**White House Conference on Aging**
Tuesday May 5 15
Room 2A LOB
300, Capital Avenue, Hartford, CT
Testimony of Velandy Manohar, MD, Certified ABPN- Adult Psychiatry, Psychosomatic Medicine, and Added Qualifications in Addiction Psychiatry

I am Velandy Manohar, MD. I am attaching my Resume to the Testimony. I was unable to prepare this before the meeting because I was informed of this meeting on Monday afternoon. I offer information I have archived on various aspects of Alzheimer's. I was very glad I attended most of the session because I gained much useful information presented in a very clear and stimulating manner. I am offering this very useful description of Alzheimer's and a well-documented dissertation on all the key clinical aspects of Alzheimer's Disease. Please feel free to share as you see fit please

## Medical News Today [MNT]

### Fast facts about Alzheimer's

- More than 5 million people in the US are living with Alzheimer's, and this number is expected to **rise to as many as 16 million by 2050**
- Alzheimer's is the sixth leading cause of death in the US
- More than two thirds of Americans with Alzheimer's are women.[Not sure to me if that is an artifact related to greater longevity of women over men in the key age groups above 65 especially after 85. Age and family history are the top two risk factors for Alzheimer's Disease. Sadly both are unavoidable risk factors. VM]

### How common is Alzheimer's disease?

In the US, the most recent census has enabled researchers to give **estimates** of how many people have Alzheimer's disease. In 2010, some 4.7 million people of 65 years of age and older were living with Alzheimer's disease in the US.[1]
The **2013 statistical report** from the Alzheimer's Association gives a proportion of the population affected - **just over a tenth of people in the over-65 age group have the disease in the US. In the over-85s, the proportion goes up to about a third.**[2]

As our **dementia** page outlines, there is a handful of different types, but Alzheimer's disease is the problem behind most cases of memory loss and cognitive decline:[2] **The Alzheimer's Association says it accounts for between 60% and 80% of all cases of dementia. Vascular dementia, which is caused by stroke not Alzheimer's, is the second most common type of dementia.**

### What causes Alzheimer's disease?

Like all types of dementia, Alzheimer's is caused by brain cell death.[3] It is a neurodegenerative disease, which means there is progressive brain cell death that happens over a course of time.
**The total brain size shrinks with Alzheimer's - the tissue has progressively fewer nerve cells and connections**.[3,4]

While they cannot be seen or tested in the living brain affected by Alzheimer's disease, postmortem/autopsy will always show tiny inclusions in the nerve tissue, called plaques and tangles:[3,4]

- **Plaques are found between the dying cells in the brain - from the build-up of a protein called beta-amyloid (you may hear the term "amyloid plaques").**
- **The tangles are within the brain neurons - from a disintegration of another protein, called tau.**

For a detailed visualization of what goes on in the Alzheimer's disease process, progressing from the normal brain to increasing dementia changes, the Alzheimer's Association has produced a journey of 16 slides. See the illustrations: **Inside the brain: an interactive tour.** [This is interesting and informative. There are 16 slides. It is available in 14 Languages from Arabic to Viet Namese on the MNT Website. VM]

**VELANDY MANOHAR, M.D.,**
**Distinguished Life Fellow APA**
**Steering committee member- Psychotherapy Caucus of the Am. Psychiatric Association**
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**MEDICAL EDUCATION AND TRAINING**

| | |
|---|---|
| **BOARD CERTIFIED –ABPN-PSYCHOSOMATIC MEDICINE #240** | 2005 |
| BOARD ELIGIBLE-ABMS-PAIN MEDICINE | 2004 |
| CERTIFIED IN OFFICE BASED BUPRENORPHINE TREATMENT AND HAVE OBTAINED SPECIAL DEA # TO PRESCRIBE SUBOXONE TO NARCOTIC ADDICTS | FEB 2003 |
| **CERTIFIED IN ADMINISTRATIVE PSYCHIATRY (APA)** | April 1997 |
| CERTIFIED BY ABPN: ADDED QUALIFICATION IN ADDICTION PSYCHIATRY | March 1993 |
| **RECERTIFIED IN ADDICTION PSYCHIATRY (#259)** | March 2003 |
| **CERTIFIED BY ABPN: PSYCHIATRY #017946** | **June 1978** |

RESEARCH FELLOW IN PSYCHIATRY WITH DR. JACK MENDELSON 1971-1972
HARVARD MEDICAL SCHOOL AT BOSTON CITY HOSPITAL
BOSTON, MA

CHIEF RESIDENT IN THE HARVARD PSYCHIATRY SERVICE AT 1970-1971
BOSTON CITY HOSPITAL
BOSTON, MA

SECOND YEAR PSYCHIATRY RESIDENT 1969-1970
HARVARD MEDICAL SCHOOL AT BOSTON CITY HOSPITAL
BOSTON, MA

FIRST YEAR PSYCHIATRY RESIDENT 1968-1969
MENTAL HEALTH INSTITUTE
INDEPENDENCE, IA

ROTATING INTERNSHIP 1967-1968
KUAKINI HOSPITAL
HONOLULU, HI

SENIOR HOUSE SURGENCY 1965-1966
GOVERNMENT GENERAL HOSPITAL
CHENNAI, INDIA
ROTATING INTERNSHIP 1964-1965
GOVERNMENT GENERAL HOSPITAL
CHENNAI, INDIA

MEDICAL DEGREE 1965
MADRAS UNIVERSITY
CHENNAI, INDIA

MEDICAL EDUCATION GRADUATED FROM 1963
MADRAS MEDICAL COLLEGE
CHENNAI, INDIA

## PROFESSIONAL APPOINTMENTS

**MOST RECENT POSITION:**

**COMMUNITY HEALTH CENTER- MIDDLETOWN, CT 06457 DEC 2006 to Dec 2014**
Supervising Psychiatrist- 675, Main Street, Middletown, CT 06457, **Preceptor of APRN Residents**
**An innovative first in the nation Program created by Ms. Margaret Flinter. Actively engaged in developing the Pod Model of Integrated care that promotes a Family Medical home concept to reduce disparities optimize efficiencies, promote healthy living, empower patient involvement, early and effective coordinated treatment and coordinated acre within the CHC** and collaborative care with Health Care entities and private practices in the community by safe and innovative EHR systems**. Provided direct care, consultations and helped integrated care with in CHC and between CHC and collaborating Hospital and HC system. I build up my personal patient panel from 5-6 in Dec 2006 to 460 when I finally left CHC in Dec 2014**

**APPOINTED SECOND LEVEL APPEAL REVIEWER PSYCHIATRIC TREATMENT (QUALITY AND UTILIZATION MANAGEMENT CONCERNS) BY QUALIDIGM- JULY 2003 to present**

**Appointed Examiner for Part II Oral Examination for Adult Psychiatry by AM. BOARD OF PSYCHIATRY AND NEUROLOGY JULY 2003**

**PSYCHIATRIC CONSULTANT TO INNOVATIVE RESIDENTIAL PROGRAM FOR PREGNANT DRUG ADDICTS WITH OR WITHOUT OTHER LITTLE CHILDREN, WOMEN AND CHILDRENS PROGRAM, EASTERN DRIVE, MIDDLETOWN 2003-2006**

**UCONN MEDICAL SCHOOL 1998-2006**
**FARMINGTON, CT**
**ASSISTANT PROFESSOR OF PSYCHIATRY**
**Developed ambulatory psychiatry rotation for third and fourth year students**

**MIDDLESEX HOSPITAL, MIDDLETOWN, CT 1977- 2006**

**DIRECTOR OF ALCOHOL SERVICES 1977-1988**
**DIRECTOR OF SUBSTANCE ABUSE AND DUAL DIAGNOSIS SERVICES 1988-2006**

**SENIOR ATTENDING PHYSICIAN 1984-2006**
**Psychiatrist Clinical experience: Worked in the In- Patient Unit almost 30 years in Mx. Hospital and I year in MHI, Iowa, C-L service for 29 years in Middlesex and 9 years in Boston City Hosp. (both ED and Medical, Surgical and Ob floors (in the days of HIV and highly prevalent SUD), but especially ED, ICU, IMCU; OP: In MHI, Iowa, BCH, Mx Hospital, PHP and IOP at Mx Hospital. As member of the Bio-Ethics Committee I helped develop the POLST- a two page form to document the wishes of the patient or those responsible for making those wishes known with respect to Life support interventions.**

**PSYCHIATRIC FACULTY 1977-2006**
**FAMILY PRACTICE RESIDENCY PROGRAM**

**BIO-ETHICS COMMITTEE - PSYCHIATRY REPRESENTATIVE 1977-2006**

**PHARMACY COMMITTEE - PSYCHIATRY REPRESENTATIVE 1977-2000**

**ADE SUB-COMMITTEE OF PHARMACY COMMITTEE-HOSPITAL WIDE, CHAIR**

**NATIONAL BOARD OF MEDICAL EXAMINERS**
**SPECIALTY SPECIFIC STANDARDS DEVELOPMENT FOR USMLE-2 Panel member 2003**

**CHARTER MEMBER: CT MULTI-CULTURAL HEALTH PARTNERSHIP-CT. DPH** **JULY 2008**
**Participated actively in the Access Committee and helped develop the grant program to support adoption of the Ask me 3 processes to increase engagement of patients in their treatment.**

**WHITING FORENSIC DIVISION ADVISORY AND REVIEW BOARD- MEMBER** **2008**
**REAPPOINTED BY GOVERNOR MALLOY** **2013**

**CONNECTICUT MEDICAL EXAMINING BOARD (CMEB)** **1995-2007**
**Designated to assist the Board to draft Guidelines to manage Pain which has been adopted for the State of CT**

**NON BOARD Hearing PANEL MEMBER (CMEB)** **2008 to present**

**MEDICAL ADVISORY BOARD OF THE COMMISSIONER OF THE DMV** **Currently 2013**

**DESIGNATED BY CT. MEDICAL EXAMINING BOARD TO PARTICIPATE IN ACONFERENCE SPONSORED BY FEDERATION OF STATE MEDICAL BOARDS to develop principles/concepts for state regulation/oversight of office based treatment of opioid addicts –Suboxone program**
**FEB 2003**

**APPOINTED SECOND LEVEL APPEAL REVIEWER PSYCHIATRIC TREATMENT (QUALITY AND UTILIZATION MANAGEMENT CONCERNS) BY QUALIDIGM, CT.** **JULY 2003**

**APPOINTED EXAMINER FOR PART II ORAL EXAMINATION FOR ADULT PSYCHIATRY BY AM BOARD OF PSYCHIATRY AND NEUROLOGY** **JULY 2003**

**PREVIOUS POSITIONS:**

PSYCHIATRIC CONSULTANT 1993-1996
RUSHFORD TREATMENT CENTER
MIDDLETOWN. CT

**DIRECTOR OF HIV PRE AND POST TESTING COUNSELING SITE.** **1982**
**MIDDLESEX HOSPTIAL, MIDDLETOWN. CT (FIRST IN MIDDLETOWN)**

**DIRECTOR OF AIDS RISK REDUCTION PROGRAM** **1982**
**MIDDLETOWN. CT (ONE OF THE ORIGINAL EIGHT SITES FUNDED BY CADAC)**

CONSULTING PSYCHIATRIST 1985-1986
INTER-COMMUNITY MENTAL HEALTH CENTER
GLASTONBURY AND WETHERSFIELD, CT

**PSYCHIATRIST IN CHARGE** **1980-1985**
**DUAL DIAGNOSIS FLOOR, MIDDLETOWN HEALTH CARE CENTER**
**THE FIRST ECF IN CONNECTICUT TOTALLY DEDICATED TO PSYCHIATRIC PATIENTS (DEVELOPED AND INTEGRATED APPROACH WITH MS. J. HALLIGAN)**
**MIDDLETOWN, CT**

**ASSOCIATE VISITING PHYSICIAN** **1976-1977**
**BOSTON CITY HOSPITAL**
**BOSTON, MA**

**DIRECTOR OF PARA PROFESSIONAL TRAINING PROGRAMS** **1971-1977**
**ALCOHOL DIVISION OF THE HARVARD PSYCHIATRY SERVICE**
**BOSTON CITY HOSPITAL**
**BOSTON, MA**

PSYCHIATRIC CONSULTANT TO THE REHAB TEAM 1970-1977
THE LONG ISLAND CHRONIC DISEASES HOSPITAL
QUINCY, MA

ASSISTANT PROFESSOR OF PSYCHIATRY 1975-1977
BOSTON UNIVERSITY SCHOOL OF MEDICINE
BOSTON, MA

INSTRUCTOR OF PSYCHIATRY 1972-1973
HARVARD MEDICAL SCHOOL
BOSTON, MA

TEACHING FELLOW 1969-1971
HARVARD MEDICAL SCHOOL
BOSTON, MA

**PROFESSIONAL TASK FORCE INVOLVEMENT**

Invited by the Chairman of the Department of Psychiatry 1995
To develop protocols for the treatment of acute intoxication
and withdrawal in Manchester memorial hospital

Member of the Clinical Pathway committee in Middlesex 1995
hospital which developed the protocols for the management
of alcohol withdrawal

I convened the Middletown task group which established the
first non-hospital detox in Middletown (one of the two demonstration projects in the state
it is part of the Rushford treatment center, Middletown, CT.

Member AIDS consortium in Middlesex county called the AIDS project. 1992

Member dual diagnosis task force which designed the protocol for acute care and evaluation adopted by five Middletown agencies, including the Middlesex hospital ER, Rushford and DMH (the only such algorithm based collaborative arrangement in the state at that time).
1990

Member of the task force which developed the collaborative treatment protocols that provided coordinated care for dual diagnosis patients in Middletown. This plan was funded in the form of a MISA CADAC grant administered with key staff housed in Rushford and DMH in Middletown and at Gateway in Old Saybrook. The only grant funded MISA program at that time
in the State 1990

**EDUCATIONAL CONSULTANT/ TRAINER**

**Community Health Center, Middletown, CT: Preceptor for APRN Residency program** 2010 to date

ONA WILCOX COLLEGE OF NURSING AND STAFF DEVELOPMENT
MIDDLESEX HOSPITAL, MIDDLETOWN, CT
Associate degree program for nurses 1977- 2000

IN HOSPITAL GRAND ROUNDS FOR PHYSICIANS (Mx Hospital).
IN HOSPTIAL PROGRAMS FOR PHYSICIANS AND NURSES 1977 -2006

MANCHESTER MEMORIAL HOSPITAL MANCHESTER, CT
Familiarize clinical staff with the procedures involved in the new detox protocols,
CADAC sponsored courses on neuropharmacology. 1979

EASTERN AREA EDUCATIONAL AND TRAINING PROGRAMS: From Maine to Virginia.
Group and Family Counseling for people working
in the alcohol and drug abuse field.

MIDDLETOWN MAYOR'S "D-DAY" 1988-1990
Presentations of Alcohol and Drug Abuse
Two drunken driving demonstrations in Middletown. CT

MIDDLESEX COMMUNITY COLLEGE
Sponsored seminars on diagnosis and treatment of Alcohol dependence.

MIDDLESEX CHAMBER OF COMMERCE
Sponsored seminars on diagnosis and treatment, EAP,
Managed Care approach to treatment.

MIDDLESEX HOSPITAL, VNA, AND MANY OTHER ORGANIZATIONS
Presentations on stress, smoking cessation, Chronic pain,
HIV testing, psychosocial issues in the management of
People with AIDS, management of dual diagnosis patients.

MIDDLESEX HOSPITAL, SUPERVISING PSYCHIATRIST
SMOKING CESSATION PROGRAM, DUAL DX PARTIAL PROGRAM

**PARTICIPATION IN PROFESSIONAL ORGANIZATIONS:**

**Nancy Berger Member Award- CT. Multi-Cultural Health Partnership 2012**

**Past President of Asian American Caucus of APA 2007- 2011**

**Recipient of the Roger Coleman, MD Memorial Award- CT. Psychiatry Society- for superlative service to persons with mental illness 2010**

**Recipient of the Cornelius Boulehouwer, MD: Service to CT. Psychiat. Society Award 2003**

**Distinguished Fellow-American Psychiatric Association 2003**

Member, CT Psychiatric Society and Am. Psychiatric Association

Member, Connecticut State Medical Examining Board. 1995
appointed by the Governor and Approved by the Legislature.

Member, Medical Advisory Committee to the Commissioner of Motor Vehicles.

Member: CT. State Medical Society and Middlesex County Medical Association

Chair of the Confidentiality Committee of Connecticut State 1988-1989
Psychiatric Society (CPS)

**Chair of the Chronic Patient Committee of the CPS** 1989-1999
(Prepared detailed analysis of the Annual Implementation Plans of DMH for the Council of the CPS).

Chair of the ad hoc committee of the CPS to monitor and report on the practices of PRO Behavioral health, a behavioral health, Managed care contractor for MD Health Plan.

President - Mx-New Haven Chapter of CPS

Member, Impaired Physicians Committee of the APA 1993- 1995

**Awarded Honorary Membership of the Connecticut Federation of Alcohol and Drug Abuse Counselors.**

**Founding Member and Past President of the New England Chapter of**

**The American Association of Psychiatrists from India.**
**Past President of the American Association of Psychiatrists from India**. **1990 -92**

Member, Practice Research Network of Am. Psychiatric Association

**Charter Member - Smithsonian Institution National Museum of African American History and Culture 2012**

**My works on Dr. Martin Luther King Jr. and related subjects have been accepted into the NMAAHC Musuem Collection. 2013**

**FEDERAL AND STATE GOVT. RELATED WORK:**

WHILE I WAS WORKING IN BOSTON: 1969-1977

**I ASSISTED SEN. QUINLAN AND HIS COMMITTEE TO PREPARE LEGISLATION TO ADDRESS DRUNK DRIVING IN 1973. It was signed into law in 1974(Chapter 647, Gen. Laws of the Commonwealth of MA)**

**I WAS THE PSYCHIATRIST FOR THE DEMONSTRATION PROJECT CALLED BOSTON ASAP** that addressed both the enforcement and legal aspects on the one hand and on the other provided necessary counseling services.

**TESTIFIED TO THE U.S. SENATE SUB-COMMITTEE ON HEALTH PREVENTION OF ALCOHOL AND DRUG PROBLEMS (SEN. HATHAWAY) 1977**

**CONSULTANT: OFFICE OF PREVENTION NIAAA; REPLICATION PROJECT 1977**

**CONSULTANT: NATIONAL CENTER FOR ALCOHOL EDUCATION-GROUP THERAPY 1977**

**LATER IN CT**: **1977 to date**.

**DRUNKEN DRIVING LEGISLATION**:

**I worked with Sen. Tulisano, Edith Prague, MADD and SADD to enact per se legislation to address challenges posed by drunken driving.** In addition **i worked with the commissioner of the DMV as a member of the Medical Advisory Board to establish intervention programs in jail and ambulatory basis.**

CONNECTICUT GENERAL ASSEMBLY (CGA)
**I TESTIFIED BEFORE THE JUDICIARY, PUBLIC HEALTH COMMITTEES**
DWI (per se law), funding for HIV programs, confidentiality of records of PWA and HIV testing results, establishment of non-hospital detox programs, funding of programs for addicted pregnant individuals.

**CGA: 2011**: **FROM APRIL TO JUNE 2011**: I advocated for the passage of SB 1083, which prohibits step edits imposed on medications used for managing pain disorders. This bill passed both the House and the Senate and is now on the way to the Governor's office for the final signature to make PA 11-169 into Law. The Op Ed on the subject of pain management was one of the tools I used to influence the legislators.

**CGA: 2015**

**Testified to Judiciary Committee on A**. In support of **Physician Aid In Dying Bill 07015**. **B**. **In Support of** SB650 **An Act Concerning Temporary Restraining Orders**; HB6848 **An Act Protecting Victims of Domestic Violence**; and HB6962 **An Act Concerning Firearm Safety**

**Testified to Education Committee in support of SB 1060- Legislation to eliminate the use of Seclusion Rooms and Restraints in Schools.**

**Testified to Appropriations Committee- I am opposed to the proposed cuts to the Dept. of Mental Health and Addiction and the DPH Budget. I am especially opposed to the cuts in funding of School Based Health Centers. This would gut any of the reforms proposed by the Sandy Hook Commission and the well thought bipartisan State Innovation Plan for expanding and enhancing access and quality of care for children and their families while increasing accountability and responsibility. [Please scroll down.]**

**Provided Testimony On Line to Public Health Committee on Proposed Senate Bill 815 Bipartisan Proposals on Hospitals and Health Care 03 11 2015 in addition to key decision makers.**

**DMH-THE STATE MENTAL HEALTH PLANNING COUNCIL: MEMBER**
**Representative of CT. Psychiatric Society to State MH PC**

**CT. Hospital Association:**
**Member, regional oversight committee established to resolve conflicts between DMH facilities and General Hospital Emergency Departments**

**CADAC/DMHAS: COMMITTEE ON HEALTH SYSTEM REFORM AND DEVELOPMENT OF A SUBSTANCE ABUSE/MH MANAGED CARE SYSTEM.**

**DEPT. of CONSUMER PROTECTION: CANNABIS REGULATIONS.**
**I provided detailed written testimony on the recategorization of Cannabis to the Commissioner Arthur Rubinstein. Mr. G. Berner this might have been the only testimony offered on the day of the hearing. 2013**

**SANDY HOOK COMMUNITY CATASTROPHE. SINCE DEC 14 2012**
**I provided extensive and specific written testimony on various domains of such heart rending mass murders to: Mayor S. Jackson Chair of the Governor's Commission, U.S. Reps Larson and Courtney, Sens. Richard Blumenthal and Chris Murphy, State Reps. Phil Miller, Matt Lesser, State Sen. Art Linares, Stillman, Bartolomeo as well as: the leaders of the State Legislature including the President Pro Temp, Speaker, Majority and Minority leaders, Newtown Reps, the Co- Chairs and members of the three work groups studying mental health, gun violence and school safety issues.**

**CT. VETERANS AFFAIRS DEPT: STAND DOWN EVENT SEPT 12 2008, 2009, 2010, 2011, 2012**
I participated with colleagues from community health center to provide veterans and their families' information pertaining to psychological, social and medical consequences of their war experiences.

