 58–66.

Rochon, P.A., Normand, S.L., Gomes, T., Gill, S.S., Anderson, G.M., Melo, M., Sykora, K., Lipscombe, L., Bell, C.M., Gurwitz, J.H. Antipsychotic therapy and short-term serious events in older adults with dementia. *Archives of Internal Medicine*. 2008; **168(10)**: 1090–1096.

Schneider, L.S., Dagerman, K.S., Insel, P. Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. *Journal of the American Medical Association*. 2005; **294**: 1934–1943.

Seitz, D., Purandare, N., Conn, D. Prevalence of psychiatric disorders among older adults in long-term care homes: a systematic review. *International Psychogeriatrics*. 2010; **22**: 1025–1039.

Seitz, D.P., Adunuri, N., Gill, S.S., Gruneir, A., Herrmann, N., Rochon, P. Antidepressants for agitation and psychosis in dementia. *Cochrane Database of Systematic Review*. 2011; **2**: CD008191.

Seitz, D.P., Gruneir, A., Conn, D.K., Rochon, P.A. Cholinesterase inhibitor use in U.S. nursing homes: Results from the national nursing home survey. *Journal of the American Geriatric Society*. 2009; **57(12)**: 2269–2274.

Serfaty, M., Kennell-Webb, S., Warner, J., Blizard, R., Raven, P. Double-blind randomised placebo-controlled trial of low dose melatonin for sleep disorders in dementia. *International Journal of Geriatric Psychiatry*. 2002; **17(12)**: 1120–1127.

Singer, C., Tractenberg, R.E., Kaye, J., Schafer, K., Gamst, A., Grundman, M., Thomas, R., Thal, L.J. A multicenter, placebo-controlled trial of melatonin for sleep disturbance in Alzheimer's disease. *Sleep*. 2003; **26**: 893–901.

Sommer, O.H., Aga, O., Cvancarova, M., Olsen, I.C., Selbaek, G., Engedal, K. Effect of oxcarbazepine in the treatment of agitation and aggression in severe dementia. *Dementia and Geriatric Cognitive Disorders*. 2009; **27**: 155–163.

Street, J.S., Clark, W.S., Gannon, K.S., Cummings, J.L., Bymaster, F.P., Tamura, R.N., Mitan, S.J., Kadam, D.L., Sanger, T.M., Feldman, P.D., et al. Olanzapine treatment of psychotic and behavioral symptoms in patients with Alzheimer disease in nursing care facilities: a double-blind, randomized, placebo-controlled trial. The HGEU Study Group. *Archives of General Psychiatry*. 2000; **57**: 968–976.

Tariot, P.N., Cummings, J.L., Katz, I.R., Mintzer, J., Perdomo, C.A., Schwam, E.M., Whalen, E. A randomized, double-blind, placebo-controlled study of the efficacy and safety of donepezil in patients with Alzheimer's disease in the nursing home setting. *Journal of the American Geriatric Society*. 2001; **49(12)**: 1590–1599.

Tariot, P.N., Erb, R., Podgorski, C.A., Cox, C., Patel, S., Jakimovich, L., Irvine, C. Efficacy and tolerability of carbamazepine for agitation and aggression in dementia. *American Journal of Psychiatry*. 1998; **155**: 54–61.

Tariot, P.N., Raman, R., Jakimovich, L., Schneider, L., Porsteinsson, A., Thomas, R., Mintzer, J., Brenner, R., Schafer, K., Thal, L., et al. Divalproex sodium in nursing home residents with possible or probable Alzheimer Disease complicated by agitation: a randomized, controlled trial. *American Journal of Geriatric Psychiatry*. 2005; **13**: 942–949.

Tariot, P.N., Schneider, L., Katz, I.R., Mintzer, J.E., Street, J., Copenhaver, M., Williams-Hughes, C. Quetiapine treatment of psychosis associated with dementia: A double-blind, randomized, placebo-controlled clinical trial. *American Journal of Geriatric Psychiatry*. 2006; **14(9)**: 767–776.

Trinh, N.H., Hoblyn, J., Mohanty, S., Yaffe, K. Efficacy of cholinesterase inhibitors in the treatment of neuropsychiatric symptoms and functional impairment in Alzheimer disease: a meta-analysis. *Journal of the American Medical Association*. 2003; **289**: 210–216.

Wang, L.Y., Shofer, J.B., Rohde, K., Hart, K.L., Hoff, D.J., McFall, Y.H., Raskind, M.A., Peskind, E.R. Prazosin for the treatment of behavioral symptoms in patients with Alzheimer disease with agitation and aggression. *American Journal of Geriatric Psychiatry*. 2009; **17**: 744–751.