**In 2011 and 2012 I worked with Post-Doctoral Psychology Fellows working in the Community Health Center created an assessment methodology to identify PTSD, Combat stress and Depression and developed a triage and referral system** including the representatives of the CT. Military Support System and VA who are also helping Veterans and their families in a nearby tent.

**I prepared detailed educational material that was distributed at the Stand Down and by various means since 2008 to political and military leader's as well medical colleagues and NGOs. I will be glad to provide copies of these reports.**

**My colleague, a therapist at the Community Health Center, Middletown, CT and I participated (as a consultant) in the CT. Military Support Program.**

**GI BILL BENEFIT LIMITATIONS: FEDERAL MONTGOMERY- GI BILL**
I initiated and successfully completed a campaign during President Reagan's tenure to change the eligibility requirements to enable recovering alcohol dependent veterans to use their GI benefits beyond the ten year window if during these ten years they were unable to do so due to disability caused by addiction. **Willful Misconduct exception written into the original Montgomery GI Bill prevented Veterans Mr. Traynor and Mr. McKelvey from being able to access and utilize their educational benefits in the specified time limits because of their struggles with Alcohol use disorders. Their Appeal failed in the Supreme Court in 1988**. **Associate Justice Harry Blackmun** responded to my detailed brief in support of the appeal of Mr Traynor and McKelvey and stated said the decision was based on the existing Law. Supporters of Veterans sought to amend Montgomery G.I. Bill. **On Oct 20, 1988 Congress Bill enacted legislation in PL 100-689, Section 2049 which provided that the "disabling effects of Chronic Alcoholism shall not be considered to be the result of willful misconduct" in determining whether or not veterans with the histories of Alcoholism will receive Educational benefits**.

**SEPT 12 REPORTS: These reports prepared originally in 2008 about health concerns arising from OIF, OEF and OND and updated since then for each of Stand Down events for distribution. Stand Down**

**events are held at the State Veterans Hospital in Rocky Hill , CT.** Thousands of veterans, active duty service members and their families as well as dignitaries and military brass come to the one day event

**AR 635-20, CHAPTER 5-13 DISCHARGES FROM THE MILITARY.** Documented grave abuses of our service men and women who were intentionally misdiagnosed with Personality Disorder, coerced to accept this and dumped on the side of the road (e.g. **SGT. Chuck Luther**) instead of being treated for PTSD, TBI, Substance Use Disorder, or Mood Disorder. **This report (47 pages and 65 references) helped persuade Hon. Rep. Robert. E. Filner, Chairman of the Committee on Veterans Affairs to hold a full committee hearing on Sept.15, 2010. The Yale Legal Center for Veterans is the litigator for the FOI case filed by the Viet Nam Veterans of America on behalf of Sgt. Chuck Luther in New Haven Federal Court.** This is the same group that has taken up the appeal of Mr. William Dolphin according to Alaine Griffin's report in the Hartford Courant on 11 17 12.

**THE TRINEXUS REPORT: PREPARED AND DISTRIBUTED TO KEY LEADERS IN THE GOVT AND MILITARY IN THE SPRING OF 2011 HGHLIGHTED THE MAJOR LEADERSHIP FAILURES AND BREAK DOWN OF ETHICAL STANDARDS WITHIN THE MILIATARY WITH DEVASTATING EFFECTS ON SERVCIE MEMBERS. Besides the Chapter 5-13 discharges mentioned above there have been other notable failures of Command leadership.** I selected three 1. The terrible mass murder perpetrated by Major Hasan. The training files at WRAMC had very damaging information that was kept out of sight. 2. The extensive prevalence of Military sexual assault and trauma and rape of patients in VA Hospitals, 3 the dumping of the entire blame for a military debacle at Wanat- E. Afghanistan on young dead Lieutenant. There are common threads in all of these situations including senior officers. So also in the tragic death , subsequent shameful cover up of the circumstances of Cpl Pat Tillman's death with three bullet holes grouped closely and the award of Silver Star by General Stanley Mc Chrystal when he knew the statement accompanying this award was no the truth. He was subsequently relieved of his command fro severely criticizing his superiors including the Commander in Chief the President.

**AMERICAL PSYCHIATRIC ASSOCIATION:**

**Psychotherapy Caucus of the Am Psychiatric Association: One of the founding members under Chairmanship of Dr. Eric Plakun, MD of Austen Riggs Center, Stockbridge, MA . May 2014.**

**I organized field response from American Association of Psychiatrists from India and peers in the community to the DSM- IV. 1994**

**PROVIDED PERSONAL INPUT OF THE PRACTICE GUIDELINES DEVELOPEDBY THE APA** for anorexia/bulimia, major depression, schizophrenia, bipolar disorder, alcohol, cocaine and opiate dependence, psychiatric evaluation, placement criteria for adults and adolescents suffering from psychiatric illnesses. Most Recent input was on MDD in 2010.

**NATIONAL ASSOCIATION OF FREE CLINICS, February 3 2010**
1800 Diagonal Road Suite 600, Alexandria VA 22314
**FREE CLINIC**: **ON FEBRUARY 03 2010, I** volunteered a whole day of service to the first and only Free Clinic offered to the public at large in the XL Center in Hartford, CT. I was one of 1200 volunteers and I was the only psychiatrist. At the location I was able to work out a plan of action with 7-8 LCSW clinicians and 1 Psychologist to offer assessment and treatment recommendations and even help patients make appointments using the more private booths I had helped to create for the occasion by corresponding with organizers ahead of the event. (I will send you my report if requested). I organized similar free clinic in Chennai, Tamil Nadu, India in 1967 during the State Congress Party exhibition.

**PUBLICATIONS:**

**Joe O'Donnell, "The God Solution: Spirituality as a Coping Mechanism and Healing Tool for Mental Illness and Addiction" for which I interviewed you. You are featured prominently in Chapter 5, about why the medical establishment has been slow to integrate spirituality into mental health care, and how you've found ways to do it yourself. Thanks so much for giving me the opportunity to interview you and I look forward to hearing your comments. [I will send you a copy upon request.VM]**
**May 2013**

**APA ANNUAL CONVENTION** **May 2010**

**Workshop on Suicide among Asian American College students prepared and submitted by Dr Russell Lim, MD and undersigned was presented on Saturday May 22nd 2010 in New Orleans, LA**

**CT. Multi-Cultural Health Partnership**

**I am one of 16 featured participants in a discussion on racial disparities in health care access and outcomes- CD developed by the CT. Multicultural Health Partnership- 2009.**

**Mx. Hospital, Hospice Program**

**I participated in development of Video-recording of the persons speaking on the "Religious traditions of Death" I am featured in the Unabridged and abridged versions. CD of both versions and my essay on a good death and the Sanatana Dharma Perspective as I understand it and can enunciate the belief system is available for perusal at your request.**

**Personal Interests:**

I have prepared manuscripts on iconography, architecture, scripture and philosophy of Santana Dharma (Hinduism) being readied for publication specific essays and chapters available at request. Tentative name for all the eight parts- Swagatam Sharanagatam (Sanskrit)" all hail and welcome, be thou my refuge."

**Letter to the Editor, Middletown Press- "Stigmatizing of Psychiatric Patients**".

Book Reviewer: Journal of the American Academy of Psychiatrists in Alcoholism and Addictions. (In the past)

Field editor: journal of hospital and community psychiatry (now psychiatric services) (in the past)

Reviewer/consultant: evidence based mental health journal (in the past)

**HONORS AND AWARDS:**

**Reappointed to Whiting Forensic Advisory Board by Governor Malloy 2014-2017**

**Roger Coleman Memorial Award**: CT. Psychiatric Society- presented to every one of the about a score of volunteers who provided assistance following the Sandy Hook School shooting for exemplary devotion to patients and commitment to quality care **June 2013**

**Marine Corps League of CT**: Honored for Advocacy and service to Veterans and Active Duty Service Members and their families **May 2013**

**Smithsonian National Museum of African American History and Culture**:

Accepted my writings on Dr. Martin Luther King Jr and related subjects into their collection **May 2013**

**Nancy Berger Member Award- Ct. Multi-Cultural Health Partnership 2012**

**Roger Coleman Memorial Award- CT. Psychiatric Society for Superlative service to persons with mental illness 2010**

**Distinguished Life Fellow: Am. Psychiatric Association- 2005**

Distinguished Service Award- Indo-Am. Psychiatric Association- 2005

Distinguished Service Award- CT. Valley Hindu Temple Society- 2004

**CT. Secretary of State- Public Service Award 2003**

**Cornelius Boulehouwer, MD Award for service to the CT. Psychiatric Society** **2003**

Fellowship of the Indian Psychiatric Society

Honorary Membership of the CT. Federation of Alcoholism counselors

**Service award from Community Addictions Programs: Springfield, MA** **1977**

**Service award from Dimock Community Health Center – Alcoholism Services**

**Roxbury, MA** **1977**

**Service award - Community Council for Alcohol and Drug Abuse Prevention Middletown, CT** **1992**

**Aids Leadership Award -Nominated by Commissioner, of Public Health,**

**Hartford, CT** **1992**

# New Approach Cuts Depression, Anxiety in Dementia Caregivers

Deborah Brauser

November 26, 2014

A novel intervention may provide long-term improvement in mood levels in caregivers looking after family members with dementia, new research suggests.

A randomized trial of 209 caregivers showed that those who underwent the START (Strategies for Relatives) program had significantly better scores on the Hospital Anxiety and Depression Scale (HADS) compared with those who received treatment as usual (TAU).

In addition, START was found to be cost-effective for both the caregivers and the dementia patients they supported.

"START...improved carers' depression and anxiety symptoms and quality of life not only in the short term, but also up to 24 months later. This is the first trial to show such results," write investigators led by Gill Livingston, MD, MBChB, FRCPsych, from the Division of Psychiatry at University College London in the United Kingdom.

The study was published online November 19 in *Lancet Psychiatry*.

**Heavy Burden**

"Two-thirds of people with dementia live at home supported mainly by family carers," write the investigators, adding that approximately 40% of these caregivers have clinical depression or anxiety.

Although past studies have shown that the START program can be effective for treating caregivers, most only looked at short-term outcomes.

The current randomized, parallel-group trial was created to assess long-term clinical results and cost-effectiveness of using START to treat psychological symptoms in caregivers of family members with dementia — and to examine whether the program was also beneficial to the patients with dementia.

Between November 2009 and June 2011, 260 UK caregivers were recruited from three mental health agencies and one neurologic outpatient clinic. All participants provided patient support at least once per week; 209 were included in the final analysis.

Study participants were randomly assigned to receive either START (n = 140) or TAU (n = 69). START consisted of 8 manual-based sessions conducted during a period of 2 to 4 months and supervised by psychology graduates. The sessions touched on topics such as stress and well-being, behavioral strategies, and communication styles.

The program was developed from the US Coping with Caregiving intervention, and each session ended with a relaxation session featuring a tailored relaxation CD. All sessions were conducted in the participants' homes unless participants cited a preference for an in-office setting.

TAU, on the other hand, "was based on National Institute for Health and Care Excellence (NICE) guidelines, with services based around the person with dementia." Measures for the caregivers included total scores, depression scores, and anxiety scores on the HADS (known as HADS-T, HADS-D, and HADS-A, respectively). Higher scores signified more symptoms. The Health Status Questionnaire (HSQ) was also used to measure quality of life.

Initial results were presented this past summer at the Alzheimer's Association International Conference (AAIC) in Copenhagen, Denmark, and were reported by *Medscape Medical News* at that time.

At an on-site press conference, Dr Livingston reported that the caregivers who received TAU were seven times more likely to experience depression and anxiety than those receiving START at the end of 2 years.

The START group was "much, much less likely to be depressed than those in the nonintervention group. This was a massive, massive difference," she said.

Although overall caregiver cost for those undergoing START was £170 ($290 USD) higher than for the TAU group, overall patient costs were £571 ($975 USD) lower.

**New Results**

Additional results from the new journal article showed that the START group had a significantly better adjusted mean score on the HADS-T than the TAU group at the 24-month follow-up (mean difference, -2.58 points; 95% confidence interval [CI], -4.26 to -0.90; *P* = .003).

"Adjusted models for continuous scores" showed that, compared with TAU, START provided significant beneficial effects during a 24-month period on the HADS-A (mean difference, -1.16) and the HADS-D (mean difference, -1.45).

Scores on the HSQ-Mental Health, which measures quality of life, were also significantly improved in the START group compared with the TAU group (mean difference, 7.47; 95% confidence interval [CI], 2.87 - 12.08).

There were no between-group differences on any of the quality of life–Alzheimer's disease measures used to assess the patients.

However, the investigators note that START was cost-effective for both the caregivers and the patients, with "67% probability of cost-effectiveness at the £20,000 per QALY [quality-adjusted life year] willingness-to-pay threshold, and 70% at the £30,000 threshold."

"The number of people with dementia is rapidly growing, and policy frameworks assume that their families will remain the frontline providers of (unpaid) support," write the researchers.

"This cost-neutral intervention, which substantially improves family-carers' mental health and quality of life, should therefore be widely available."

**Enduring Benefit**

In an accompanying editorial, Sube Banerjee, MD, FRCPsych, from the Centre for Dementia Studies at Brighton and Sussex Medical School at the University of Sussex in the United Kingdom, writes that these findings were "strong and important" and show enduring benefits.

"This well conducted study addresses an important area for intervention for which the evidence base is sparse. Family carers are a vital resource for the management of people with dementia," writes Dr Banerjee.

"Although many carers derive personal satisfaction from caring, the experience can also be detrimental — physically, psychologically, and financially."

He notes that any intervention that can decrease negative outcomes should be welcomed and that START "has a strong theoretical basis."

Program benefits cited by Dr Banerjee include its being straightforward and manualized, that it can be given in a residential home by non–clinically trained individuals who are readily available, and that it is relatively low in cost.

"On the basis of these results, the START intervention should be offered as individual therapy to all family carers of people with dementia as part of the support with a timely diagnosis," he writes.

At this summer's AAIC, press conference moderator Ralph Nixon, MD, chair of the Alzheimer's Association Medical and Scientific Advisory Council, noted that the study showcases the importance of caregivers.

By preparing them for what lies ahead and teaching them necessary coping skills, START can help caregivers preserve their own mental health, which will ultimately result in better care for their dementia patients, said Dr Nixon.

*Dr Livingston, 10 of the 11 other study authors, and Dr Nixon have reported no relevant financial relationships. The remaining study author reports receiving fees, grants, and other payments from GE Healthcare and grants from Lundbeck. Dr Banerjee reports having received consultancy and speakers' fees, research funding, and education support from pharmaceutical companies that manufacture antidepressants, antidementia medications, and other drugs.*

# Just 2 Months' Exposure to Anticholinergics Affects Cognition

Pauline Anderson

May 22, 2013

Older adults using anticholinergic (AC) medications for just 2 months to manage sleep problems, urinary incontinence, and other ailments could be at increased risk of developing mild cognitive impairment (MCI), a new study suggests.

The association between AC medication use and cognition appears to depend not only on the length of exposure but also on the strength of the medication burden. The study showed that the risk for cognitive impairment was increased by 50% in adults receiving at least 3 mild ACs for more than 90 days and by 100% in those receiving 1 or more severe ACs for more than 60 days.

The results highlight the importance of limiting prescriptions for ACs in older adults and helps fill some research gaps, said study author Malaz Boustani, MD, associate director, Indiana University Center for Aging Research, and associate professor, medicine, Indiana University School of Medicine, Indianapolis.

"Before, we didn't know if you would have a problem with cognition if you were exposed to ACs for just 1 day, or if it had to be 2 days, 3 days, 5 days, 6 days," he said. "Now, we know that if you've been exposed to stronger ACs, you need 60 days, and if you were exposed to a little bit milder ACs, you need 90 days."

The study was published online in the journal *Alzheimer's & Dementia.*

## Cognitive Impairment

Participants were from the Indianapolis Dementia Screening and Diagnosis (IDSD) study, which targeted patients aged 65 years and older receiving primary care within the Wishard Health Services (WHS) system from January 2002 to October 2003.

They received a formal diagnostic assessment that included standardized neuropsychological testing, a neurologic examination, medical record review, and a structured interview. A team consisting of a psychologist, neuropsychologist, geriatrician, and geriatric psychiatrist made the final diagnosis of MCI or dementia.

Of the 3690 eligible participants, 562 were considered to have cognitive impairment requiring further evaluation, after they made at least 1 mistake on the 6-item screener that measures temporal orientation and new learning ability and then scored 24 or below on the abbreviated version of the Community Screening Instrument for Dementia, which evaluates multiple cognitive domains (language, memory, attention, and calculation, among others).

Of the 285 participants who completed the full diagnostic assessment, 129 received a diagnosis of dementia, 93 received a diagnosis of MCI, and 63 were normal.

The researchers merged the IDSD screening and diagnostic data with the Regenstrief Medical Record System, an electronic system that captures more than 85% of the drug-dispensing data of all participants receiving care within the WHS system.

A team of experts categorized medications as mild (an Anticholinergic Cognitive Burden [ACB] score of 1) or severe (an ACB score of 2 or 3). Exposure was based on the AC burden as well as on the duration of AC exposure and the number of ACs taken at the same time. Burden was categorized as no burden (receiving no drug with an ACB score), mild burden (receiving at least 1 drug with an ACB score of 1), and severe burden (receiving at least 1 drug with an ACB score of 2 or 3).

Drugs with mild AC effects were those with serum AC activity or in vitro affinity to muscarinic receptors, but no known clinically relevant negative cognitive effects. Those with established and clinically relevant cognitive AC effects were considered severe.

### Exposure Patterns

Various exposure patterns showed that duration and burden increased cognitive impairment. Holding the AC burden at an ACB of 1 and the number of medications at fewer than 3, the study found that compared with patients with an exposure time of less than 90 days, those with an exposure time of 90 days or longer had a higher rate of cognitive impairment (19.69% vs 15.07%), although the difference was not statistically significant ($P = .16$).

When the AC burden was held at an ACB of 1 but with the number of medications at 3 or more, the rates of impairment were 23.08% with exposure time of 90 days or more and 14.97% for exposure time of less than 90 days ($P = .02$).

There was a marginally significant difference for the patients with exposure time of 60 days or more vs those with less than 60 days: With an ACB of 2 or 3 and the number of medications at 1 or more, the rates of cognitive impairment were 22.5% vs 15.07% ($P$ = .05).

Receiving at least 3 mild ACs for 90 days increased the odds of having a diagnosis of MCI by more than 170%, but this exposure didn't increase the probability of dementia diagnosis. "Most of the previous studies lumped MCI and dementia together, but in our study we were able to dissect them separately," said Dr. Boustani. "We found that these medications are a risk factor for the development of MCI, but they are not risk factor for developing dementia."

We found that these medications are a risk factor for the development of MCI, but they are not risk factor for developing dementia. Dr. Malaz Boustani

MCI is potentially a reversible condition, said Dr. Boustani. He noted that other research has concluded that the probability of converting from MCI back to normal cognition within 1 year is twice that of converting from MCI to AD.

"We have the opportunity to possibly reverse MCI if we stop exposure to these definite ACs, and perhaps stop progression to a more debilitating cognitive disorder such as AD."

Physicians "absolutely" overprescribe ACs, said Dr. Boustani. Patients might push for these drugs in the belief that if they simply take a pill, their symptoms will go away. Also, physicians typically don't have the time to discuss medication alternatives with individual patients. "They take the easy way out, which is to just simply spend 10 seconds writing a prescription," said Dr. Boustani.

## Alternative Approaches

**When possible, physicians should substitute AC medications with those that have fewer cognitive adverse effects or with nonpharmacologic alternatives, said Dr. Boustani. For example, he said, instead of taking oxybutynin (*Ditropan*, Janssen Pharmaceuticals) to treat urinary incontinence, patients could try pelvic exercise, biofeedback, and scheduled toileting.**

For sleep problems, instead of "jumping" straight to diphenhydramine (*Benadryl PM*, McNeil-PPC), they might use sleep hygiene tactics, such as having a quiet, dim sleeping area and avoiding alcohol and other stimulants before bed, or they might use alternative non-AC sleep aids. And patients with peripheral neuropathy might take gabapentin (*Neurontin*, Pfizer) instead of nortriptyline.

All too often, said Dr. Boustani, patients continue to take AC medications even when they're not working.

A **limitation of the study was the presence of undetected cases of dementia or MCI in the cognitively normal group. The study also did not systematically measure medication adherence or include AC burden from over-the-counter medications and did not account for possible confounding factors, such as socioeconomic status, education level, depressive symptoms, *APOE* genotype, and alcohol and tobacco use. There is also the "remote" possibility that patients with unrecognized cognitive symptoms might be treated more with ACs, said the authors.**

Asked for his views of the study, Chris Fox, MD, Dementia Research Innovation Group, Norwich School of Medicine, United **Kingdom, who has researched ACs in dementia, noted that it's the first to look at the threshold of time exposure to medicines with AC effects.**

However, he said, while the study found that 3 months of exposure increases the risk for MCI, "we do not know from this data whether this leads to increased risk of more persistent cognitive impairment."

**To address that question, said Dr. Fox, 3 things are needed: a larger sample size, longer duration of follow-up, and better methods of assessing whether people prescribed these medicines are actually taking them.**

*Dr. Boustani was supported by the Paul A. Beeson Career Development Award in Aging from the National Institute on Aging, the Hartford Foundation, the Atlantic Philanthropy, and the American Federation of Aging Research. Dr. Fox has disclosed no relevant financial relationships.*

*Alzheimer's & Dementia*. Published online November 26, 2012. Abstract

# Benzodiazepine Use Linked to Dementia Risk

Megan Brooks

October 02, 2012

October 2, 2012 — Older adults who use benzodiazepines have about a 50% greater chance of developing dementia than their peers who don't use benzodiazepines, French researchers observed in a large population-based study.

This finding, added to evidence of increased risk for falls and fractures in elderly who use benzodiazepine, "should incite (health providers) to carefully assess expected benefits versus putative risks, and to limit prescriptions to a few weeks," lead author of the study and PhD student Sophie Billioti de Gage, PharmD, from the University of Bordeaux Segalen in France, told *Medscape Medical News*.

"In any case, uncontrolled use should be cautioned against," she said.

The study was published online September 27 in the *British Medical Journal*.

**"Bad Drugs for Older Adults"**

Greg A. Sachs, MD, who reviewed the study for *Medscape Medical News*, said it is "yet another study that suggests that benzodiazepines are bad drugs for older adults."

Dr. Sachs is chief of the Division of General Internal Medicine and Geriatrics, Indiana University School of Medicine, and investigator at the IU Center for Aging Research, Regenstrief Institute, Indianapolis. He was not involved in the study.

"Many of these drugs," Dr. Sachs said, "are on 'Do Not Prescribe' lists for older adults. If used at all, they should be used for short periods of time (10 days or less) and in the lowest dose possible to achieve benefit for the target symptom." Benzodiazepines "should not be used long term for either sleep or anxiety; safer alternatives exist."

The analysis included 1063 men and women (mean age, 78.2 years) from the PAQUID (Personnes Agées Quid) project, a prospective, population-based study of cognitive aging and dementia involving a total of 3777 participants from France. The study started in 1987 and follow-up lasted 20 years, with clinic visits every 2 to 3 years.

All participants in the current analysis were free of dementia at the outset and did not start taking benzodiazepines until at least the third year of follow-up. Ninety-five (8.9%) reported benzodiazepine use at the 5-year visit, indicating new use between years 3 and 5. Year 5 was baseline for the analysis.

During the 15-year follow-up period, 253 (23.8%) cases of dementia were confirmed: 30 (32%) in benzodiazepine users and 223 (23.0%) in nonusers.

The 15-year incidence rate of dementia per 100 person-years was higher in benzodiazepine users than nonusers (4.8 vs 3.2).

The multivariable adjusted hazard ratio (HR) for dementia with new use of benzodiazepines was 1.60 (95% confidence interval [CI], 1.08 - 2.38). This result was unchanged when further adjusted for depressive symptoms (HR, 1.62; 95% CI, 1.08 - 2.43).

The result "remained robust" in a secondary pooled analysis of patients who initiated a benzodiazepine between follow-up visits 8 and 15 (HR, 1.46; 95% CI, 1.10 - 1.94). This added a total of 116 additional new users during follow-up to the 95 new users at year 5.

Similarly, in a nested-case control study (467 case-patients with dementia and 1810 controls), the adjusted odds ratio (OR) with ever use vs never use was 1.55 (95% CI, 1.24 - 1.95). The results were similar in past users (OR, 1.56; 95% CI, 1.23 - 1.98) and recent users (OR, 1.48; 95% CI, 0.83 - 2.63).

The PAQUID investigators say their findings are consistent with 3 recent case-control studies that found an increased risk for dementia in benzodiazepine users.

Two of the studies from Taiwan (Wu et al, 2011, Wu et al, 2009) used health insurance data and showed an increased risk for dementia in long-term users ( > 6 months; adjusted OR, 1.24; 95% CI, 1.01 - 1.53) and current users (adjusted OR, 2.71; 95% CI, 2.46 - 2.99).

The third study, a nested case-control study among French people, found an increased risk for dementia in former users (adjusted OR, 2.3; 95% CI, 1.2 - 4.5).

Other studies, however, have not found an increased risk for dementia among elderly people using benzodiazepines.

Dr. Billioti de Gage told *Medscape Medical News* that "contrary to most of the previous study on the topic, our study is based on a long period of follow-up (up to 15 years) and was carried out in a large representative cohort of elderly participants. This allows to take into account the somewhat long prodromal period of dementia and to generalize the conclusions."

**"Positive Distinguishing Factors"**

Dr. Sachs said there are several "positive distinguishing factors about this study." It was large; it followed patients over many years with little dropout; it was prospective and longitudinal rather than cross-sectional; the diagnosis of dementia involved both neuropsychological testing and examination by a neurologist; and the researches had excellent information about drug use from patients, he explained.

The exclusion of people who were already receiving benzodiazepines at time of study entry and for a period of a few years "run in" is another key strength, he said.

"This is important regarding the notion of 'reverse causation' — that people could end up taking benzodiazepines because of symptoms of depression or anxiety that are early symptoms relating to a developing dementia. Without doing that, it could bias the study toward people with dementia already brewing getting benzodiazepines at a higher rate, instead of the notion that it is contributing to dementia development," Dr. Sachs said.

The analyses were "carefully done" and the findings were "explored and confirmed using more than one approach. The PAQUID study is one of the higher quality cohort studies examining dementia," he added.

Dr. Billioti de Gage said, "patients should be told about the potential adverse effects of these drugs, including long-term risk when initiating benzodiazepines and about the necessity of gradual discontinuation when stopping the treatment."

She and her colleagues say further study is needed to determine whether long-term use of benzodiazepines in people younger than age 65 years is also associated with an increased risk for dementia and uncover possible correlations between dosage or cumulative length of exposure and dementia.

Dr. Sachs agrees. The analysis "cannot tell us anything about long versus short acting meds, specific meds, dose, or duration of therapy," he told *Medscape Medical News*. Also, the small numbers of people on benzodiazepines in the study is a limitation, he added.

Another limitation, he said, is that the analysis is primarily focused on "ever use" of benzodiazepines, "and that means we do not have information here on whether stopping the meds would help prevent dementia. In fact, because of the 'ever use' approach to analysis, I'd be concerned that someone misinterpret this and think 'why bother stopping' once someone has been exposed."

Dr. Sachs also noted that "far greater numbers of people who developed dementia had not been exposed to benzodiazepines than those who had; so while it increases relative risk, how much it contributes to development of dementia should not be overplayed; this still was an observational study, so assigning causation is hard to do no matter how well the study is done."

*This research was conducted by the INSERM U657 research team co-funded by INSERM (Institut National de la Santé et de la Recherche Médicale) and Université Bordeaux Segalen. Additional support was provided by a 2010 grant from IRESP (Institut de Recherche en Santé Publique) acting on behalf of the French Ministry of Health (Direction Générale de la Santé, Direction de la Recherche, des Études, de l'Évaluation et des Statistiques); by a 2011 grant from the French Ministry of Health (Direction Générale de la Santé); and by Caisse Nationale des Travailleurs Salariés, Régime Social des Indépendants, Caisse Nationale de Solidarité pour l'Autonomie, and Institut National de Prévention et d'Education pour la Santé. SBdG is a part-time researcher in the INSERM 657 Unit, and her salary is paid by IRESP.*

*BMJ*. Published online September 27, 2012. Abstract

# Sex and Dementia: Is it Love or Assault?

Arthur L. Caplan,

April 16, 2015

Hi. I'm Art Caplan, from the Division of Medical Ethics at the NYU Langone Medical Center.

**Not long ago, a 78-year-old man in Iowa, a representative for that state in the House of Congress, was arrested and charged after being accused of having sex with his wife.[1] That may seem startling and unusual, but the circumstances make it clear why this has happened, and they raise some important ethical issues that physicians and healthcare teams are going to have to wrestle with.**

This gentleman had remarried late in life to a woman also in her 70s, and they spent a lot of time together and loved each other and things were fine. But, sadly, she was diagnosed with Alzheimer disease. That forced her ultimately to go into a nursing home. And the husband did not leave her or divorce her, and it was clear that he still wanted to maintain intimacy with her.

**During one of his visits to his wife in the nursing home, her roommate said she heard "sexual' noises" and reported that she thought he probably had had sex with his wife.[2]**

**His daughter-in-law wanted that followed up and examined. The daughter-in-law was very upset. The ethical issue is not when does "no" mean "no," but rather, what if you can't say "yes"?[2]**

**This issue is a growing problem for all of us in the United States because Alzheimer's-one of our most feared and dreaded diseases-is starting to afflict more and more people. We're starting to be able to diagnose it with better tests. And soon, I think, we'll have some better scanning information about early-onset Alzheimer's even before symptoms occur.**

Because Alzheimer's is becoming so prevalent, physicians have to come up with a better plan for managing the disease. One sad fact is that a lot of doctors don't feel comfortable revealing the diagnosis, or suspicion, of Alzheimer's to their patients.[3] In fact, a 2008 analysis showed that only 40% of doctors regularly disclose the diagnosis of Alzheimer's to their patients.[4]

**It is certainly acceptable to say that you don't want to deliver bad news all at once. With a disease for which we don't really have any current cures, it may take a few visits-information being given out over time-to let the patient know what's going on.**

**I do strongly believe that patients do need to know the diagnosis. They're not going to know how to make plans for the time they have. Their family members have to make arrangements and decide how they want to manage. And, as we've seen with the case of the gentleman under arrest, there are going to be some important questions about what life will be like when competency begins to fail.**

**Could a person and should a person say, while they're still competent but suspected of having Alzheimer's, "Look-here is what I want you to play on television. And this is the relationship I want to have with my husband: If he still wants to have relations with me, then that's great. Let him. Let's do that in a private area-let's make sure we make some provision for that. If it's something that would hurt me or cause me to be physically harmed in some way, if I become fragile or develop fragile bones, then we should not allow that to happen."**

That discussion, as tough as it is, is something that should take place before a person becomes incompetent. People need to know the truth about Alzheimer's, and they need to be able to plan for it.

They need to decide the following:

- What do they want to do in terms of their relationships with their loved ones?
- Who is going to take care of them?
- Where would they want to go?
- How do they want to manage their end-of-life care should they get illnesses or diseases that threaten their ability to live? Do they want aggressive treatment, or don't they?

- Would they want to be in experimental trials?

- Many new drugs are starting to appear, we're hopeful for at least slowing some of the symptoms and dysfunction of Alzheimer's. Do they want to be given those, or do they not want to be involved with that? Does cost matter?

So there is a lot to talk about. We're not going to be able to talk about any of this unless you get to the point where you're comfortable, somehow, with disclosing and discussing that diagnosis.

As I say, just dumping the information on a person who is fragile may not be the way to go. Maybe the talk has to happen with other family members or a trusted friend present. Maybe you want to urge the person to come back for a second visit, saying "I want to reconfirm something," just to make sure they're not overwhelmed.

**And you've got to be ready to support them and counsel them about steps that they need to take and things they need to start thinking about-everything from sex to where they live, to how they are going to have their medical care given or not given in the time that remains for them.**

**This is Art Caplan at the Division of Medical Ethics at NYU. Thanks. Please leave your comments below.**

- References

# Eating More Carbs May Signal Frontotemporal Dementia

Pauline Anderson

December 22, 2014

If older patients are suddenly craving sweets, gaining weight, and developing swallowing difficulties, consider a diagnosis of frontotemporal dementia (FTD), a new study suggests.

Results show that patients with certain types of FTD eat significantly more carbohydrates and sugar than healthy controls or those with Alzheimer's disease (AD), and that these changes don't appear to be explained by being hungrier.

Patients presenting with such eating behaviors should raise a red flag, study author Olivier Piguet, PhD, associate professor, University of New South Wales, and Principal Research Fellow, Neuroscience Research, Australia, told *Medscape Medical News*.

"Someone in their 50s or early 60s showing these changes in eating preferences and the amount of food that they eat would certainly indicate that something might be going on in their brain that needs exploring further."

The study, published in the December issue of *JAMA Neurology*, is the first to quantify abnormal eating behaviors in patients with FTD, said Dr Piguet.

**Eating Disturbance**

"Changes in eating behavior are part of the criteria for the diagnosis of behavior variant FTD, but no one has really looked at exactly what that means," said Dr Piguet. "This study is really the first one to try to measure what it means when we say these patients have an eating disturbance."

The analysis included 75 patients with dementia: 21 with personality or behavioral disturbance (behavioral variant FTD [bvFTD]), 26 with language disturbances (semantic dementia or SD), and 28 with AD, as well as 18 age- and education-matched healthy controls.

Caregivers completed the Appetite and Eating Habits Questionnaire (APEHQ), which includes 34 questions examining changes in eating behaviors with regard to swallowing, appetite, eating habits, food preferences, and other oral behaviors (eg, eating objects such as cigarette butts). For each question, researchers calculated a composite score that included frequency and severity and derived an overall score for each domain.

Investigators found the bvFTD group had significantly higher scores than the AD group for all 5 APEHQ domains: swallowing ($P = .003$), appetite change ($P = .007$), eating habits ($P = .001$), food preferences ($P = .001$), and other oral behaviors ($P = .009$).

Caregivers also completed the Cambridge Behavioral Inventory, which includes four questions related to eating behaviors: sweet preference, eating the same foods, changes in appetite, and table manners.

The table manners item was included because of anecdotal evidence that patients with behavioral disturbances lose this etiquette. "Caregivers will report that 'my husband is stealing food from someone else's plate' or piling up food on their plate," said Dr Piguet.

There were significantly greater changes related to sweet preference ($P < .001$), eating the same foods ($P = .001$), and table manners ($P = .007$) in the bvFTD group compared with the AD group.

Some of the findings were unexpected.

"The finding that the behavior variant patients changed their preferences in terms of the foods they like and their tendency to focus more on sweet foods confirms something we knew already, although we were able to quantify that," commented Dr Piguet. "But we also found that this tendency to prefer sweet foods was also present in the group with semantic dementia, which was surprising."

Although patients with semantic dementia increased their carbohydrate intake to some degree, the increase among those with bvFTD was "more prominent," said Dr Piguet, "again confirming anecdotal evidence that we were able to measure with the questionnaire."

Caregivers also measured patients' level of hunger and satiety using a visual analogue scale before and after meals during a 24-hour period (with higher scores indicating more hunger). The bvFTD group had a significantly higher overall hunger-satiety index score than the semantic dementia ($P$ = .02) and AD ($P$ = .03) groups, but not the control group ($P$ = .38).

These results suggest that "these patients don't eat because they feel full," but simply because "the food is there and they eat it," said Dr Piguet.

**Weight Concerns**

The bvFTD and SD groups had significantly greater waist circumference compared with the control group, and the bvFTD group had significantly greater waist circumference compared with those with AD.

These patients, said Dr. Piguet, are "getting into the danger zone" with body mass indexes "hovering around the 30 mark, which raises concerns about their general health, their cardiovascular health and risks for related illnesses such as diabetes."

An earlier paper by the same research group found atrophy in the hypothalamus — the area of the brain that plays a central role in eating regulation — in patients with FTD, said Dr Piguet. "The brain is receiving incorrect messages from the periphery in terms of hunger and satiety and is then responding to these messages in an incorrect manner."

The changes, he added, can lead to disordered behavior when it comes to eating. "These patients tend to want to eat the food that they have in front of them; they have difficulty in inhibiting or stopping their eating."

In FTD, atrophy predominantly affects the frontal lobes and temporal brain areas; in AD, in contrast, other brain regions are affected. "You rarely see these behavior changes in patients with AD," noted Dr Piguet.

Reached for comment on these findings, Ronald Petersen, MD, PhD, director, Mayo Alzheimer's Disease Research Center, Mayo Clinic, Rochester, Minnesota, said the study results illustrate disinhibition on the part of patients with bvFTD.

"Foods that are sweet are very attractive to most of us, and people with bvFTD lack the ability to deny themselves the pleasure," said Dr Petersen. "They can't reason that this type of excessive ingestion of sweets will lead to weight gain and other health consequences."

These patients, he added, lack the ability to foresee the consequences and act impulsively. "This is due to frontal lobe dysfunction since that part of the brain is involved in our ability to judge the consequences of behavior."

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*JAMA Neurol*. 2014;71:1540-1546. Abstract

# Medical News Today

## Fast facts about Alzheimer's

- More than 5 million people in the US are living with Alzheimer's, and this number is expected to rise to as many as 16 million by 2050
- Alzheimer's is the sixth leading cause of death in the US
- More than two thirds of Americans with Alzheimer's are women.

## How common is Alzheimer's disease?

In the US, the most recent census has enabled researchers to give **estimates** of how many people have Alzheimer's disease. In 2010, some 4.7 million people of 65 years of age and older were living with Alzheimer's disease in the US.[1]

The **2013 statistical report** from the Alzheimer's Association gives a proportion of the population affected - **just over a tenth of people in the over-65 age group have the disease in the US. In the over-85s, the proportion goes up to about a third.**[2]

As our **dementia** page outlines, there is a handful of different types, but Alzheimer's disease is the problem behind most cases of memory loss and cognitive decline:[2]

**The Alzheimer's Association says it accounts for between 60% and 80% of all cases of dementia. Vascular dementia, which is caused by stroke not Alzheimer's, is the second most common type of dementia.**

## What causes Alzheimer's disease?

Like all types of dementia, Alzheimer's is caused by brain cell death.[3] It is a neurodegenerative disease, which means there is progressive brain cell death that happens over a course of time.

**The total brain size shrinks with Alzheimer's - the tissue has progressively fewer nerve cells and connections**.[3,4]

While they cannot be seen or tested in the living brain affected by Alzheimer's disease, postmortem/autopsy will always show tiny inclusions in the nerve tissue, called plaques and tangles:[3,4]

- **Plaques are found between the dying cells in the brain - from the build-up of a protein called beta-amyloid (you may hear the term "amyloid plaques").**
- **The tangles are within the brain neurons - from a disintegration of another protein, called tau.**

For a detailed visualization of what goes on in the Alzheimer's disease process, progressing from the normal brain to increasing dementia changes, the Alzheimer's Association has produced a journey of 16 slides. See the illustrations: **Inside the brain: an interactive tour.**

The abnormal protein clumps, inclusions, in the brain tissue are always present with the disease, **but there could be another underlying process that is actually causing the Alzheimer's - scientists are not yet sure.**[3]

This sort of change in brain nerves is also witnessed in other disorders,[3] and researchers want to find out more than just that there are protein abnormalities - they also want to know how these develop so that a cure or prevention might be discovered.

## Risk factors

Some things are more commonly associated with Alzheimer's disease - not seen so often in people without the disorder. These factors may therefore have some direct connection. **Some are preventable or modifiable factors (for example**, reducing the risk of **diabetes** or **heart disease** may in turn cut the risk of dementia).

If researchers gain more understanding of the risk factors, or scientifically prove any "cause" relationships for Alzheimer's, this could help to find ways to prevent it or develop treatments.