Zhong, K.X., Tariot, P.N., Mintzer, J., Minkwitz, M.C., Devine, N.A. Quetiapine to treat agitation in dementia: a randomized, double-blind, placebo-controlled study. *Current Alzheimer Research*. 2007; **4**: 81–93.

Optimizing the use of psychotropic medications

Avorn, J., Soumerai, S.B., Everitt, D.E., et al. A randomized trial of a program to reduce the use of psychoactive drugs in nursing homes. *New England Journal of Medicine*. 1992; **327**: 168–173.

Ballard, C., Hanney, M.L., Theodoulou, M., et al. The dementia antipsychotic withdrawal trial (DART-AD): long-term follow-up of a randomised placebo-controlled trial. *Lancet Neurology*. 2009; **8**: 151–157.

Banerjee, S. The use of antipsychotic medication for people with dementia: time for action. A report for the Minister of State for Care Services. 2009; London, United Kingdom.

Bird, M., Llewellyn Jones, R.H., Korten, A., et al. A controlled trial of a predominantly psychosocial approach to BPSD: treating causality. *International Psychogeriatrics*. 2007; **19**: 874–891.

Bridges-Parlet, S., Knopman, D., Steffes, S. Withdrawal of neuroleptic medications from institutionalized dementia patients: results of a double-blind, baseline-treatment-controlled pilot study. *Journal of Geriatric Psychiatry and Neurology*. 1997; **10**: 119–126.

Cohen-Mansfield, J., Lipson, S., Werner, P., et al. Withdrawal of haloperidol, thioridazine, and lorazepam in the nursing home: a controlled, double-blind study. *Archives of Internal Medicine*. 1999; **159**: 1733–1740.

Cornege-Blokland, E., Kleijer, B.C., Hertogh, C.M., et al. Reasons to Prescribe Antipsychotics for the Behavioral Symptoms of Dementia: A Survey in Dutch Nursing Homes Among Physicians, Nurses, and Family Caregivers. *Journal of the American Medical Directors Association*. 2010.

Crotty, M., Halbert, J., Rowett, D., et al. An outreach geriatric medication advisory service in residential aged care: a randomised controlled trial of case conferencing. *Age Ageing*. 2004; **33**: 612–617.

Eide, E., Schjott, J. Assessing the effects of an intervention by a pharmacist on prescribing and administration of hypnotics in nursing homes. *Pharmacy World and Science*. 2001; **23**: 227–231.

Fossey, J., Ballard, C., Juszczak, E., et al. Effect of enhanced psychosocial care on antipsychotic use in nursing home residents with severe dementia: cluster randomised trial. *British Medical Journal*. 2006; **332**: 756–761.

Furniss, L., Burns, A., Craig, S.K., et al. Effects of a pharmacist's medication review in nursing homes. Randomised controlled trial. *British Journal of Psychiatry*. 2000; **176**: 563–567.

Hagen, B.F., Armstrong-Esther, C., Quail, P., et al. Neuroleptic and benzodiazepine use in long-term care in urban and rural Alberta: characteristics and results of an education intervention to ensure appropriate use. *International Psychogeriatrics*. 2005; **17**: 631–652.

Kamble, P., Chen, H., Sherer, J.T., et al. Use of antipsychotics among elderly nursing home residents with dementia in the US: an analysis of National Survey Data. *Drugs and Aging*. 2009; **26**: 483–492.

Kim, H., Whall, A.L. Factors associated with psychotropic drug usage among nursing home residents with dementia. *The Nursing Residency*. 2006; **55**: 252–258.

Koopmans, R.T., Zuidema, S.U., Leontjevas, R., et al. Comprehensive assessment of depression and behavioral problems in long-term care. *International Psychogeriatrics*. 2010; **22**: 1054–1062.

Kovach, C.R., Logan, B.R., Noonan, P.E., et al. Effect of the Serial Trial Intervention on discomfort and behavior of nursing home residents with dementia. *American Journal of Alzheimer's Disease and Other Dementias*. 2006; **21**: 147–153.

Lövheim, H., Sandman, P.O., Kallin, K., et al. Relationship between antipsychotic drug use and behavioral and psychological symptoms of dementia in old people with cognitive impairment living in geriatric care. *International Psychogeriatrics*. 2006; **18**: 713–726.

Meador, K.G., Taylor, J.A., Thapa, P.B., et al. Predictors of antipsychotic withdrawal or dose reduction in a randomized controlled trial of provider education. *Journal of the American Geriatric Society*. 1997; **45**: 207–210.