Risk factors associated with Alzheimer's disease include:[5,6]

***Unavoidable risk factors***

- Age - the disorder is more likely in older people, and a greater proportion of over-85-year-olds have it than of over-65s.[2]
- Family history (inheritance of genes) - having Alzheimer's in the family is associated with higher risk. This is the second biggest risk factor after age.[7]
- Having a certain gene (the apolipoprotein E or APOE gene) puts a person, depending on their specific genetics, at three to eight times more risk than a person without the gene.[6] Numerous other genes have been found to be associated with Alzheimer's disease, even recently (see developments below).[7]
- Being female (more women than men are affected).

***Potentially avoidable or modifiable factors***

- Factors that increase blood vessel (vascular) risk - including diabetes, high **cholesterol** and **high blood pressure**. (These also increase the risk of stroke, which itself can lead to another type of **dementia**.)
- Low educational and occupational attainment.
- Prior head injury. (While a **traumatic brain injury** does not necessarily lead to Alzheimer's, some research links have been drawn, with increasing risk tied to the severity of trauma history.)[8]
- **Sleep disorders (the breathing problem sleep apnea, for example).**
- **Estrogen** **hormone replacement therapy**.
- Anticholinergic Drug Use[VM]
- Benzodiazepine Drug Use[VM]

## Early-onset Alzheimer's disease

Genetics are behind early-onset familial Alzheimer's disease, which presents typically between the ages of 30 and 60 years and affects people who have a family history of it.

**Due to one of three inherited genes, it is also known as young-onset, and it is uncommon - accounting for under 5% of all Alzheimer's cases.**[6,9]

The Alzheimer's Association says in its **early-onset information** that it can sometimes be "a long and frustrating process" to get this diagnosis confirmed since doctors do not expect to find Alzheimer's in younger people. For the younger age groups, doctors will look for other dementia causes first. Healthcare professionals, the nonprofit says, may also "incorrectly attribute" symptoms to **stress** and so on, or may not agree on the diagnosis.[10]

## Recent developments in understanding causes and risk factors from MNT news

**Eleven new Alzheimer's risk genes** have been identified. The findings, published in ***Nature Genetics*** in **October 2013**, **mean the total number of genes found to be associated with Alzheimer's disease was 21.** Large research collaborations resulted in the breakthrough to help understand genetic factors behind the dementia. Just over 70,000 individuals were analyzed, **comparing the genes of 25,580 people who had Alzheimer's against 48,466 healthy controls, enabling the scientists to pinpoint genes that may put people at higher risk.**

**Alzheimer's onset could be triggered by sleep disturbances** - **Chronic sleep problems can inflame a number of health problems, from widespread pain to speeding up Cancer**. Though sleep disturbances have been observed in people with Alzheimer's disease, whether this is a cause or effect has been unknown. Now, **researchers say individuals with chronic sleep disruptions could face earlier onset of Alzheimer's.** Their pre-clinical study was published in the journal *Neurobiology of Aging*.

**DNA methylation in brain 'linked to Alzheimer's disease'** - **DNA methylation - the biochemical alteration of the building blocks of DNA - can indicate whether DNA is biologically active within a region of the human genome.** Now, researchers at Brigham and Women's Hospital in Boston, MA, and Rush University Medical Center in Chicago, IL, **have demonstrated how DNA methylation in the brain is implicated in Alzheimer's disease.**

**Increased Alzheimer's risk linked to long-term benzodiazepine use** - Long-term users of benzodiazepines, drugs used to treat **anxiety** and **insomnia**, **may be at increased risk of developing Alzheimer's disease, according to a new study published in the *BMJ*.**

**Brain network vulnerable to Alzheimer's and schizophrenia identified** - **New research has emerged that reveals a specific brain network - that is the last to develop and the first to show signs of neurodegeneration - is more vulnerable to unhealthy aging as well as to disorders that emerge in young people, shedding light on conditions such as Alzheimer's disease and schizophrenia.**

## Signs and symptoms

**The information in this section connects closely to some of that about tests and diagnosis below because symptoms noticed by patients, or people close to them, are exactly the same signs that healthcare professionals look for during testing.**

Symptoms can be diagnosed at any stage of Alzheimer's dementia and the **progression through the stages of the disease is monitored after an initial diagnosis, too, when the developing symptoms dictate how care is managed.**

Of course, the very nature of the symptoms can be confusing for both a patient and the people around them, with different levels of severity. For this reason, and because symptoms could signal any of a number of diagnoses, it is always worthwhile seeing a doctor.

For doctors to make an initial diagnosis of Alzheimer's disease, they must first be satisfied that there is **dementia** - **guidelines spell out what dementia consists of. It involves cognitive or behavioral symptoms that show a decline from previous levels of "functioning and performing" and interfere with ability "to function at work or at usual activities."**[11]
The cognitive decline is in at least **TWO** of the five symptom areas listed below (from **guidelines** jointly produced by the National Institute on Aging and the Alzheimer's Association):[11]

## What is Alzheimer's disease? Causes, symptoms and treatment

Last updated: Monday 23 February 2015

**1. Worsened ability to take in and remember new information, for example:**

- "Repetitive questions or conversations
- Misplacing personal belongings
- Forgetting events or appointments
- Getting lost on a familiar route."

**2. Impairments to reasoning, complex tasking, exercising judgment:**

- "Poor understanding of safety risks
- Inability to manage finances
- Poor decision-making ability
- Inability to plan complex or sequential activities."

**3. Impaired visuospatial abilities (but not, for example, due to eye sight problems):**

- "Inability to recognize faces or common objects or to find objects in direct view
- Inability to operate simple implements, or orient clothing to the body."

**4. Impaired speaking, reading and writing:**

- "Difficulty thinking of common words while speaking, hesitations
- Speech, spelling, and writing errors."

**5. Changes in personality and behavior, for example:**

- Out-of-character mood changes, including agitation; less interest, motivation or initiative; apathy; social withdrawal
- Loss of empathy
- Compulsive, obsessive or socially unacceptable behavior.

**Once the number and severity of these example symptoms confirm dementia, the best certainty that they are because of Alzheimer's disease is given by:**

- **A gradual onset "over months to years" rather than hours or days** (the case with some other problems)
- **A marked worsening of the individual person's normal level of cognition in particular areas.**[11]

**The most common presentation marking Alzheimer's dementia is where symptoms of memory loss are the most prominent, especially in the area of learning and recalling new information.** But the initial presentation can also be one of mainly language problems, in which case the greatest symptom is struggling to find the right words.[11]

**If visuospatial deficits are most prominent, meanwhile, these would include inability to recognize objects and faces, to comprehend separate parts of a scene at once (simultanagnosia),** and a type of difficulty with reading text (alexia). Finally, the most prominent deficits in "executive dysfunction" would be to do with reasoning, judgment and problem-solving.[11]

## Stages of Alzheimer's disease

**The progression of Alzheimer's can be broken down into three basic stages**:[12]

- Preclinical (no signs or symptoms yet)
- Mild cognitive impairment
- Dementia.

**The Alzheimer's Association has broken this down further, describing seven stages along a continuum of cognitive decline based on symptom severity - from a state of no impairment, through mild and moderate decline, and eventually reaching "very severe decline."**

The association has published the **seven stages** online.[13] It is not usually until stage four that a diagnosis is clear - here it is called mild or early-stage Alzheimer's disease, and "a careful medical interview should be able to detect clear-cut symptoms in several areas."

**Alzheimer's disease typically progresses slowly in three general stages — mild (early-stage), moderate (middle-stage), and severe (late-stage).** Since Alzheimer's affects people in different ways, each person will experience symptoms - or progress through Alzheimer's stages - differently.

## Overview of disease progression

The symptoms of Alzheimer's disease worsen over time, although the rate at which the disease progresses varies. On average, a person with Alzheimer's lives four to eight years after diagnosis, but can live as long as 20 years, depending on other factors.

Changes in the brain related to Alzheimer's begin years before any signs of the disease. This time period, which can last for years, is referred to as preclinical Alzheimer's disease.

The stages below provide an overall idea of how abilities change once symptoms appear and should only be used as a general guide. They are separated into three different categories: mild Alzheimer's disease, moderate Alzheimer's disease and severe Alzheimer's disease. Be aware that it may be difficult to place a person with Alzheimer's in a specific stage as stages may overlap

### Mild Alzheimer's- Early Stage

In the early stages of Alzheimer's, a person may function independently. He or she may still drive, work and be part of social activities. Despite this, the person may feel as if he or she is having memory lapses, such as forgetting familiar words or the location of everyday objects.

Friends, family or neighbors begin to notice difficulties. During a detailed medical interview, doctors may be able to detect problems in memory or concentration. Common difficulties include:

- Problems coming up with the right word or name
- Trouble remembering names when introduced to new people
- Having greater difficulty performing tasks in social or work settings
- Forgetting material that one has just read
- Losing or misplacing a valuable object
- Increasing trouble with planning or organizing.

Although the onset of Alzheimer's disease cannot yet be stopped or reversed, an early diagnosis can allow a person the opportunity to live well with the disease for as long as possible and plan for the future.

## Moderate Alzheimer's disease-Middle Stage

Moderate Alzheimer's is typically the longest stage and can last for many years. As the disease progresses, the person with Alzheimer's will require a greater level of care.

You may notice the person with Alzheimer's confusing words, getting frustrated or angry, or acting in unexpected ways, such as refusing to bathe. Damage to nerve cells in the brain can make it difficult to express thoughts and perform routine tasks.

## At this point, symptoms will be noticeable to others and may include:

- Forgetfulness of events or about one's own personal history
- Feeling moody or withdrawn, especially in socially or mentally challenging situations
- Being unable to recall their own address or telephone number or the high school or college from which they graduated
- Confusion about where they are or what day it is
- The need for help choosing proper clothing for the season or the occasion
- Trouble controlling bladder and bowels in some individuals
- Changes in sleep patterns, such as sleeping during the day and becoming restless at night
- An increased risk of wandering and becoming lost
- Personality and behavioral changes, including suspiciousness and delusions or compulsive, repetitive behavior like hand-wringing or tissue shredding

During the moderate stage of Alzheimer's, individuals may have greater difficulty performing tasks such as paying bills, but they may still remember significant details about their life.

## Severe Alzheimer's Disease- [Late Stage]

In the final stage of this disease, individuals lose the ability to respond to their environment, to carry on a conversation and, eventually, to control movement. They may still say words or phrases, but communicating pain becomes difficult. As memory and cognitive skills continue to worsen, personality changes may take place and individuals need extensive help with daily activities.

### At this stage, individuals may:

- Require full-time, around-the-clock assistance with daily personal care
- Lose awareness of recent experiences as well as of their surroundings
- Require high levels of assistance with daily activities and personal care
- Experience changes in physical abilities, including the ability to walk, sit and, eventually, swallow
- Have increasing difficulty communicating
- Become vulnerable to infections, especially pneumonia

### Supporters need to Get support at regular intervals

Late-stage care decisions can be some of the hardest families face. Connect with other caregivers who have been through the process on our online message boards and get helpful resources in our Caregiver Center.

#### Help is available

Your local Alzheimer's Association chapter can connect you with the resources you need to cope with the symptoms and challenges of Alzheimer's. Find a chapter in your community

Our free 24/7 Helpline provides information, referral and care consultation by professionals in more than 200 languages.

Our Greenfield Library houses more than 5,000 books, journals and resources. Access it online.

# Tool May Help Detect, Monitor Multiple Symptoms of Aging

Megan Brooks

January 09, 2015

A new tool may provide a simple and reliable way to detect and monitor cognitive, functional, and psychological symptoms in aging adults, according to the tool's developers, who are from the Regenstrief Institute and Indiana University Center for Aging Research, in Indianapolis.

The Healthy Aging Brain Care (HABC) Monitor "helps busy physicians accurately measure and monitor the severity of symptoms, providing valuable information that the patient's entire care team needs," Malaz Boustani, MD, MPH, notes in a statement.

"We have been using this tool in the Eskenazi Health System for more than 2 years," Dr Boustani, medical director of the Eskenazi Health Healthy Aging Brain Center, in Indianapolis, told *Medscape Medical News.*

"We use it every time the patient comes to the clinic, just like you'd take a patient's blood pressure at every visit. I can compare it with the last visit, and I have a dashboard to track the numbers and decide if my care plan is working or if I should make modifications," he said.

**Quick and Easy**

The HABC Monitor includes 27 items on a 4-point scale to assess cognitive, functional, and psychological symptoms. There are self-report and caregiver versions, which can be completed online or with paper and pencil in 2 to 3 minutes. The tool asks caregivers and patients questions such as, during the past 2 weeks, how often have you (or your loved one) had problems with the following:

- Repeating the same things over and over, such as questions or stories
- Forgetting the correct month or year
- Handling complicated financial affairs, such as balancing a checkbook, income taxes, and paying bills
- Planning, preparing, or serving meals
- Taking medications in the right dose at the right time
- Walking or physical ambulation
- Taking less interest or pleasure in doing things, hobbies, or activities
- Feeling anxious, nervous, tense, fearful, or panic
- Hearing voices, seeing things, or talking to people who are not there
- Wandering, pacing, or doing things repeatedly

Dr Boustani and colleagues previously validated the caregiver report version of the HABC Monitor for measuring and monitoring symptoms (Monahan et al, *Clin Interv Aging*. 2012;7:143-157).

In an article published online December 5 in *Clinical Interventions in Aging*, they report a validation study of the patient self-report version of the tool.

Participants included 291 adults aged 65 years and older from Eskenazi Health primary care clinics; 56% were African-American, and 76% were women.

The researchers note that the self-report version of the HABC Monitor demonstrated "good reliability and validity as a clinically practical multidimensional tool for assessing and monitoring symptoms of older adults attending primary care clinics."

The self-report tool performed equally well as the caregiver report tool. However, if a patient self-reports a perfect cognitive score, the researchers note that further testing should be performed to rule out the possibility that the patient is denying or is unaware of their cognitive symptoms.

A lack of longitudinal data to estimate test-retest reliability of the self-report version during brief periods or to test sensitivity to change during longer periods is a limitation of the current study, the researchers note.

A future study should assess the sensitivity to change of the self-report version to that of "valid but lengthier" tools, such as the Neuropsychiatric Inventory, they suggest.

**Beneficial Concept**

Commenting for *Medscape Medical News*, Keith Fargo, PhD, director of scientific programs and outreach at the Alzheimer's Association, said, "This research is about early and accurate detection and cognitive assessment, and the Alzheimer's Association is supportive of ongoing research in that area. This concept of ongoing assessment and evaluation of a person's cognitive state is a beneficial concept, and there is a need for this kind of tool [to be] used under the supervision of a healthcare professional."

Dr Fargo noted that the Alzheimer's Association "for several years now has been making efforts toward having cognitive assessment included, for example, in the Medicare annual wellness visit, because we do think it's important for physicians to have a baseline on all of their patients and then be able to track that over time to see whether there is a deviation from that baseline so they can intervene as early as possible."

*The study was funded by the National Institute of Mental Health and the National Institute on Aging. The HABC Monitor is copyrighted by Dr Boustani, two colleagues, and the Indiana University School of Medicine. The authors have disclosed no relevant financial relationships.*

*Clin Interv Aging.* 2014;9:2123-2132. Full text

Medscape
Reuters Health Information

# The State of Senior Health: It Depends on Your State

By Mark Miller

June 25, 2014

CHICAGO (Reuters) - What are the best and worst places to stay healthy as you age? **For answers, take out a map and follow the Mississippi River from north to south. The healthiest people over 65 are in Minnesota, the sickest in Mississippi.**

That's among the findings of the America's Health Rankings Senior Report released in May by the United Health Foundation. **The report ranks the 50 states by assessing data covering individual behavior, the environment and communities where seniors live, local health policy and clinical care.**

Minnesota took top honors for the second year in a row, ranking high for everything from the rate of annual dental visits, volunteerism, high percentage of quality nursing-home beds and low percentage of food insecurity. **This year's runners-up are Hawaii, New Hampshire, Vermont and Massachusetts.** (See how your state fared here: http://bit.ly/1pdwTUS).

The researchers base their rankings on 34 measures of health. But here's one you won't find in the report: state compliance with the Affordable Care Act (ACA). While the health reform law isn't mainly about seniors, it has one important feature that can boost the health of lower-income older people: the expansion of Medicaid.

The ACA aims to expand health insurance coverage for low-income Americans through broadened Medicaid eligibility, with the federal government picking up 100% of the tab for the first three years (2014-2016) and no less than 90% after that. But when the U.S. Supreme Court affirmed the ACA's legality in 2012, it made the Medicaid expansion optional, and 21 states have rejected the expansion for ideological or fiscal reasons.

And guess what: **Most of the states with the worst senior health report cards also rejected the Medicaid expansion.**

**Nearly all Americans over age 65 are covered by Medicare. But the Medicaid expansion also is a key lever for improving senior health because it extends coverage to older people who haven't yet become eligible for Medicare**. That means otherwise uninsured low-income seniors are able to get medical care in the years leading up to age 65 - and they are healthier when they arrive at Medicare's doorstep.

**Two studies from non-partisan reports verify this. The U.S. Government Accountability Office reported late last year that seniors who had continuous health insurance coverage in the six years before enrolling in Medicare used fewer and less costly medical services during their first six years in the program; in their first year of Medicare enrollment, they had 35% lower average total spending.**

The GAO study confirmed the findings of a 2009 report by two researchers at the Harvard Medical School. **That study looked at individuals who were continuously or intermittently uninsured between age 51 and 64; these patients cost Medicare an additional $1,000 per person due mainly to complications from cardiovascular disease, diabetes and delayed surgeries for arthritis**.

**Fifty-two percent of Medicaid-rejecting states ranked in the study's bottom third for senior health, including two very large states, Texas and Florida**. Many of these states also can be found in a list of states with the highest rates of poverty among people over 65.

**What emerges is a north-south divide on senior health**. "**Many states that haven't expanded Medicaid are in the South, and there's a clear link between socioeconomic status and health status," says Tricia Neuman**, senior vice-president at the Henry J Kaiser Family Foundation and director of the foundation's Medicare policy program. **"Insurance may not be the only answer, but it certainly is helpful."[Poverty and related SDOH including dietary choices and access to HC are important factors.VM]**

The United Health Foundation - a non-profit funded by the insurer UnitedHealth Group - didn't consider insurance coverage in its study, **but it did consider poverty**. **Minnesota's rate was 5.4% - well below the 9.3% national rate. Mississippi ranked dead last, with a 13.5% poverty rate.**

**In states that rejected the Medicaid expansion, we are witnessing a victory of politics over compassion and morality**. **Jonathan Gruber**, an economics professor at the Massachusetts Institute of Technology and a key architect of health reform in Massachusetts and under the ACA, **summed it up in an interview with HealthInsurance.org earlier this year, saying that**

**these states "are willing to sacrifice billions of dollars of injections into their economy in order to punish poor people. It really is just almost awesome in its evilness."**

# Connecticut Rating 12th overall

***Strengths***

- High percentage of dental visits
- Low percentage of seniors living in poverty
- Low premature death rate

***Challenges***

- High percentage of hospital deaths
- Low use of hospice care
- High prevalence of chronic drinking

***Highlights***

- While Connecticut ranks in the top 10 for smoking among seniors, more than 40,000 seniors still smoke.
- Connecticut ranks well for all outcomes combined. The state ranks in the top 10 for hip fracture hospitalizations, able-bodied seniors, and rate of premature death.
- In the past year, obesity among seniors increased from 23.7 percent to 26.5 percent; 143,000 seniors are obese in Connecticut.
- In the past year, use of hospice care among seniors increased by 38 percent, and hospital deaths among seniors decreased by 12 percent.
- The percentage of underweight seniors decreased from 1.9 percent of adults aged 65 and older to 1.2 percent.

***Disparities***

- In Connecticut, 62.3 percent of seniors with a college education report their health is very good or excellent compared to only 14.5 percent of seniors with less than a high school education.

- See more at: http://www.americashealthrankings.org/Senior/CT#sthash.bFPg2PDZ.dpuf

(The opinions expressed here are those of the author, a columnist for Reuters.)

CT Overall rank is 11th

**Obesity:**

Education: <HS 30.5%, HS Grad 30.1%, Some College 30%, College Grad 19.2%

Gender: Male 25.5%, Female 24.4%

Age: 18-44: 22%, 45-64: 24%, 65and > 26%

Income: <25,000: 33.8%, >75,000: 22.8

Race: White: 23.3%, Black: 32.5%, Hispanic: 32%, Asian: 9%

Urbanization: Urban 27.3%, Suburban 24%, Rural 22%

# Brain Insulin Resistance Marker May Diagnose Alzheimer's

Megan Brooks

November 25, 2014

A neuronal protein that is defective in Alzheimer's disease (AD) and detectable in blood may be able to predict the disease up to 10 years before clinical symptoms appear, early research hints.

The protein, insulin receptor substrate-1 (IRS-1), plays a key role in insulin signaling in the brain. Brain insulin resistance occurs in AD even in the absence of peripheral insulin resistance, but until now, no brain biomarker of brain insulin resistance has been discovered.

The new research suggests that dysfunctionally phosphorylated IRS-1 in neural-derived blood exosomes may be a specific biomarker of brain insulin resistance in AD.

Dimitrios Kapogiannis, PhD, from the National Institute on Aging in Baltimore, Maryland, reported the findings at the Society for Neuroscience 2014 Annual Meeting.

**"Near Perfect"**

The researchers assessed the level of IRS-1 and its state of phosphorylation in neural-derived plasma exosomes in a cross-sectional study involving 48 patients with AD without diabetes, 20 elderly cognitively normal participants with diabetes, 16 patients with frontotemporal dementia, and 84 cognitively normal control participants.

They found that patients with AD had several-fold higher p-Ser312-IRS-1 and Ser312/p-panY ratios and lower p-panY-IRS-1 than all other patient groups. The Ser312/p-panY ratio achieved a 0.99 receiver operating characteristic area under the curve.

These markers "near-perfectly discriminate" patients with AD from cognitively normal elderly adults, adults with diabetes, and those with frontotemporal dementia, the researchers report in a conference abstract.

In a longitudinal analysis of 22 patients with AD who provided blood samples 1 to 10 years before diagnosis, preclinical and clinical levels of these proteins were indistinguishable; preclinical levels of all three differed significantly from those of control participants ($P < .001$).

"By measuring these proteins in the bloodstream, we were able to differentiate patients with AD from controls with almost 100% accuracy, and there is good hope that we may be able to predict the disease before clinical symptoms begin because these proteins are already abnormal when you look at them up to 10 years in advance," Dr Kapogiannis said in an interview with *Medscape Medical News*.

"That is the hope: diagnose the disease and predict it at a preclinical stage," he added.

**Active Area of Research**

The exosome-based technology used in the study will be further developed by NanoSomiX, a California-based biotechnology company that develops blood assays for neurodegenerative diseases and that is supporting the research.

Dr Kapogiannis emphasized that a blood test for AD is not around the corner.

"The emphasis should be on down the road because these are findings from case-control studies in a small number of patients and the findings need to be replicated and validated in larger studies, but still the findings are very clear cut and reached very high levels of statistical significance," he said.

Simon Lovestone, PhD, from King's College London and the Institute of Psychiatry, United Kingdom, who is not involved in the research, said it's "interesting for two reasons: the link to insulin signaling and the use of exosomes.

There are plenty of other studies to make one think both these elements are real and worth pursuing in AD. Combining both makes this a potentially exciting study."

Asked for comment on these findings, Dean M. Hartley, PhD, director of science initiatives at the Alzheimer's Association, told *Medscape Medical News* that the search for preclinical biomarkers of AD to facilitate early diagnosis is a "very active" area of research.

"A simple blood test that is performed in a doctor's office is certainly something we see as a direction of the future, but this is very much still in the research phase," he said.

*The study was supported by the Intramural Research Program of the National Institute on Aging, National Institutes of Health, and NanoSomiX. The authors have disclosed no relevant financial relationships.*

Society for Neuroscience 2014 Annual Meeting: Poster 197.03. Presented November 16, 2014.

# Brain Training to Keep Dementia at Bay: Buyer Beware

Deborah Brauser

November 21, 2014

Growing evidence suggests brain training may help maintain cognition and lower dementia risk, resulting in the rise of a billion dollar brain training industry. However, new research examining the efficacy of such programs suggests not all are created equal and that it may be a case of buyer beware.

A meta-analysis of 51 randomized clinical trials (RCTs) that included more than 4800 older participants showed that group-based brain training under the supervision of a trainer was significantly more effective for overall cognition, memory, and processing speed than self-directed, home-based training programs.

"Our results send a key message to the public. They show that brain training carried out in a center can improve cognition in older adults, but commercial products promoted for solo training use at home just don't work. There are better ways to spend your time and money," senior author Michael Valenzuala, PhD, associate professor and leader of the Regenerative Neuroscience Group at the Brain and Mind Research Institute (BMRI) at the University of Sydney, Australia, said in a release.

In addition, training one to three times per week was effective, but more than that appeared to neutralize benefits.

"The brain's plastic mechanisms may saturate if training is too frequent. Like strenuous physical exercise, we recommend at least one rest day between training sessions," lead author Amit Lampit, postdoctoral research fellow at BMRI, said in the same release.

"The brain may need a rest day between rigorous exercise, much like the body," Dr Lampit told *Medscape Medical News.*

The study was published online November 18 in *PLoS Medicine.*

**Pop-up "Industry"**

It is estimated that by 2050, 100 million individuals worldwide will have developed dementia. With new research suggesting that brain training can help maintain cognition and lower dementia risk, a whole "brain training industry" has popped up, investigators note.

"There has been a lot of controversy about cognitive training and whether it can improve cognition in older adults," said Dr Lampit.

"We felt that both the public and scientific discussion was not well informed enough and based more on opinions than hard evidence. As a result, the marketing had got ahead of the science. And we felt scientific discussion was becoming reactionary," he added.

The researchers sought to "quantitatively assess" whether computerized cognitive training (CCT) can improve cognition in a systematic analysis.

They examined data on 51 RCTs published through July 2014, which included 4885 adults aged 60 years or older (60% women) who did not have dementia or other impairments. All studies assessed effects of at least 4 hours of CCT on cognitive performance (n = 2527) vs a control group (n = 2358).

CCT consisted of standardized computer tasks or video games on personal computers, mobile devices, or gaming consoles in a home (n = 19) or group setting (n = 32).

The RCTs were conducted in the United States (n = 25), Europe (n = 16), Canada (n = 3), and Australia (n = 2), as well as Israel, China, Taiwan, the Republic of Korea, and Japan (n = 1 each).

Dr Lampit noted that he was surprised to have found so many RCTs on this topic. "This allowed us to investigate many questions that have not been addressed before."

Results showed a "small but significant" overall effect on cognition for CCT vs control interventions ($P < .001$).

In addition, "small to moderate effect sizes" were shown for improved nonverbal and verbal memory ($P = .002$ and .02, respectively), working memory ($P < .001$), processing speed ($P = .002$), and visuospatial skills ($P = .01$).

There was no significant association between CCT and improvements in executive function or attention.

**Not a Magic Bullet**

When examining CCT delivery modes, group-based training was significantly more effective for overall cognitive performance compared with home-based administration (*Hedges g*, 0.29 vs .09, respectively; $P < .001$).

Group-based training was also more effective for processing speed, nonverbal memory, visuospatial skills (all, $P < .01$), and working memory ($P < .05$).

Training in which one ($P < .001$) or two to three sessions per week ($P < .001$) were administered showed a significant effect, but those in which more than three sessions per week were administered did not.

"It is possible there is a maximal dose for CCT, after which factors such as cognitive fatigue may interfere with training gains," write the investigators.

The 25 studies that examined both frequency and delivery mode showed a significant improvement in cognitive performance for patients who underwent group-based CCT for two or three sessions per week ($P < .001$).

Finally, there was no significant efficacy for training that specifically focused on working memory and only weak evidence for training that lasted less than 30 minutes per session.

"We now understand how to prescribe brain training based on the highest standards of medical evidence," said Dr Valenzuela.

However, "this is not a magic bullet. We still don't know if this type of activity can prevent or delay dementia. Much more research is needed," he added.

**Uncertain Evidence Base**

Druin Burch, from the Public Library of Science in Cambridge, United Kingdom, writes in an accompanying editorial that the findings show that CCT is "modestly effective" in this patient population, which is a valuable conclusion to both academics and to companies who sell these types of training programs.

"CCT has a market approaching a billion dollars a year and an uncertain evidence base," writes Dr Burch.

He notes, however, that although improvement from group-based CCT "may approximate an average relative improvement of 1 point on the Mini–Mental State Examination," none of the outcome measures were based on actual daily living activities.

Dr Burch adds that the meta-analysis was also limited by the time frame used to assess for changes and that the investigators could not evaluate whether these changes persisted.

"Valenzuela and colleagues show effects that are statistically significant but uncertain in their impact on human capacity and performance," he writes.

"Does a billion-dollar gap exist between our knowledge about 'standardized computerized tasks with clear cognitive rationale' and the industry selling them? Valenzuela and colleagues' overview of the evidence for CCT...suggests it does," writes Dr Burch.

"It makes clear what remains to be discovered and suggests promising lines of inquiry. Their paper is of use to those planning thoughtful research in the field."

*Dr Valenzuela has reported receiving research funding and honoraria from the Brain Department LLC for a project unrelated to the current meta-analysis and that the Regenerative Neuroscience Group receives "in-kind research support in the form of no-cost software" from BrainTrain Inc. Dr Burch reported no relevant financial relationships other than being a consulting editor for* PLoS Medicine.

*PLoS Med*. Published online November 18, 2014. Article, Editorial

# Donepezil May Slow Hippocampal Atrophy in Prodromal AD

Laird Harrison

February 04, 2015

Donepezil (*Aricept*, Esai) slows atrophy of the hippocampus in patients with prodromal Alzheimer's disease, a new randomized study shows.

"After 1 year we were surprised to see a 42% reduction of hippocampal atrophy in prodromal Alzheimer's patients," lead researcher Bruno Dubois, MD, told *Medscape Medical News*. "This is a very strong result."

Dr Dubois, a neurology professor at Hôpital La Salpêtrière, Paris, France, and his colleagues at 15 French institutions published their findings online January 14 in *Alzheimer's & Dementia*.

However, the study did not show any effects on cognition, disappointing researchers who had hoped to identify a subgroup of patients who might especially benefit from the medication.

## Early Intervention

Researchers have been working to identify patients with prodromal Alzheimer's disease: mild cognitive impairment that foreshadows progression to full-blown disease. They hope that by intervening early enough they might prevent the disease from progressing.

Earlier studies showed that the hippocampus shrinks rapidly in patients with mild cognitive impairment as that condition progresses to Alzheimer's disease. Donepezil slows atrophy of the hippocampus in patients with mild to moderate Alzheimer's disease, as well as slowing the patients' cognitive decline, but few researchers have looked at donepezil in patients with mild cognitive impairment.

To fill that gap, Dr Dubois and colleagues used a memory test, the Free and Cued Selective Reminding Test (FCSRT), to identify patients most likely to have prodromal Alzheimer's disease. The test has been correlated with hippocampal volume and changes in cerebrospinal fluid characteristic of Alzheimer's disease.

They recruited 216 people over age 50 who had no dementia but scored low on the FCSRT. They randomly assigned 103 to take a placebo and 113 to take donepezil, 10 mg/day.

They used brain MRI to measure the volume of the patients' hippocampus at baseline, 6 months, and 1 year.

Adverse reactions occurred more frequently in the donepezil group and included muscle spasms, nightmares, diarrhea, headache, nausea, sleep disorder, abdominal pain, and vertigo.

Partly because of the adverse reactions, several patients dropped out. After a year, 81 remained in the placebo group and 75 remained in the donepezil group.

In these remaining patients, the donepezil group lost 1.89% of hippocampal volume over the year, while the placebo group lost 3.47%. The difference was statistically significant ($P < .001$).

Although apolipoprotein has been linked to the decline in hippocampal volume in people with Alzheimer's disease, hippocampal volume did not differ between *APOE4* carriers in the 2 groups.

The researchers gave their patients a battery of neuropsychological tests but didn't find any significant differences between the two groups.

This last finding means this study has no implications for current clinical practice, Dr Dubois said.

## Direction for Future Research

Keith Fargo, PhD, director of scientific programs and outreach at the Alzheimer's Association, agreed.

"At this point it's more about giving direction to additional research," said Dr Fargo, who was not associated with this study. "The literature in this area has been somewhat mixed, and this paper answers a question. But all research has to be followed up on."

One possibility for future researchers is to look further for neuropsychological benefits from donepezil in this category of patients.

"If you follow people longer, if you had more people in the study, would you see benefits to cognition, would you see benefits to daily living, for example?" Dr Fargo asked.

Dr Dubois said he and his colleagues are planning to continue analyzing their current data, looking further at the effect of donepezil on other brain structures.

*This study was funded by Eisai, the company that markets donepezil as Aricept. The authors and commenter have disclosed no relevant financial relationships.*

*Alzheimers Dement.* Published online January 14, 2015. Abstract

# Novel Drug Targets 'Huge Unmet Need' in Schizophrenia

Nancy A. Melville

April 10, 2015

COLORADO SPRINGS, Colorado — Encenicline (Forum Pharmaceuticals**), a novel α-7 nicotinic acetylcholine receptor partial agonist, shows improvement of cognitive impairment in schizophrenia in a phase 2 randomized, controlled trial, potentially ushering in a long-anticipated treatment for an aspect of the disease not addressed by antipsychotics.**

"**These data shows that pro-cognitive effects in schizophrenia were observed for encenicline as assessed by two independent cognitive measures and a functional measure**," said Ilise Lombardo, MD, who is vice president of clinical research and medical affairs at Forum Pharmaceuticals, Watertown, Massachusetts, in presenting the findings here at the 15th International Congress on Schizophrenia Research (ICOSR).

Although cognitive impairment occurs in nearly all (98%) patients with schizophrenia, antipsychotics do not adequately offer improvement, Dr Lombardo said.

"**Antipsychotics remain the mainstay of pharmacotherapy for schizophrenia with limited, if any, benefit in improving cognitive impairment. There is a clear need for pharmacological agents that target cognitive impairment.**"

With its unique mechanism seen as potentially helping to improve memory and cognitive function, encenicline is being studied as an adjunct to antipsychotics in treating cognitive impairment in schizophrenia as well as Alzheimer's disease.

For the phase 2, multicenter, double-blind study**, 319 patients with a diagnosis of schizophrenia for 3 or more years were randomly assigned 1:1:1 to receive encenicline in doses of 0.27 mg or 0.9 mg once daily or placebo for 12 weeks.**

The results showed significant cognitive improvements in the encenicline groups in both dose groups at various measures.

For the primary efficacy endpoint of Overall Cognitive Index score, as well as **Trails 2 and 4 tasks from the Neuropsychological Test Battery (NTB), patients receiving the 0.27-mg dose had significant improvement over placebo (*P* = .03 for both).**

In a subset of 154 patients only in the United States, both dose groups showed a trend toward improved cognition in the MATRICS Consensus Cognitive Battery tests, but the improvement from baseline was greater in the higher-dose 0.9-mg group (*P* = .06 compared with placebo) than the 0.27-mg group.

**Pro-Cognitive Effect**

**Improvement in clinical function was further seen in the measures of the Schizophrenia Cognition Rating Scale, with the 0.9-mg group showing a significant improvement over placebo (*P* = .01) in terms of the mean change from baseline.**

**Patients in the 0.9-mg group also showed significant improvements in the Positive and Negative Syndrome Scale (PANSS) Cognition Impairment domain compared with placebo (*P* = .029) as well as for PANSS-negative subscale scores (*P* = .028).**

Dr. Lombardo noted that the primary outcome data were difficult to interpret because, **the higher dose has consistently shown greater improvement**

"Those data were inconsistent with the other measures of cognition and all of the measures of function and other assessments in this study, as well as, importantly, in the phase 1 data on schizophrenia," she said.

"**In all of those other measures, we did see the more robust effect was in the higher dose than the lower dose.**"

**There were no treatment-emergent adverse events in the treatment groups that were considered serious, and covariate analyses have shown no notable effects of smoking, sex, or baseline severity**, Dr Lombardo said.

She noted that two 6-month, phase 3 trials are underway for encenicline, involving 700 patients each.

**The approach of targeting nicotinic acetylcholine receptors for cognitive improvement in schizophrenia has attracted particular interest because of deficiencies shown in patients with the condition, according to a phase 2 study on the first drug in the class of α-7 nicotinic acetylcholine receptor partial agonists, the agent 3-(2,4-dimethoxybenzylidene) anabaseine (DMXB-A).[Smoking cigarettes has agonist effects on Alpha 7 Nicotinic Acetyl Choline receptor.VM]**

"[Schizophrenia] patients' heavy smoking suggests attempted self-medication through this mechanism," wrote the authors, who included Robert Freedman, MD, from the University of Colorado Denver's School of Medicine in Aurora.

Dr Freedman told *Medscape Medical News* that the drug class has shown some promising signs in animal studies.

"A pro-cognitive effect was suggested (with the α-7 nicotinic acetylcholine receptor partial agonist) by the preclinical evidence in laboratory animals," he said. "**The mechanism of action, activating a nicotinic receptor, is far different from most current antipsychotics."**

"**The exception is clozapine, which releases large amounts of acetylcholine from the brain's synapses as one of its many effects, and thereby indirectly activates nicotinic receptors."**

While the need for a therapy to specifically address cognitive function in schizophrenia has yet to be met, it's not from a lack of trying.

A review published in *Schizophrenia Bulletin* in 2013 underscored the efforts, describing a multitude of shortcomings in more than 100 clinical trials examining treatment of cognitive impairment in schizophrenia.

**Huge Unmet Need**

"**This has been an area of substantial interest but no drug to date has worked, despite multiple attempts,**" Philip D. Harvey, PhD, the Leonard M. Miller Professor of Psychiatry and Behavioral Sciences at the University of Miami Miller School of Medicine in Florida, told *Medscape Medical News.*

"**Antipsychotic medications do nothing for cognition, and cognitive impairment is associated with disability," he said.**

"Meanwhile, cognitive remediation interventions have shown that improving cognitive function leads to improvement in everyday activities for these patients."

Dr Harvey noted that some earlier efforts in developing a drug in the α-7 nicotinic receptor class have not successfully advanced, largely because of a very short half-life of the compounds.[Including cigarette smoking effects being short acting.VM]

"The earlier compounds did have a signal for efficacy, but due to the short half-life they had to be administered multiple times a day and that's just not practical for patients with severe mental illness."

Anticipation in psychiatry is high for a drug that successfully overcomes the challenges, he stressed.

"Everyone in the field is very excited about the idea that a drug like this would have efficacy," he said. "It really could fill a hugely unmet need."

*The study was funded by Forum Pharmaceuticals. Dr Lombardo is an employee of Forum Pharmaceuticals. Dr Freedman has disclosed no relevant financial relationships. Dr Harvey is a consultant for Forum Pharmaceuticals but has no financial interests in the development of encenicline.*

15th International Congress on Schizophrenia Research (ICOSR). Abstract 2207646. Presented March 30, 2015.

Medscape

# Big Data: Could It Ever Cure Alzheimer's Disease?

Masud Husain

Brain. 2014;137(10):2623-2624.

When, with the benefit of hindsight, people look back at the history of biomedical sciences at the turn of the 21st century, the focus will inevitably turn to dementia, and in particular Alzheimer's disease. How did brain scientists and clinicians of that generation—our generation—deal with this global health issue? Did we make the right choices, or will we seem woefully inadequate, our judgements quaintly naïve?

One strategy that will surely come under scrutiny is the investment in big data sets. In Alzheimer's disease there has been a surge in recent years towards 'Big Data' initiatives, reflecting a general drive that has galvanized other disciplines, in medicine and beyond (Cukier and Mayer-Schonberger, 2013). From business to government, many have been seduced by the possibilities that Big Data seems to offer for a whole range of problems. However, not everyone is convinced, and the debate on its merits is now in full swing in the media (Harford, 2014; Ozimek, 2014).

The same kind of reflection might also be healthy for the neurosciences. Indeed, recent concerns over the Human Brain Project, which aims to simulate the brain on supercomputers, demonstrate how contentious some Big Data projects have become. Backed by €1 billion funding from the European Commission this initiative represents a massive investment, but the size—and quality—of the potential payback remain questionable to many ('Open message to the European Commission concerning the Human Brain Project', 2014).

For brain diseases, Alzheimer's disease provides the key example to consider. New initiatives announced this year follow in the footsteps of the Alzheimer's Disease Neuroimaging Initiative (ADNI), a major international collaboration that is now a decade old. ADNI has an impressive track record of data sharing and publications, as well as of attracting grants and investment from industry, with a total of more than $200 million backing it.

Earlier this year the OECD published its report on informatics and 'the potential for Big Data to be a "game changer" in global efforts to accelerate innovation in neurodegenerative research' (OECD, 2014). Then followed the announcement of the Alzheimer's disease Big Data DREAM Challenge: a major collaborative, open science initiative that aims to identify biomarkers for the condition ('Big Data Challenge for Alzheimer's Disease' 2014). These developments call not only for large-scale information repositories, but also for development of analytical tools to mine such data sets effectively.

This journal plays a role in presenting the direction of travel of the research community. We aspire to reflect in its pages some of the best science that is being performed. But *Brain* hopes also to provoke and stimulate debate. Although we do not have the gift of foresight, we can as a community consider what the realistic potential of Big Data is. As the man on the street might rightly ask: Could it cure Alzheimer's disease? Is 'big' the answer?