Nijk, R.M., Zuidema, S.U., Koopmans, R.T.C.M. Prevalence and correlates of psychotropic drug use in Dutch nursing home patients with dementia. *International Psychogeriatrics*. 2009; **21**: 485–493.

Patterson, S.M., Hughes, C.M., Crealey, G., et al. An evaluation of an adapted U.S. model of pharmaceutical care to improve psychoactive prescribing for nursing home residents in Northern Ireland (Fleetwood Northern Ireland Study). *Journal of the American Geriatric Society*. 2010; **58**: 44–53.

Pitkala, K.H., Laurila, J.V., Strandberg, T.E., et al. Behavioral symptoms and the administration of psychotropic drugs to aged patients with dementia in nursing homes and in acute geriatric wards. *International Psychogeriatrics*. 2004; **16**: 61–74.

Ray, W.A., Taylor, J.A., Meador, K.G., et al. Reducing antipsychotic drug use in nursing homes. A controlled trial of provider education. *Archives of Internal Medicine*. 1993; **153**: 713–721.

Roberts, M.S., Stokes, J.A., King, M.A., et al. Outcomes of a randomized controlled trial of a clinical pharmacy intervention in 52 nursing homes. *British Journal of Clinical Pharmacology*. 2001; **51**: 257–265.

Rovner, B.W., Steele, C., Shmuely, D.S., et al. A randomised trial of dementia care in nursing homes. *Journal of the American Geriatric Society*. 1996; **44**: 7–13.

Ruths, S., Straand, J., Nygaard, H.A., et al. Effect of antipsychotic withdrawal on behavior and sleep/wake activity in nursing home residents with dementia: a randomized, placebo-controlled, double-blinded study. The Bergen District Nursing Home Study. *Journal of the American Geriatric Society*. 2004; **52**: 1737–1743.

Salzman, C., Jeste, D.V., Meyer, R.E., et al. Elderly patients with dementia-related symptoms of severe agitation and aggression: consensus statement on treatment options, clinical trials methodology, and policy. *Journal of Clinical Psychiatry*. 2008; **69**: 889–898.

Schmidt, I., Claesson, C.B., Westerholm, B., et al.: The impact of regular multidisciplinary team interventions on psychotropic prescribing in Swedish nursing homes. *Journal of the American Geriatric Society*. 1998; **46**: 77–82.

Selbaek, G., Kirkevold, O., Engedal, K. The prevalence of psychiatric symptoms and behavioural disturbances and the use of psychotropic drugs in Norwegian nursing homes. *International Journal of Geriatric Psychiatry*. 2007; **22**: 843–849.

Smalbrugge, M., Jongenelis, L., Pot, A.M., et al. Incidence and outcome of depressive symptoms in nursing home patients in the Netherlands. *American Journal of Geriatric Psychiatry*. 2006; **14**: 1069–1076.

Thapa, P.B., Meador, K.G., Gideon, P., et al. Effects of antipsychotic withdrawal in elderly nursing home residents. *Journal of the American Geriatric Society*. 1994; **42**: 280–286.

van Dijk, K.N., de Vries, C.S., van den Berg, P.B., et al. Drug utilisation in Dutch nursing homes. *European Journal of Clinical Pharmacology*. 2000; **55**: 765–771.

van Reekum, R., Clarke, D., Conn, D., et al. A randomized, placebo-controlled trial of the discontinuation of long-term antipsychotics in dementia. *International Psychogeriatrics*. 2002; **14**: 197–210.

Verrue, C.L., Petrovic, M., Mehuys, E., et al. Pharmacists' interventions for optimization of medication use in nursing homes: a systematic review. *Drugs and Aging*. 2009; **26**: 37–49.

Westbury, J., Jackson, S., Gee, P., et al. An effective approach to decrease antipsychotic and benzodiazepine use in nursing homes: the RedUSe project. *International Psychogeriatrics*. 2010; **22**: 26–36.

Wetzels, R.B., Zuidema, S.U., de Jonghe, J.F.M., et al. Prescribing pattern of psychotropic drugs in nursing home residents with dementia. *International Psychogeriatrics*. 2011; **23**: 1249–1259.

Wood-Mitchell, A., James, I.A., Waterworth, A., et al. Factors influencing the prescribing of medications by old age psychiatrists for behavioural and psychological symptoms of dementia: a qualitative study. *Age Ageing*. 2008; **37**: 547–552.

Zuidema, S.U., Verhey, F.R.J., Derksen, E., et al. Prevalence of neuropsychiatric symptoms in a large sample of Dutch nursing home patients with dementia. *International Journal of Geriatric Psychiatry*. 2007; **22**: 632–638.

Role of the interdisciplinary team

Bartels, S.J., Moak, G.S., Dums, A.R. Models of mental health services in nursing homes. *Psychiatric Services*. 2002; **53**: 1390–1396.

Crooks, E.A., Geldmacher, D.S. Interdisciplinary approaches to Alzheimer's disease management. *Clinics in Geriatric Medicine*. 2004; **20(1)**: 121–139.

Draper, B.M., Low, L. Evidence-based service delivery. *Psychogeriatric Service Delivery*. 2005; Oxford, United Kingdom: Oxford University Press.

Ferrell, B.A. The management of pain in long-term care. *Clinical Journal of Pain*. 2004; **20(4)**: 240–243.

Glaister, J.A., Blair, C. Improved education and training for nursing assistants: Keys to promoting the mental health of nursing home residents. *Issues in Mental Health Nursing*; **29**: 863–872.

Grahn, B., Ekdahl, C., Borgquist, L. Motivation as a predictor of changes in quality of life and working ability in multidisciplinary rehabilitation. A two-year follow-up of a prospective controlled study in patients with prolonged musculoskeletal disorders. *Disability & Rehabilitation: An International Multidisciplinary Journal*. 2004; **20**: 285–297.

Greene, J.A. *Manual of Nursing Home Practice*. 2000; Washington, DC, United States: American Psychiatric Association.

Hertogh, C.M.P.M., Deerenberg-Kessler, W., Ribbe, M.W. The problem-oriented multidisciplinary approach in Dutch nursing home care. *Clinical Rehabilitation*. 1996; **10**: 135–142.

Jeste, D.V., Alexopoulos, G.S., Bartels, S.J., Cummings, J.L., Gallo, J.J., Gottlieb, G.L., Halpain, M.C., Palmer, B.W., Patterson, T.L., Reynolds, C.F., Lebowitz, B.D. Consensus statement on the upcoming crisis in geriatric mental health. *Archives of General Psychiatry*. 1999; **56**: 848–853.

Leipzig, R.M., Granville, L., Simpson, D., Brownell Anderson, M., Sauvigne, K., Sahlins, J. *Social Work Practice in Nursing Homes*. 2009; University Park, Illinois, United States: Lyceum Books.

Lichtenberg, P.A., et al. Standards for psychological services in long-term care facilities. *Gerontologist*. 1998; **38**: 122–127.

Lidell, E., Fridlund, B. Long-term effects of a comprehensive rehabilitation programme after myocardial infarction. *Scandinavian Journal of Caring Sciences*. 1996; **10**: 67–74.

Lawlor, B. Managing behavioural and psychological symptoms in dementia. *The British Journal of Psychiatry*. 2002; **181**: 463–465.

Oliver, S. Leadership in healthcare. *Musculoskeletal Care*. 2006; **4**: 38–47.

Nowalk, M.P., Prendergast, J.M., Bayles, C.M., D'Amico, F.J., Colvin, G.C. A randomized trial of exercise programs among older individuals living in two long-term care facilities: The FallsFREE Program. *Journal of the American Geriatrics Society*. 2001; **49**: 859–865.

Reeves, S., Macmillan, K., van Soeren, M. Leadership of interprofessional health and social care teams: a socio-historical analysis. *Journal of Nursing Management*. 2010; **18**: 258–264.

Rubenstein, L.Z., Stuck, A.E., Siu, A.L., Wieland, D. Impacts of geriatric evaluation and management programs on defined outcomes: Overview of the evidence. *Journal of the American Geriatrics Society*. 1991; **39(Supplement)**: 8S–16S.

Schmidt, I., Claesson, C.B., Westerholm, B., Nilsson, L.G., Svarstad, B.L. The impact of regular multidisciplinary team interventions on psychotropic prescribing in Swedish nursing homes. *Journal of the American Geriatrics Society*. 1998; **46(1)**: 77–82.

Schmidt, I.K., Svarstad, B.L. Nurse-physician communication and quality of drug use in Swedish nursing homes. *Social Science and Medicine*. 2002; **54(12)**: 1767–1777.

Snowdon, J. Mental health service delivery in long-term care homes. *International Psychogeriatrics*, 2010; **22(7)**: 1063–1071.

Zeiss, A. Providing Interdisciplinary Geriatric Team Care: What Does It Really Take? *Clinical Psychology: Science and Practice*. 2003; **10(1)**: 115–119.

Zeiss, A.M., Steffen, A.M. Interdisciplinary health care teams in geriatrics: An international model. *Comprehensive Clinical Psychology*. 1998; London, United Kingdom: Pergamon Press.