That big collections might generally be useful is not the issue. In the Victorian era, for example, the energy and philanthropy of men like Augustus Pitt Rivers and Henry Wellcome provided not only fascinating insights into cultures across the globe, but also influenced the development of scientific enquiry. The utility of the vast collections they, and others, amassed is not in doubt. But what did those collections actually explain? That is the question that lies at the heart of current concerns: *What is the explanatory power of Big Data?*

Enthusiasts of the new approach counter that 'Big Data is about *what*, not *why*. We don't always need to know the cause of a phenomenon; rather, we can let the data speak for itself' (Cukier and Mayer-Schonberger, 2013). Letting the data speak is, in many ways, to be encouraged but it risks the possibility that we won't be able to make sense of the vast array of information we obtain. Even if we did, what would it show apart from correlation? Could it ever uncover causal mechanisms? That would seem very unlikely.

But advocates of Big Data initiatives in Alzheimer's disease might understandably argue that first we need to find the 'signal' before we start to understand what it means. Indeed, they might point out that although traditional scientific endeavours have uncovered potential genetic and molecular mechanisms underlying Alzheimer's disease, those approaches also do not provide adequate explanations for the protean manifestations of the condition, in terms of either behaviour (how different patients present with the illness) or brain network dysfunction (how different brain regions and their connections appear to be affected). Bringing together those very different levels of explanation would seem to be crucial to any proper understanding of the condition.

Perhaps the debate about Big Data is exposing some very important general issues about the way that neuroscience is drifting. The trajectories might be quite different depending upon the parochial interests and expertise of different sectors of the community. So one virtue of Big Data might be that it can potentially bring together different levels of data—from genes and molecules through to imaging and cognitive function—and thereby expose the lack of integration across these. In this sense, it provides a real opportunity to glimpse the 'big picture', and the holes in that canvas, rather than keeping the focus tightly on what we know best. Regardless of the pros and cons, the Big Data approach is here. Better we make the most of it and exploit it to its maximum—while understanding its limitations—than simply appealing to the argument that 'Small is beautiful' (Schumacher, 1973).


- References

# Brain Training to Keep Dementia at Bay: Buyer Beware

Deborah Brauser

November 21, 2014

Growing evidence suggests brain training may help maintain cognition and lower dementia risk, resulting in the rise of a billion dollar brain training industry. However, new research examining the efficacy of such programs suggests not all are created equal and that it may be a case of buyer beware.

A meta-analysis of 51 randomized clinical trials (RCTs) that included more than 4800 older participants showed that group-based brain training under the supervision of a trainer was significantly more effective for overall cognition, memory, and processing speed than self-directed, home-based training programs.

"Our results send a key message to the public. They show that brain training carried out in a center can improve cognition in older adults, but commercial products promoted for solo training use at home just don't work. There are better ways to spend your time and money," senior author Michael Valenzuala, PhD, associate professor and leader of the Regenerative Neuroscience Group at the Brain and Mind Research Institute (BMRI) at the University of Sydney, Australia, said in a release.

In addition, training one to three times per week was effective, but more than that appeared to neutralize benefits.

"The brain's plastic mechanisms may saturate if training is too frequent. Like strenuous physical exercise, we recommend at least one rest day between training sessions," lead author Amit Lampit, postdoctoral research fellow at BMRI, said in the same release.

"The brain may need a rest day between rigorous exercise, much like the body," Dr Lampit told *Medscape Medical News.*

The study was published online November 18 in *PLoS Medicine.*

**Pop-up "Industry"**

It is estimated that by 2050, 100 million individuals worldwide will have developed dementia. With new research suggesting that brain training can help maintain cognition and lower dementia risk, a whole "brain training industry" has popped up, investigators note.

"There has been a lot of controversy about cognitive training and whether it can improve cognition in older adults," said Dr Lampit.

"We felt that both the public and scientific discussion was not well informed enough and based more on opinions than hard evidence. As a result, the marketing had got ahead of the science. And we felt scientific discussion was becoming reactionary," he added.

The researchers sought to "quantitatively assess" whether computerized cognitive training (CCT) can improve cognition in a systematic analysis.

They examined data on 51 RCTs published through July 2014, which included 4885 adults aged 60 years or older (60% women) who did not have dementia or other impairments. All studies assessed effects of at least 4 hours of CCT on cognitive performance (n = 2527) vs a control group (n = 2358).

CCT consisted of standardized computer tasks or video games on personal computers, mobile devices, or gaming consoles in a home (n = 19) or group setting (n = 32).

The RCTs were conducted in the United States (n = 25), Europe (n = 16), Canada (n = 3), and Australia (n = 2), as well as Israel, China, Taiwan, the Republic of Korea, and Japan (n = 1 each).

Dr Lampit noted that he was surprised to have found so many RCTs on this topic. "This allowed us to investigate many questions that have not been addressed before."

Results showed a "small but significant" overall effect on cognition for CCT vs control interventions ($P < .001$).

In addition, "small to moderate effect sizes" were shown for improved nonverbal and verbal memory ($P = .002$ and .02, respectively), working memory ($P < .001$), processing speed ($P = .002$), and visuospatial skills ($P = .01$).

There was no significant association between CCT and improvements in executive function or attention.

**Not a Magic Bullet**

When examining CCT delivery modes, group-based training was significantly more effective for overall cognitive performance compared with home-based administration (*Hedges g*, 0.29 vs .09, respectively; $P < .001$).

Group-based training was also more effective for processing speed, nonverbal memory, visuospatial skills (all, $P < .01$), and working memory ($P < .05$).

Training in which one ($P < .001$) or two to three sessions per week ($P < .001$) were administered showed a significant effect, but those in which more than three sessions per week were administered did not.

"It is possible there is a maximal dose for CCT, after which factors such as cognitive fatigue may interfere with training gains," write the investigators.

The 25 studies that examined both frequency and delivery mode showed a significant improvement in cognitive performance for patients who underwent group-based CCT for two or three sessions per week ($P < .001$).

Finally, there was no significant efficacy for training that specifically focused on working memory and only weak evidence for training that lasted less than 30 minutes per session.

"We now understand how to prescribe brain training based on the highest standards of medical evidence," said Dr Valenzuela.

However, "this is not a magic bullet. We still don't know if this type of activity can prevent or delay dementia. Much more research is needed," he added.

**Uncertain Evidence Base**

Druin Burch, from the Public Library of Science in Cambridge, United Kingdom, writes in an accompanying editorial that the findings show that CCT is "modestly effective" in this patient population, which is a valuable conclusion to both academics and to companies who sell these types of training programs.

"CCT has a market approaching a billion dollars a year and an uncertain evidence base," writes Dr Burch.

He notes, however, that although improvement from group-based CCT "may approximate an average relative improvement of 1 point on the Mini–Mental State Examination," none of the outcome measures were based on actual daily living activities.

Dr Burch adds that the meta-analysis was also limited by the time frame used to assess for changes and that the investigators could not evaluate whether these changes persisted.

"Valenzuela and colleagues show effects that are statistically significant but uncertain in their impact on human capacity and performance," he writes.

"Does a billion-dollar gap exist between our knowledge about 'standardized computerized tasks with clear cognitive rationale' and the industry selling them? Valenzuela and colleagues' overview of the evidence for CCT...suggests it does," writes Dr Burch.

"It makes clear what remains to be discovered and suggests promising lines of inquiry. Their paper is of use to those planning thoughtful research in the field."

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*PLoS Med*. Published online November 18, 2014. Article, Editorial

# Benzodiazepine Use Linked to Dementia Risk

Megan Brooks

October 02, 2012

October 2, 2012 — Older adults who use benzodiazepines have about a 50% greater chance of developing dementia than their peers who don't use benzodiazepines, French researchers observed in a large population-based study.

This finding, added to evidence of increased risk for falls and fractures in elderly who use benzodiazepine, "should incite (health providers) to carefully assess expected benefits versus putative risks, and to limit prescriptions to a few weeks," lead author of the study and PhD student Sophie Billioti de Gage, PharmD, from the University of Bordeaux Segalen in France, told *Medscape Medical News*.

"In any case, uncontrolled use should be cautioned against," she said.

The study was published online September 27 in the *British Medical Journal*.

**"Bad Drugs for Older Adults"**

Greg A. Sachs, MD, who reviewed the study for *Medscape Medical News*, said it is "yet another study that suggests that benzodiazepines are bad drugs for older adults."

Dr. Sachs is chief of the Division of General Internal Medicine and Geriatrics, Indiana University School of Medicine, and investigator at the IU Center for Aging Research, Regenstrief Institute, Indianapolis. He was not involved in the study.

"Many of these drugs," Dr. Sachs said, "are on 'Do Not Prescribe' lists for older adults. If used at all, they should be used for short periods of time (10 days or less) and in the lowest dose possible to achieve benefit for the target symptom." Benzodiazepines "should not be used long term for either sleep or anxiety; safer alternatives exist."

The analysis included 1063 men and women (mean age, 78.2 years) from the PAQUID (Personnes Agées Quid) project, a prospective, population-based study of cognitive aging and dementia involving a total of 3777 participants from France. The study started in 1987 and follow-up lasted 20 years, with clinic visits every 2 to 3 years.

All participants in the current analysis were free of dementia at the outset and did not start taking benzodiazepines until at least the third year of follow-up. Ninety-five (8.9%) reported benzodiazepine use at the 5-year visit, indicating new use between years 3 and 5. Year 5 was baseline for the analysis.

During the 15-year follow-up period, 253 (23.8%) cases of dementia were confirmed: 30 (32%) in benzodiazepine users and 223 (23.0%) in nonusers.

The 15-year incidence rate of dementia per 100 person-years was higher in benzodiazepine users than nonusers (4.8 vs 3.2).

The multivariable adjusted hazard ratio (HR) for dementia with new use of benzodiazepines was 1.60 (95% confidence interval [CI], 1.08 - 2.38). This result was unchanged when further adjusted for depressive symptoms (HR, 1.62; 95% CI, 1.08 - 2.43).

The result "remained robust" in a secondary pooled analysis of patients who initiated a benzodiazepine between follow-up visits 8 and 15 (HR, 1.46; 95% CI, 1.10 - 1.94). This added a total of 116 additional new users during follow-up to the 95 new users at year 5.

Similarly, in a nested-case control study (467 case-patients with dementia and 1810 controls), the adjusted odds ratio (OR) with ever use vs never use was 1.55 (95% CI, 1.24 - 1.95). The results were similar in past users (OR, 1.56; 95% CI, 1.23 - 1.98) and recent users (OR, 1.48; 95% CI, 0.83 - 2.63).

The PAQUID investigators say their findings are consistent with 3 recent case-control studies that found an increased risk for dementia in benzodiazepine users.

Two of the studies from Taiwan (Wu et al, 2011, Wu et al, 2009) used health insurance data and showed an increased risk for dementia in long-term users ( > 6 months; adjusted OR, 1.24; 95% CI, 1.01 - 1.53) and current users (adjusted OR, 2.71; 95% CI, 2.46 - 2.99).

The third study, a nested case-control study among French people, found an increased risk for dementia in former users (adjusted OR, 2.3; 95% CI, 1.2 - 4.5).

Other studies, however, have not found an increased risk for dementia among elderly people using benzodiazepines.

Dr. Billioti de Gage told *Medscape Medical News* that "contrary to most of the previous study on the topic, our study is based on a long period of follow-up (up to 15 years) and was carried out in a large representative cohort of elderly participants. This allows to take into account the somewhat long prodromal period of dementia and to generalize the conclusions."

**"Positive Distinguishing Factors"**

Dr. Sachs said there are several "positive distinguishing factors about this study." It was large; it followed patients over many years with little dropout; it was prospective and longitudinal rather than cross-sectional; the diagnosis of dementia involved both neuropsychological testing and examination by a neurologist; and the researches had excellent information about drug use from patients, he explained.

The exclusion of people who were already receiving benzodiazepines at time of study entry and for a period of a few years "run in" is another key strength, he said.

"This is important regarding the notion of 'reverse causation' — that people could end up taking benzodiazepines because of symptoms of depression or anxiety that are early symptoms relating to a developing dementia. Without doing that, it could bias the study toward people with dementia already brewing getting benzodiazepines at a higher rate, instead of the notion that it is contributing to dementia development," Dr. Sachs said.

The analyses were "carefully done" and the findings were "explored and confirmed using more than one approach. The PAQUID study is one of the higher quality cohort studies examining dementia," he added.

Dr. Billioti de Gage said, "patients should be told about the potential adverse effects of these drugs, including long-term risk when initiating benzodiazepines and about the necessity of gradual discontinuation when stopping the treatment."

She and her colleagues say further study is needed to determine whether long-term use of benzodiazepines in people younger than age 65 years is also associated with an increased risk for dementia and uncover possible correlations between dosage or cumulative length of exposure and dementia.

Dr. Sachs agrees. The analysis "cannot tell us anything about long versus short acting meds, specific meds, dose, or duration of therapy," he told *Medscape Medical News*. Also, the small numbers of people on benzodiazepines in the study is a limitation, he added.

Another limitation, he said, is that the analysis is primarily focused on "ever use" of benzodiazepines, "and that means we do not have information here on whether stopping the meds would help prevent dementia. In fact, because of the 'ever use' approach to analysis, I'd be concerned that someone misinterpret this and think 'why bother stopping' once someone has been exposed."

Dr. Sachs also noted that "far greater numbers of people who developed dementia had not been exposed to benzodiazepines than those who had; so while it increases relative risk, how much it contributes to development of dementia should not be overplayed; this still was an observational study, so assigning causation is hard to do no matter how well the study is done."

*This research was conducted by the INSERM U657 research team co-funded by INSERM (Institut National de la Santé et de la Recherche Médicale) and Université Bordeaux Segalen. Additional support was provided by a 2010 grant from IRESP (Institut de Recherche en Santé Publique) acting on behalf of the French Ministry of Health (Direction Générale de la Santé, Direction de la Recherche, des Études, de l'Évaluation et des Statistiques); by a 2011 grant from the French Ministry of Health (Direction Générale de la Santé); and by Caisse Nationale des Travailleurs Salariés, Régime Social des Indépendants, Caisse Nationale de Solidarité pour l'Autonomie, and Institut National de Prévention et d'Education pour la Santé. SBdG is a part-time researcher in the INSERM 657 Unit, and her salary is paid by IRESP.*

*BMJ*. Published online September 27, 2012. Abstract

# Obesity Tied to Brain Volume Loss

Megan Brooks

November 21, 2014

Being overweight or obese is associated with poorer brain health in cognitively healthy adults in their 60s, according to new data from the long-running Australian PATH Through Life Study.

After adjustment for multiple factors, participants who were overweight or obese had smaller hippocampal volume at baseline and experienced greater hippocampal atrophy over 8 years than their normal-weight peers.

"The results further underscore the importance of reducing the rate of obesity through education, population health interventions, and policy," Nicolas Cherbuin, PhD, from the Australian National University in Canberra, Australia, said in a statement.

He reported the findings in Washington, DC, at the Society for Neuroscience 2014 Annual Meeting.

**Increased Dementia**

Obesity is a "major concern" and has been linked to an increased risk for dementia, Dr Cherbuin said during a media briefing. The hippocampus plays a key role in long-term memory, and hippocampal atrophy is a hallmark of cognitive decline.

Dr Cherbuin reported on 420 cognitively healthy adults aged 60 to 64 years participating in the PATH study on aging. As part of the study, body mass index (BMI) was recorded and high-resolution T1-weighted MRI was performed at study outset and then 4 and 8 years later.

At baseline, BMI was negatively correlated with left hippocampal volume (estimate per unit BMI above 25: –10.65 $mm^3$; $P$ = .027) and right hippocampal volume (estimate: –8.18 $mm^3$; $P$ = .097).

During follow-up, participants with higher BMI experienced greater atrophy in the left ($P$ = .001) but not the right ($P$ = .058) hippocampus, even after adjustment for age, sex, education, diabetes, hypertension, smoking, and depression.

Each 2-point increment in BMI at baseline was associated with a 7.2% decrease in left hippocampal volume during follow-up. "This is particularly significant in an aging population, and further research should be conducted to determine how obesity affects thinking abilities," Dr Cherbuin said.

"We did not investigate the relationship between shrinkage and function, but other studies in this research field have shown that greater shrinkage in the hippocampus is linked with a greater risk of cognitive decline and a greater risk of dementia as well," he said.

In an interview with *Medscape Medical News*, Ralph DiLeone, PhD, from Yale University in New Haven, Connecticut, who moderated the media briefing, said more information on outcomes would be of interest.

"Because the hippocampus is so important for memory function, mood regulation and is implicated in cognitive aging and dementia, it will be very interesting to see if the researchers can correlate some of those brain changes with specific behavioral deficits or disease states," he said.

*The research was supported with funds from the Australian National Health and Medical Research Council, the Australian Research Council, the Dementia Collaborative Research Centre – Early Detection and Prevention, and the Australian National Computing Infrastructure. The authors have disclosed no relevant financial relationships.*

Society for Neuroscience 2014 Annual Meeting. Abstract 19.04. Presented November 15, 2014.

# Sex and Dementia: Is it Love or Assault?

Arthur L. Caplan,

April 16, 2015

Hi. I'm Art Caplan, from the Division of Medical Ethics at the NYU Langone Medical Center.

**Not long ago, a 78-year-old man in Iowa, a representative for that state in the House of Congress, was arrested and charged after being accused of having sex with his wife.[1] That may seem startling and unusual, but the circumstances make it clear why this has happened, and they raise some important ethical issues that physicians and healthcare teams are going to have to wrestle with.**

This gentleman had remarried late in life to a woman also in her 70s, and they spent a lot of time together and loved each other and things were fine. But, sadly, she was diagnosed with Alzheimer disease. That forced her ultimately to go into a nursing home. And the husband did not leave her or divorce her, and it was clear that he still wanted to maintain intimacy with her.

**During one of his visits to his wife in the nursing home, her roommate said she heard "sexual' noises" and reported that she thought he probably had had sex with his wife.[2]**

**His daughter-in-law wanted that followed up and examined. The daughter-in-law was very upset. The ethical issue is not when does "no" mean "no," but rather, what if you can't say "yes"?[2]**

**This issue is a growing problem for all of us in the United States because Alzheimer's-one of our most feared and dreaded diseases-is starting to afflict more and more people. We're starting to be able to diagnose it with better tests. And soon, I think, we'll have some better scanning information about early-onset Alzheimer's even before symptoms occur.**

Because Alzheimer's is becoming so prevalent, physicians have to come up with a better plan for managing the disease. One sad fact is that a lot of doctors don't feel comfortable revealing the diagnosis, or suspicion, of Alzheimer's to their patients.[3] In fact, a 2008 analysis showed that only 40% of doctors regularly disclose the diagnosis of Alzheimer's to their patients.[4]

**It is certainly acceptable to say that you don't want to deliver bad news all at once. With a disease for which we don't really have any current cures, it may take a few visits-information being given out over time-to let the patient know what's going on.**

**I do strongly believe that patients do need to know the diagnosis. They're not going to know how to make plans for the time they have. Their family members have to make arrangements and decide how they want to manage. And, as we've seen with the case of the gentleman under arrest, there are going to be some important questions about what life will be like when competency begins to fail.**

**Could a person and should a person say, while they're still competent but suspected of having Alzheimer's, "Look-here is what I want you to play on television. And this is the relationship I want to have with my husband: If he still wants to have relations with me, then that's great. Let him. Let's do that in a private area-let's make sure we make some provision for that. If it's something that would hurt me or cause me to be physically harmed in some way, if I become fragile or develop fragile bones, then we should not allow that to happen."**

That discussion, as tough as it is, is something that should take place before a person becomes incompetent. People need to know the truth about Alzheimer's, and they need to be able to plan for it.

They need to decide the following:

- What do they want to do in terms of their relationships with their loved ones?
- Who is going to take care of them?
- Where would they want to go?
- How do they want to manage their end-of-life care should they get illnesses or diseases that threaten their ability to live? Do they want aggressive treatment, or don't they?

- Would they want to be in experimental trials?

- Many new drugs are starting to appear, we're hopeful for at least slowing some of the symptoms and dysfunction of Alzheimer's. Do they want to be given those, or do they not want to be involved with that? Does cost matter?

So there is a lot to talk about. We're not going to be able to talk about any of this unless you get to the point where you're comfortable, somehow, with disclosing and discussing that diagnosis.

As I say, just dumping the information on a person who is fragile may not be the way to go. Maybe the talk has to happen with other family members or a trusted friend present. Maybe you want to urge the person to come back for a second visit, saying "I want to reconfirm something," just to make sure they're not overwhelmed.

**And you've got to be ready to support them and counsel them about steps that they need to take and things they need to start thinking about-everything from sex to where they live, to how they are going to have their medical care given or not given in the time that remains for them.**

**This is Art Caplan at the Division of Medical Ethics at NYU. Thanks. Please leave your comments below.**

- References

# Eating More Carbs May Signal Frontotemporal Dementia

Pauline Anderson

December 22, 2014

If older patients are suddenly craving sweets, gaining weight, and developing swallowing difficulties, consider a diagnosis of frontotemporal dementia (FTD), a new study suggests.