Zwarenstein, M., Goldman, J., Reeves, S. Interprofessional collaboration: effects of practice-based interventions on professional practice and healthcare outcomes. *Cochrane Database of Systematic Review*. 2009; **3**: CD000072.

Education and staff training

Dementia Training Study Centres and Dementia Collaborative Research Centres. Australian Government, Department of Health and Ageing. 2009; www.health.gov.au/internet/main/publishing.nsf/Content/ageing-mailfax-2009-1202.htm

Aylward, S., Stolee, P., Keat, N., Van Johncox, M.A. Effectiveness of continuing education in long-term care: A literature review. *The Gerontologist*. 2003; **43**: 259–271.

Beeber, A.S., Zimmerman, S., Fletcher, S., Mitchell, C.M., Gould, E. Challenges and strategies for implementing and evaluating dementia care staff training in long-term care settings. *Alzheimer's Care Today*. 2010; **11**: 17–39.

National guidelines for seniors' mental health: The assessment and treatment of mental health issues in long-term care homes. Canadian Coalition for Seniors' Mental Health. 2006; http://www.ccsmh.ca/en/natlGuidelines/initiative.cfm.

Hsu, M.C., Moyle, W., Creedy, D., Venturato, L. An investigation of aged care mental health knowledge of Queensland aged care nurses. *International Journal of Mental Health Nursing*. 2005; **14**: 16–23.

Hyer, K., Molinari, V., Kaplan, M., Jones, S. Credentialing dementia training: the Florida experience. *International Psychogeriatrics*. 2010; **22**: 864–873.

Kuske, B., Hanns, S., Luck, T., Angermeyer, M.C., Behrens, J., Riedel-Heller, S.G. Nursing home staff training in dementia care: a systematic review of evaluated programs. *International Psychogeriatrics*. 2007; **19**: 818–841.

McCabe, M., Davidson, T., George, K. Effectiveness of staff training programs for behavioural problems among older people with dementia. *Aging and Mental Health*. 2007; **11**: 505–519.

McAiney, C.A., et al. Evaluation of the sustained implementation of a mental health learning initiative in long-term care. *International Psychogeriatrics*. 2007; **19**: 842–858.

Rampatige, R., Dunt, D., Doyle, C., Day, S., van Dort, P. The effect of continuing professional education on health care outcomes: lessons for dementia care. *International Psychogeriatrics*. 2009; **21**: S34–S43.

Moyle, W., Hsu, M., Lieff, S., Vernooij-Dassen, M. Recommendations for staff education and training for older people with mental illness in long-term aged care. *International Psychogeriatrics*. 2010; **22(7)**: 1197–1106.

Teri, L., Huda, P., Gibbons, L.E., Young, H., van Leynseele, J. STAR: A dementia-specific training program for staff in assisted living residences. *The Gerontologist*. 2005; **45(5)**: 686–693.

Visser, S.M., McCabe, M.P., Hudgson, C., Buchanan, G., Davison, T.E., George, K. Managing behavioural symptoms of dementia: Effectiveness of staff education and peer support. *Aging and Mental Health*. 2008; **12**: 47–55.

Guidelines

Consensus statement on improving the quality of mental health care in U.S. nursing homes: management of depression and behavioral symptoms associated with dementia. *Journal of the American Geriatrics Society*. 2003; **51**: 1287–1298.

Depression: clinical practice guidelines. American Medical Directors Association. 2003; Columbia, Maryland, United States.

National guidelines for the assessment and treatment of mental health issues in long-term care homes. 2006; Toronto, Ontario, Canada: Canadian Coalition for Seniors' Mental Health.

Sokoloff, L., Feldman, S., Conn, D.K., Simons, K., Walsh, L., Dunal, L., Goodman, R., Khatri, N., Huijbregts, M. Implementation of a mental health guideline in a long-term care home: A participatory action approach. *Journal of Research in Interprofessional Practice and Education*. 2012; **2**: 134–151.

INTERNATIONAL PSYCHOGERIATRIC ASSOCIATION
www.ipa-online.org

The IPA Complete Guides to

Behavioral and Psychological Symptoms of Dementia

Specialists Guide

BPSD

MODULE 1: An introduction to BPSD

MODULE 2: Clinical issues

MODULE 3: Etiology

MODULE 4: Role of family caregivers

MODULE 5: Non-pharmacological treatments

MODULE 6: Pharmacological management

MODULE 7: Cross-cultural and transnational considerations

MODULE 8: Long-term care

Nurses Guide

The IPA Complete Guides to BPSD are available in three editions to meet a variety of practice needs.

Primary Care Physicians Guide

Specialists • Primary Care Physicians • Nurses

ISBN 978-0-9829509-0-6