Results show that patients with certain types of FTD eat significantly more carbohydrates and sugar than healthy controls or those with Alzheimer's disease (AD), and that these changes don't appear to be explained by being hungrier.

Patients presenting with such eating behaviors should raise a red flag, study author Olivier Piguet, PhD, associate professor, University of New South Wales, and Principal Research Fellow, Neuroscience Research, Australia, told *Medscape Medical News*.

"Someone in their 50s or early 60s showing these changes in eating preferences and the amount of food that they eat would certainly indicate that something might be going on in their brain that needs exploring further."

The study, published in the December issue of *JAMA Neurology*, is the first to quantify abnormal eating behaviors in patients with FTD, said Dr Piguet.

**Eating Disturbance**

"Changes in eating behavior are part of the criteria for the diagnosis of behavior variant FTD, but no one has really looked at exactly what that means," said Dr Piguet. "This study is really the first one to try to measure what it means when we say these patients have an eating disturbance."

The analysis included 75 patients with dementia: 21 with personality or behavioral disturbance (behavioral variant FTD [bvFTD]), 26 with language disturbances (semantic dementia or SD), and 28 with AD, as well as 18 age- and education-matched healthy controls.

Caregivers completed the Appetite and Eating Habits Questionnaire (APEHQ), which includes 34 questions examining changes in eating behaviors with regard to swallowing, appetite, eating habits, food preferences, and other oral behaviors (eg, eating objects such as cigarette butts). For each question, researchers calculated a composite score that included frequency and severity and derived an overall score for each domain.

Investigators found the bvFTD group had significantly higher scores than the AD group for all 5 APEHQ domains: swallowing ($P = .003$), appetite change ($P = .007$), eating habits ($P = .001$), food preferences ($P = .001$), and other oral behaviors ($P = .009$).

Caregivers also completed the Cambridge Behavioral Inventory, which includes four questions related to eating behaviors: sweet preference, eating the same foods, changes in appetite, and table manners.

The table manners item was included because of anecdotal evidence that patients with behavioral disturbances lose this etiquette. "Caregivers will report that 'my husband is stealing food from someone else's plate' or piling up food on their plate," said Dr Piguet.

There were significantly greater changes related to sweet preference ($P < .001$), eating the same foods ($P = .001$), and table manners ($P = .007$) in the bvFTD group compared with the AD group.

Some of the findings were unexpected.

"The finding that the behavior variant patients changed their preferences in terms of the foods they like and their tendency to focus more on sweet foods confirms something we knew already, although we were able to quantify that," commented Dr Piguet. "But we also found that this tendency to prefer sweet foods was also present in the group with semantic dementia, which was surprising."

Although patients with semantic dementia increased their carbohydrate intake to some degree, the increase among those with bvFTD was "more prominent," said Dr Piguet, "again confirming anecdotal evidence that we were able to measure with the questionnaire."

Caregivers also measured patients' level of hunger and satiety using a visual analogue scale before and after meals during a 24-hour period (with higher scores indicating more hunger). The bvFTD group had a significantly higher overall hunger-satiety index score than the semantic dementia ($P$ = .02) and AD ($P$ = .03) groups, but not the control group ($P$ = .38).

These results suggest that "these patients don't eat because they feel full," but simply because "the food is there and they eat it," said Dr Piguet.

**Weight Concerns**

The bvFTD and SD groups had significantly greater waist circumference compared with the control group, and the bvFTD group had significantly greater waist circumference compared with those with AD.

These patients, said Dr. Piguet, are "getting into the danger zone" with body mass indexes "hovering around the 30 mark, which raises concerns about their general health, their cardiovascular health and risks for related illnesses such as diabetes."

An earlier paper by the same research group found atrophy in the hypothalamus — the area of the brain that plays a central role in eating regulation — in patients with FTD, said Dr Piguet. "The brain is receiving incorrect messages from the periphery in terms of hunger and satiety and is then responding to these messages in an incorrect manner."

The changes, he added, can lead to disordered behavior when it comes to eating. "These patients tend to want to eat the food that they have in front of them; they have difficulty in inhibiting or stopping their eating."

In FTD, atrophy predominantly affects the frontal lobes and temporal brain areas; in AD, in contrast, other brain regions are affected. "You rarely see these behavior changes in patients with AD," noted Dr Piguet.

Reached for comment on these findings, Ronald Petersen, MD, PhD, director, Mayo Alzheimer's Disease Research Center, Mayo Clinic, Rochester, Minnesota, said the study results illustrate disinhibition on the part of patients with bvFTD.

"Foods that are sweet are very attractive to most of us, and people with bvFTD lack the ability to deny themselves the pleasure," said Dr Petersen. "They can't reason that this type of excessive ingestion of sweets will lead to weight gain and other health consequences."

These patients, he added, lack the ability to foresee the consequences and act impulsively. "This is due to frontal lobe dysfunction since that part of the brain is involved in our ability to judge the consequences of behavior."

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*JAMA Neurol*. 2014;71:1540-1546. Abstract

Medscape Psychiatry and Mental Health
Heartwire

# Cognition Can Falter in Chronic Heart Failure as Physical-Activity Levels Drop

Steve Stiles

January 08, 2015

BETHESDA, MD — **Declines in activity level as measured by accelerometer predicted deterioration in scores on tests of attention and executive function over a mere 12 weeks in a mixed population with reduced- or preserved-ejection-fraction heart failure (HF), reported researchers January 5, 2015 in the *Journal of Cardiac Failure* [1].**

"Surprisingly, there was no longitudinal association between physical activity and memory and language abilities," note the authors, led by Michael L Alosco (Kent State University, OH). They speculate that the lack of such an association, which in contrast has been observed in previous, mostly cross-sectional studies, may owe to differences among studied populations or that "**the longitudinal associations among physical activity, memory, and language may present with a different pattern." Indeed, according to the group, their study is the first to track the effects of changing activity levels on cognition in HF.**

Their population consisted of 57 patients with primarily NYHA class 2 stable HF aged 50 to 85 with a mean LV ejection fraction of 40.5%, who were a subgroup from a larger HF study of the effects of cardiac rehabilitation. The current cohort was taken from those who did not complete the larger study's rehab intervention, report Alosco et al.

They wore an accelerometer for 7 days and underwent comprehensive cognition testing at both baseline and after 12 weeks. The patients average daily step count went down over the period, from about 3460 to 3118 ($P$=0.02). Time spent sedentary did not change significantly, however.

At the same time, various cognitive measures didn't change much or showed slight improvement, on average, although there was wide variability. **That still left substantial numbers of patients with deficits at 12 weeks, including 10.5% of patients with T-scores (reflecting a composite of test end points) <35 for attention/executive function, 12.3% with <35 in the memory domain, and 3.5% with <35 for the language composite. Deficits were most prevalent for two components of the attention/executive-function composite, the Frontal Assessment Battery (21.1%) and the California Verbal Learning Test (19.3%).**

In multivariate analysis controlling for sex, HF severity, LVEF, and depressive symptoms, as well as baseline attention/executive-function scores, **a decline in time spent in moderate to vigorous actively over 12 weeks significantly predicted ($P$=0.04) deterioration in attention/executive-function score; the predictive value of a drop-off in light activity fell short of significance ($P$=0.08). A similar pattern of correlation was not seen for memory or language scores.**

The authors acknowledge the study's limitations, including small size and inability to control for comorbidities, medications, and other possible confounders, and propose prospective case-control studies to explore whether falloff in activity level should be considered "an important and modifiable risk factor" for some types of cognitive decline in HF.

*The study was funded by grants from the National Institutes of Health. The authors had report they have no relevant financial relationships.*

# Preventing Alzheimer's disease — with an antidepressant

**By MELISSA HEALY*contact the reporter***

Antidepressant appears to reduce accumulation of plaque that is a hallmark of Alzheimer's
Study finds citalopram lowers the concentration of beta-amyloid in the cerebrospinal fluid

Citalopram, an antidepressant better known by its commercial name Celexa, has a remarkable side effect, a new study has found: In both mice bred to develop Alzheimer's disease and in healthy human volunteers, the selective serotonin reuptake inhibitor, or SSRI, drives down the production of a protein called beta-amyloid, which in the brains of those with Alzheimer's clumps together in sticky plaques and is thought to short-circuit the brain's wiring.

In study participants free of Alzheimer's disease or any other neuropsychiatric affliction, citalopram was found to reduce the concentration of beta-amyloid in the cerebrospinal fluid (outside of the brain) by 38%. Researchers see that as a clear sign that beta-amyloid protein in the brain, too, declines in those taking the antidepressant.

In older mice bred to develop an animal version of Alzheimer's disease, a 28-day regimen of citalopram arrested the growth of beta-amyloid plaques and reduced the appearance of new plaques by 78%. In healthy volunteers, the slowdown in beta-amyloid protein production, as measured in cerebrospinal fluid by lumbar puncture, was virtually immediate, occurring within hours of their having receive two doses of citalopram at 30 mg. each.

The new research, published Wednesday in the journal Science Translational Medicine, suggests that the widely-used antidepressant -- and possibly several others in the same class -- could become a relatively simple, cheap and potentially powerful way to prevent or delay the onset of Alzheimer's when taken by those at greatest risk of developing the devastating dementia.

That promising news could not come at a more opportune time. In their wide-ranging research on Alzheimer's disease, scientists have made enormous strides in devising means to detect and diagnose Alzheimer's in its earliest stages. But they've had far less success in developing therapies to thwart the disease before its symptoms of memory loss and confusion become evident.

The result of that mismatch is that many of those at greatest risk of developing Alzheimer's dementia feel they have little to gain from early screening for the disease. They would live with the knowledge that the disease would rob them of memory, independence and even a sense of self. But they could do nothing to avert that outcome.

But Alzheimer's specialist Dr. Lon Schneider of USC says it's far too early for people fearing a future marred by the disease to start taking citalopram, particularly at the dosage levels shown to be effective in the current study. For starters, he noted, the success of

antifdepressants in preventing Alzheimer's disease rests on an assumption that has not always panned out in research: **that reducing beta-amyloid in the brain will change the course of the illness.**

Beyond that, Schneider cautioned that an article published two months ago on citalopram as treatment for agitation associated with Alzheimer's found further cognitive impairment and cardiac toxicity in those taking it. The maximum dose used in the current study -- the equivalent of 60 milligrams -- is three times higher than the highest dose recommended for those over 60, he added.

"People should not start popping citalopram or other antidepressants in the expectation that they will prevent Alzheimer's disease," said Schneider, who was not involved in the latest study. "They could be doing some substantial harm."

In the study, researchers from University of Pennsylvania in Philadelphia and Washington University Medical School in St. Louis set out to explore the untapped powers of SSRIs to reduce production of beta-amyloid. Past research has found that while SSRIs do little to improve the clearance of beta-amyloid protein from the brain, they do reduce the protein's production in the brain.

**Studies tracking the progression of Alzheimer's disease have suggested that years and even decades before symptoms appear, beta-amyloid proteins become more plentiful in the brain (and spill into cerebrospinal fluid where they are more easily measured). First, the proteins aggregate in a sort of soluble goo form, and with time, they turn into insoluble, hard plaques. Both can disrupt signals among brain cells, but as plaques proliferate, normal communication among neurons is completely broken, and dementia takes hold.**

That conversion from goo to gunk appears to accelerate when beta-amyloid proteins become more concentrated, said the researchers. **Thus, in theory, a medication that can keep concentrations of beta-amyloid low might prevent amyloid plaques from forming altogether.**

Citing their own past research, the authors of the article suggested the same effect seems to take place with a wide range of SSRIs. **In the current study, the suppression of beta-amyloid production was not only substantial but it could also be detected very rapidly, in as few as five minutes after the drug was taken by healthy human volunteers.**

The researchers found the suppression of beta-amyloid production to be greater at larger doses of citalopram, but the most effective dose tested on mice was comparable to a 50-mg dose of citalopram, a dose that is substantially higher than that commonly used to treat those with depression.

APA Office of Communications & Public Affairs <Headlines@psych.custombriefings.com>

Customized Briefing for Dr Velandy Manohar

October 3, 2012

## Leading the News

### Obama Administration Releases Guidance On Medicaid Expansion.

The New York Times (10/2, A20, Pear, Subscription Publication) reported that the Obama Administration has released its first "definitive guidance" regarding Medicaid expansion since the Supreme Court ruled on the Affordable Care Act in June. The director of the Center for Medicaid and State Operations, Cindy Mann, said in a letter, "A state may choose whether and when to expand, and if a state covers the expansion group, it may decide later to drop the coverage." She added that, "there is no deadline," but states "would pay a price for delay." The Times notes that even with this guidance, "the Administration left major questions unanswered."

## Psychiatric Treatment/Disorders

### Risk Factors For MCI May Differ By Sex, Age. Key Findings

Medscape (10/3, Brauser) reports, "Risk factors for mild cognitive impairment (MCI) differ significantly by sex and age," according to a study (10/3) published in October issue of the American Journal of Geriatric Psychiatry. Findings "from the Sydney Memory and Aging Study, which assessed more than 700 elderly individuals who were either in their 70s (the younger group) or in their 80s (the older group), showed that those with the lowest overall risk for MCI were younger women." But, the researchers also found that "the younger women who walked slowly, had poor visual acuity, and/or had a history of depression were at high risk for MCI."

### New Canadian Depression Guideline Aims For Functional Recovery.

Medscape (10/3, Johnson) reports, "The treatment of major depressive disorder (MDD) should go beyond the goal of symptom relief to include a more global target of improving patients' overall and occupational functioning," a shift that "is reflected in new consensus recommendations currently being finalized by the Canadian Network for Mood and Anxiety Treatments (CANMAT)." Network executive chairman Raymond Lam, MD, of the University of British Columbia, told delegates at the Canadian Psychiatric Association's 62nd Annual Conference, "The ideal outcome really should be functional recovery."

### Small Study Identifies Differentiating Features Of Early Onset BD, AD/HD-C.

MedWire (10/3, Grasmo) reports, "Research findings published in the Journal of Abnormal Child Psychology have identified differentiating features between early-onset bipolar disorder (BD) and combined attention-deficit/hyperactivity disorder (AD/HD-C)." The "comparison of children and adolescents with BD (n=23), AD/HD-C (n=26), BD plus AD/HD-C (n=15), and 68 healthy controls on memory tests including the Digit span and Children's Verbal Learning Test-II suggests that patients with previous psychotic symptoms and concurrent BD may have inefficient encoding of verbal material," whereas "memory problems in AD/HD-C appear to be characterized by impaired free recall."

### Small Study Identifies Executive Attention Deficits In First-Episode Schizophrenia.

MedWire (10/3) reports, "Patients with first-episode schizophrenia (FES) have impairments in executive attention but not in alerting or orienting attention," according to a study published online Sept. 22 in BMC Psychiatry. "Evaluation of attention using the Attention Network Test (ANT) among 22 FES patients with a recent history of a single psychotic episode treated only with neuroleptics showed deficits in executive attention compared with 20 mentally healthy individuals." The study authors suggested that "executive attention deficit may...be a primary impairment during the progression of schizophrenia, even when clinical manifestations of the disease are controlled by antipsychotic medication."

# New 'MIND' diet linked to reduced risk of Alzheimer's

Last updated: Wednesday 18 March 2015 at 7am PST

A new diet developed by researchers from Rush University Medical Center in Chicago, IL, could significantly reduce the risk of Alzheimer's disease, even for those who do not follow it precisely.

This is the finding of a new study published in*Alzheimer's & Dementia: The Journal of the Alzheimer's Association*.

The diet - called the Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diet - was created by nutritional epidemiologist Martha Clare Morris, PhD, and colleagues at Rush. It uses aspects of the DASH (Dietary Approaches to Stop Hypertension) diet - an eating plan based on studies supported by the National Institutes of Health - and the **Mediterranean diet**.

While both the Mediterranean and DASH diets have been shown to reduce the risk of cardiovascular problems, such as **heart attack**, **stroke** and **high blood pressure**, some studies have suggested the diets may also protect against **dementia**.

The newly created MIND diet, according to Morris and Colleagues, is easier to follow than the Mediterranean and DASH diets. It consists of 15 dietary components: 10 "brain-healthy food groups" and five unhealthy food groups.

**Green leafy vegetables, other vegetables, nuts, berries, beans, whole grains, fish, poultry, olive oil and wine make up the brain-healthy foods, while red meats, butter and stick margarine, cheese, pastries and sweets, and fried or fast food are the food groups that should be limited.**

Unlike the DASH and Mediterranean diets - in which high consumption of all fruit s is recommended - the MIND diet focuses specifically on berries. Morris explains that **blueberries** and strawberries, in particular, have been hailed for their brain benefits in past research.

## Moderate adherence to MIND diet reduced Alzheimer's risk by 35%

For their study, the researchers analyzed the food intake of 923 Chicago residents between the ages of 58 and 98 who were part of the Rush Memory and Aging Project - an ongoing study that aims to identify factors that may protect cognitive health.

Dietary information was gathered from food frequency questionnaires the participants completed between 2004 and 2013. The researchers scored participants on how closely their food intake matched either the MIND diet, Mediterranean diet or DASH diet, and incidence of **Alzheimer's disease** was assessed over an average follow-up period of 4.5 years.

The researchers found that participants whose food intake closely followed either of the three diets were at lower risk of Alzheimer's. Participants who followed the Mediterranean diet were at 54% lower risk, those who followed the MIND diet were at 53% lower risk, while followers of the DASH diet had a 39% reduced risk for Alzheimer's.

**However, the team found that participants who had a moderate adherence to the Mediterranean or DASH diets showed no reduced risk for Alzheimer's, while moderate adherence to the MIND diet still put participants at 35% lower risk of developing the disease.**

Morris says one of the most exciting things about their findings is the fact that even following the MIND diet moderately well indicated significant protection against Alzheimer's. "I think that will motivate people," she adds.

However, the researchers note that to really benefit from the MIND diet, followers should not overindulge in unhealthy foods, particularly butter, cheese and fried foods.

On eliminating participants who changed their diet at some point during follow-up, the team found that participants who followed the MIND diet for a longer duration saw the highest protection against Alzheimer's. "As is the case with many health-related habits, including physical exercise," says Morris, "you'll be healthier if you've been doing the right thing for a long time."

While further studies are needed to confirm these findings, the researchers believe the MIND diet shows promise for reducing the risk of Alzheimer's. "We devised a diet and it worked in this Chicago study," Morris adds.

Talking to *Medical News Today*, Morris said there is no reason why people should wait to try the MIND diet, however. "The dietary components of the MIND diet are also the foundations of the Mediterranean and DASH diets - both of which have been found through randomized controlled trials to have many cardiovascular benefits," she said. "It is hard to come up with a potential downside to adopting these dietary habits."

Last week, *MNT* reported on a study published in *Science Translational Medicine*, in which Australian researchers reveal how a new **ultrasound technique successfully restored memory** in mouse models of Alzheimer's.

**Written by Honor Whiteman**

The abnormal protein clumps, inclusions, in the brain tissue are always present with the disease, **but there could be another underlying process that is actually causing the Alzheimer's - scientists are not yet sure.**[3]

This sort of change in brain nerves is also witnessed in other disorders,[3] and researchers want to find out more than just that there are protein abnormalities - they also want to know how these develop so that a cure or prevention might be discovered.

## Risk factors

Some things are more commonly associated with Alzheimer's disease - not seen so often in people without the disorder. These factors may therefore have some direct connection. **Some are preventable or modifiable factors (for example**, reducing the risk of **diabetes** or **heart disease** may in turn cut the risk of dementia).

If researchers gain more understanding of the risk factors, or scientifically prove any "cause" relationships for Alzheimer's, this could help to find ways to prevent it or develop treatments.

Risk factors associated with Alzheimer's disease include:[5,6]

***Unavoidable risk factors***

- **Age -** the disorder is more likely in older people, and a **greater proportion of over-85-year-olds have it than of over-65s.**[2]
- **Family history** (inheritance of genes) - having Alzheimer's in the family is associated with higher risk. **This is the second biggest risk factor after age.**[7]
- Having a certain gene (the apolipoprotein E or APOE gene) puts a person, depending on their specific genetics, at three to eight times more risk than a person without the gene.[6] Numerous other genes have been found to be associated with Alzheimer's disease, even recently (see developments below).[7]
- Being female (more women than men are affected).

***Potentially avoidable or modifiable factors***

- Factors that increase blood vessel (vascular) risk - including diabetes, high **cholesterol** and **high blood pressure**. (These also increase the risk of stroke, which itself can lead to another type of **dementia**.)
- Low educational and occupational attainment.
- Prior head injury. (While a **traumatic brain injury** does not necessarily lead to Alzheimer's, some research links have been drawn, with increasing risk tied to the severity of trauma history.)[8]
- **Sleep disorders (the breathing problem sleep apnea, for example).**
- **Estrogen** **hormone replacement therapy**.
- Anticholinergic Drug Use[VM]
- Benzodiazepine Drug Use[VM]

## Early-onset Alzheimer's disease

Genetics are behind early-onset familial Alzheimer's disease, which presents typically between the ages of 30 and 60 years and affects people who have a family history of it.

**Due to one of three inherited genes, it is also known as young-onset, and it is uncommon - accounting for under 5% of all Alzheimer's cases.**[6,9]

The Alzheimer's Association says in its **early-onset information** that it can sometimes be "a long and frustrating process" to get this diagnosis confirmed since doctors do not expect to find Alzheimer's in younger people**. For the younger age groups, doctors will look for other dementia causes first.** Healthcare professionals, the nonprofit says, may also "incorrectly attribute" symptoms to **stress** and so on, or may not agree on the diagnosis.[10]

## Recent developments in understanding causes and risk factors from MNT news

**Eleven new Alzheimer's risk genes** have been identified. The findings, published in ***Nature Genetics*** in **October 2013**, **mean the total number of genes found to be associated with Alzheimer's disease was 21.** Large research collaborations resulted in the breakthrough to help understand genetic factors behind the dementia. Just over 70,000 individuals were analyzed, **comparing the genes of 25,580 people who had Alzheimer's against 48,466 healthy controls, enabling the scientists to pinpoint genes that may put people at higher risk.**

**Alzheimer's onset could be triggered by sleep disturbances** - **Chronic sleep problems can inflame a number of health problems, from widespread pain to speeding up Cancer**. Though sleep disturbances have been observed in people with Alzheimer's disease, whether this is a cause or effect has been unknown. Now, **researchers say individuals with chronic sleep disruptions could face earlier onset of Alzheimer's.** Their pre-clinical study was published in the journal *Neurobiology of Aging*.

**DNA methylation in brain 'linked to Alzheimer's disease'** - **DNA methylation - the biochemical alteration of the building blocks of DNA - can indicate whether DNA is biologically active within a region of the human genome.** Now, researchers at Brigham and Women's Hospital in Boston, MA, and Rush University Medical Center in Chicago, IL, **have demonstrated how DNA methylation in the brain is implicated in Alzheimer's disease.**

**Increased Alzheimer's risk linked to long-term benzodiazepine use** - Long-term users of benzodiazepines, drugs used to treat **anxiety** and **insomnia**, **may be at increased risk of developing Alzheimer's disease, according to a new study published in the *BMJ*.**

**Brain network vulnerable to Alzheimer's and schizophrenia identified** - **New research has emerged that reveals a specific brain network - that is the last to develop and the first to show signs of neurodegeneration - is more vulnerable to unhealthy aging as well as to disorders that emerge in young people, shedding light on conditions such as Alzheimer's disease and schizophrenia.**

## Signs and symptoms

**The information in this section connects closely to some of that about tests and diagnosis below because symptoms noticed by patients, or people close to them, are exactly the same signs that healthcare professionals look for during testing.**

Symptoms can be diagnosed at any stage of Alzheimer's dementia and the **progression through the stages of the disease is monitored after an initial diagnosis, too, when the developing symptoms dictate how care is managed.**

Of course, the very nature of the symptoms can be confusing for both a patient and the people around them, with different levels of severity. For this reason, and because symptoms could signal any of a number of diagnoses, it is always worthwhile seeing a doctor.

For doctors to make an initial diagnosis of Alzheimer's disease, they must first be satisfied that there is **dementia** - **guidelines spell out what dementia consists of. It involves cognitive or behavioral symptoms that show a decline from previous levels of "functioning and performing" and interfere with ability "to function at work or at usual activities."**[11]

The cognitive decline is in at least **TWO** of the five symptom areas listed below (from **guidelines** jointly produced by the National Institute on Aging and the Alzheimer's Association):[11]

What is Alzheimer's disease? Causes, symptoms and treatment.

Last updated: Monday 23 February 2015

**1. Worsened ability to take in and remember new information, for example:**

- "Repetitive questions or conversations
- Misplacing personal belongings
- Forgetting events or appointments
- Getting lost on a familiar route."

**2. Impairments to reasoning, complex tasking, exercising judgment:**

- "Poor understanding of safety risks
- Inability to manage finances
- Poor decision-making ability
- Inability to plan complex or sequential activities."

**3. Impaired visuospatial abilities (but not, for example, due to eye sight problems):**

- "Inability to recognize faces or common objects or to find objects in direct view
- Inability to operate simple implements, or orient clothing to the body."

**4. Impaired speaking, reading and writing:**

- "Difficulty thinking of common words while speaking, hesitations
- Speech, spelling, and writing errors."

**5. Changes in personality and behavior, for example:**

- Out-of-character mood changes, including agitation; less interest, motivation or initiative; apathy; social withdrawal
- Loss of empathy
- Compulsive, obsessive or socially unacceptable behavior.

**Once the number and severity of these example symptoms confirm dementia, the best certainty that they are because of Alzheimer's disease is given by:**

- **A gradual onset "over months to years" rather than hours or days** (the case with some other problems)
- **A marked worsening of the individual person's normal level of cognition in particular areas.**[11]

**The most common presentation marking Alzheimer's dementia is where symptoms of memory loss are the most prominent, especially in the area of learning and recalling new information.** But the initial presentation can also be one of mainly language problems, in which case the greatest symptom is struggling to find the right words.[11]

**If visuospatial deficits are most prominent, meanwhile, these would include inability to recognize objects and faces, to comprehend separate parts of a scene at once (simultanagnosia),** and a type of difficulty with reading text (alexia). Finally, the most prominent deficits in "executive dysfunction" would be to do with reasoning, judgment and problem-solving.[11]

## Stages of Alzheimer's disease

**The progression of Alzheimer's can be broken down into three basic stages**:[12]

- Preclinical (no signs or symptoms yet)
- Mild cognitive impairment
- Dementia.

**The Alzheimer's Association has broken this down further, describing seven stages along a continuum of cognitive decline based on symptom severity - from a state of no impairment, through mild and moderate decline, and eventually reaching "very severe decline."**

The association has published the **seven stages** online.[13] It is not usually until stage four that a diagnosis is clear - here it is called mild or early-stage Alzheimer's disease, and "a careful medical interview should be able to detect clear-cut symptoms in several areas."

**Alzheimer's disease typically progresses slowly in three general stages — mild (early-stage), moderate (middle-stage), and severe (late-stage).** Since Alzheimer's affects people in different ways, each person will experience symptoms - or progress through Alzheimer's stages - differently.

### Overview of disease progression

The symptoms of Alzheimer's disease worsen over time, although the rate at which the disease progresses varies. On average, a person with Alzheimer's lives four to eight years after diagnosis, but can live as long as 20 years, depending on other factors.

Changes in the brain related to Alzheimer's begin years before any signs of the disease. This time period, which can last for years, is referred to as preclinical Alzheimer's disease.

The stages below provide an overall idea of how abilities change once symptoms appear and should only be used as a general guide. They are separated into three different categories: mild Alzheimer's disease, moderate Alzheimer's disease and severe Alzheimer's disease. Be aware that it may be difficult to place a person with Alzheimer's in a specific stage as stages may overlap

### Mild Alzheimer's- Early Stage

In the early stages of Alzheimer's, a person may function independently. He or she may still drive, work and be part of social activities. Despite this, the person may feel as if he or she is having memory lapses, such as forgetting familiar words or the location of everyday objects.

Friends, family or neighbors begin to notice difficulties. During a detailed medical interview, doctors may be able to detect problems in memory or concentration. Common difficulties include:

- Problems coming up with the right word or name

- Trouble remembering names when introduced to new people
- Having greater difficulty performing tasks in social or work settings
- Forgetting material that one has just read
- Losing or misplacing a valuable object
- Increasing trouble with planning or organizing.

Although the onset of Alzheimer's disease cannot yet be stopped or reversed, an early diagnosis can allow a person the opportunity to live well with the disease for as long as possible and plan for the future.

**Moderate Alzheimer's disease-Middle Stage**

Moderate Alzheimer's is typically the longest stage and can last for many years. As the disease progresses, the person with Alzheimer's will require a greater level of care.

You may notice the person with Alzheimer's confusing words, getting frustrated or angry, or acting in unexpected ways, such as refusing to bathe. Damage to nerve cells in the brain can make it difficult to express thoughts and perform routine tasks.

**At this point, symptoms will be noticeable to others and may include:**

- Forgetfulness of events or about one's own personal history
- Feeling moody or withdrawn, especially in socially or mentally challenging situations
- Being unable to recall their own address or telephone number or the high school or college from which they graduated
- Confusion about where they are or what day it is
- The need for help choosing proper clothing for the season or the occasion
- Trouble controlling bladder and bowels in some individuals
- Changes in sleep patterns, such as sleeping during the day and becoming restless at night
- An increased risk of wandering and becoming lost
- Personality and behavioral changes, including suspiciousness and delusions or compulsive, repetitive behavior like hand-wringing or tissue shredding

During the moderate stage of Alzheimer's, individuals may have greater difficulty performing tasks such as paying bills, but they may still remember significant details about their life.

**Severe Alzheimer's Disease- [Late Stage]**

In the final stage of this disease, individuals lose the ability to respond to their environment, to carry on a conversation and, eventually, to control movement. They may still say words or phrases, but communicating pain becomes difficult. As memory and cognitive skills continue to worsen, personality changes may take place and individuals need extensive help with daily activities.

**At this stage, individuals may:**

- Require full-time, around-the-clock assistance with daily personal care
- Lose awareness of recent experiences as well as of their surroundings
- Require high levels of assistance with daily activities and personal care
- Experience changes in physical abilities, including the ability to walk, sit and, eventually, swallow
- Have increasing difficulty communicating
- Become vulnerable to infections, especially pneumonia

**Care takers and Care Givers must be consistently encouraged to Get support at regular intervals**

Late-stage care decisions can be some of the hardest families face. Connect with other caregivers who have been through the process on our online message boards and get helpful resources in our Caregiver Center.

**Key Message for all Care givers and Care takers – "Help is available"**

Your local Alzheimer's Association chapter can connect you with the resources you need to cope with the symptoms and challenges of Alzheimer's. Find a chapter in your community

Our free 24/7 Helpline provides information, referral and care consultation by professionals in more than 200 languages.

Our Greenfield Library houses more than 5,000 books, journals and resources. Access it online.

I welcome your comments at my e-mail address: velandy_manohar_md@comcast.net

Velandy Manohar, MD

Distinguished Life Fellow, Am Psychiatric Association

# Novel Intervention May Reverse Alzheimer's Memory Loss

Pam Harrison

October 03, 2014

A novel, comprehensive lifestyle intervention has shown promise in reversing memory loss related to Alzheimer's disease (AD), preliminary research suggests.

According to investigators, this novel intervention is aimed at "tweaking" the network of imbalances in the brain that contribute to cognitive decline.

"We've been studying the underlying mechanisms of neurodegeneration in the test tube and in transgenic mice for 25 years, and we came to the conclusion that there is an imbalance between the physiological processes that mediate plasticity in Alzheimer's disease — between synaptoblastic and synaptoclastic signaling — similar to what we see in osteoporosis, where osteoblastic signaling is chronically exceeded by osteoclastic signaling, resulting in bone loss," principal investigator Dale Bredesen, MD, professor of neurology and director, Mary S. Easton Center for Alzheimer's Disease Research, University of California, Los Angeles, told *Medscape Medical News.*

Through this lifestyle intervention, "it appears we can correct this network imbalance by tweaking it at multiple sites," Dr Bredesen added.

The study was published online September 27 in the journal *Aging*.

**Sustained, Marked Improvement**

A total of 10 patients with memory loss associated with either AD, mild cognitive impairment, or subjective cognitive impairment were recruited for the study.

Each participant was instructed to follow a personalized intervention program tailored to address specific metabolic deficits identified on laboratory testing as affecting the plasticity of the participant's brain, causing memory loss.

Nine of the 10 patients displayed subjective or objective improvement in cognition within 3 to 6 months of initiation of treatment. The single patient who failed to respond to the intervention had late-stage AD.

Six participants had discontinued working or were struggling with their jobs at study outset because of memory problems.

"All were able to return to work or continue working with improvement performance, and improvements have been sustained," said Dr Bredesen.

At the present time, one patient has been followed for 2.5 years from the initial presentation, and the patient continues to show "sustained and marked improvement."

Dr Bredesen noted that the level of improved function required to work effectively is an important outcome of any successful therapeutic intervention.

**Optimizing Metabolic Parameters**

In studies of transgenic mice, Dr Bredesen and colleagues found that beta-amyloid precursor protein (APP) signaling can be manipulated to inhibit the underlying pathophysiology that causes AD.

However, many different metabolic factors contribute to APP signaling, including hormones, inflammatory mediators, and exercise.

This suggests that the pathobiology of AD must be approached at different points of intervention and not with a single targeted agent.

"Just as for other chronic illnesses such as atherosclerotic cardiovascular disease, the goal is not simply to normalize metabolic parameters, but rather to optimize them," the investigators write.

"Based on the hypothesis that AD results from an imbalance in an extensive plasticity network, the therapy should address as many network components as possible, with the idea that a combination approach may create an effect that is more than the sum of the effects of many monotherapeutics," the researchers add.

Critical to the success of this hypothesis is the idea that there is a "threshold" at which multiple interventions will start to reverse the pathology leading to memory loss.

As Dr Bredesen points out, it has been shown by Dean Ornish, MD, founder and president of Preventive Medicine Research Institute, San Francisco, California, among others that with a large enough lifestyle change, buildup of atherosclerotic plaque and subsequent coronary artery disease can be reversed.

Similarly, in AD, if enough of the factors that contribute to the imbalance between synaptoblastic and synaptoclastic signaling in the brain can be reversed, deficits in the network that lead to memory loss can be redressed — "and you start to see improvement, which is exactly what we saw in these patients. If they follow enough of these interventions, they are able to improve," Dr Bredesen said.

**Tailored Interventions**

The interventions used in the 10 patients involved in the UCLA pilot project were tailored to each individual, but they shared similar elements. Typically, patients were asked to eliminate all simple carbohydrates from their diet.

They were also asked to increase consumption of fruit, vegetables, and nonfarmed fish and to follow a strict meal pattern with specifically timed interludes of fasting.

Exercise was a key component of all interventions, and participants were counseled on ways to reduce stress through practices such as yoga and meditation.

Participants also took a large variety of daily supplements, including vitamin D3, fish oil, coenzyme Q10, melatonin, and methylcobalamin.

And where appropriate, practitioners counseled their female patients to resume previously discontinued hormone replacement therapy.

"The program is not easy to follow," Dr Bredesen acknowledged. (None of the patients in this pilot project were able to fully follow the program).

"But what this program says is that we are all contributing to our own AD by the diet we chose to eat; by the way we sleep; by the stress we have in our lives; by our microbiome; and of course by our genetics.

"The important thing here is, we can alter cognitive decline by affecting each of these parameters."

**Growing Evidence**

Commenting on the study for *Medscape Medical News*, Heather Snyder, PhD, director, medical and scientific relations, Alzheimer's Association, Chicago, Illinois, said a number of studies have shown that lifestyle interventions can attenuate the progressive decline in cognitive function in older individuals.

Most recently, the FINGER study (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability), which was presented earlier this year at the Alzheimer's Association International Conference 2014 and was reported by *Medscape Medical News* at that time, showed that a multipronged lifestyle intervention had a significant beneficial effect on overall

cognitive performance, including memory, executive function, and psychomotor speed, in a large cohort of older participants at high risk for cognitive decline.

"The FINGER study certainly suggests that this is the kind of study we need to do in translating what Dr Bredesen did to a much larger clinical trial," Dr Snyder said.

Dr Snyder also noted that it is clear the underlying pathology driving AD is already changing well before patients manifest overt memory loss and accompanying symptoms of the disease.

"This presents us with an opportunity to identify those individuals at the earliest stage of AD, when we can intervene with a medication or some type of nonpharmacological intervention," she suggested.

Efforts to do just that are already under way with the launch of the Anti-Amyloid Treatment in Asymptomatic Alzheimer's (A4) study. The A4 study is designed to evaluate the effectiveness of an investigational drug to attenuate memory loss in patients at high risk for AD.

*Dr Bredesen and Dr Snyder report no relevant financial relationships.*

*Aging*. Published online September 27, 2014. Full text

AMA Viewpoint | April 15, 2015

# Cognitive Aging: A Report From the Institute of Medicine FREE ONLINE FIRST

Dan G. Blazer, MD, MPH, PhD[1]; Kristine Yaffe, MD[2]; Jason Karlawish, MD[3]

Viewpoint | April 15, 2015

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The Institute of Medicine recently released a report entitled *Cognitive Aging: Progress in Understanding and Opportunities for Action*, which addresses the emerging concept of cognitive aging, the importance of this issue for the nation's public health, and actions the nation needs to take to better understand and maintain the cognitive health of older adults.[1]

Cognitive aging is a lifelong process of gradual, ongoing, yet highly variable changes in cognitive function that occur as people get older. Some cognitive functions decrease predictably, such as memory and reaction time, whereas some other functions are either maintained or may even increase, such as wisdom and knowledge. Characteristics of cognitive aging are presented in the Box.

**Box.**

**Characteristics of Cognitive Aging**

**Key Features**

- Inherent in humans and animals as they age
- Occurs across the spectrum of individuals as they age regardless of initial cognitive function
- Highly dynamic process with variability within and between individuals
- Includes some cognitive domains that may not change, may decline, or may improve with aging, and there is the potential for older adults to strengthen some cognitive abilities
- Only now beginning to be understood biologically yet clearly involves structural and functional brain changes

- Not a clinically defined neurological or psychiatric disease and does not inevitably lead to neuronal death and neurodegenerative dementia (such as in Alzheimer disease)

### Risk and Protective Factors

- Health and environmental factors over the life span influence cognitive aging
- Modifiable and nonmodifiable factors include genetics, culture, education, medical comorbidities, acute illness, physical activity, and other health behaviors
- Cognitive aging can be influenced by development beginning in utero, infancy, and childhood

### Assessment

- Cognitive aging is not easily defined by a clear threshold on cognitive tests because many factors—including culture, occupation, education, environmental context, and health variables (eg, medications)—influence test performance and norms
- For an individual, cognitive performance is best assessed at several points in time

### Effect on Daily Life

- Day-to-day functions may be affected, such as driving, making financial and health care decisions, and understanding instructions given by health care professionals
- Experience, expertise, and environmental support aids (eg, lists) can help compensate for declines in cognition
- The challenges of cognitive aging may be more apparent in environments that require individuals to engage in highly technical and fast-paced or timed tasks, situations that involve new learning, or

stressful situations (eg, emotional, physical, or health-related) and are less apparent in highly familiar situations

Cognitive aging is not a disease or a quantifiable level of dysfunction. It is distinct from Alzheimer disease and other neurocognitive and psychiatric disorders that affect older adults' cognitive health, so it is best measured and studied longitudinally among adults who are free of these disorders. Animal models of aging demonstrate that neurons do not die with aging, but their synaptic structure and function are diminished, particularly in prefrontal cortical regions. The committee that prepared the report on cognitive aging concluded this finding is important because it suggests the possibility for improving cognitive health.

Cognition and cognitive health are matters of the life span. Cognitive health is described as the maintenance of optimal cognitive function with age. The evidence showed that cognitive aging and its influence on cognitive health are matters of pressing public health importance.

Individuals are deeply concerned about declines in memory and decision-making abilities as they age. They may worry that these declines are early signs of a neurodegenerative disease, particularly Alzheimer disease, and they fear losing their independence and a worsening quality of life. Maintenance of cognitive function, or "staying mentally sharp," may be the primary health concern of older adults.[2] Cognitive decline also affects older adults' family members and friends, who are concerned about the older person's continued ability to drive or make financial decisions and who often are called to assist them even if the older adult does not meet criteria for a diagnosable disorder.

An individual and society can be affected by cognitive aging because of 2 issues. First, older adults lose an estimated $2.9 billion a year, directly and indirectly, to financial fraud.[3] To address this, the committee called for financial institutions and relevant government agencies to develop and improve programs and services used by older adults to help them avoid exploitation, optimize independence, and make sound financial decisions. Second, older adults may develop problems with driving, especially because reaction time is critical and decision making must be at times almost instantaneous. Although most older adults are more experienced drivers, their driving capability may be compromised and recognition of these deficits and programs to help correct them will be essential.

Although the study of cognitive aging, especially clinical trials of interventions, is in its infancy, well-designed studies support some actions that individuals can take to promote their cognitive health: be physically active; reduce and manage cardiovascular disease risk factors, including high blood pressure, diabetes, and smoking; and regularly discuss and review with a health care professional the medications that might influence cognitive health. None of these findings are unique to cognitive aging—each is good advice for many health conditions—yet the finding that these actions may promote cognitive health as persons age emphasizes the importance of public health resources and programs to promote them. Although the evidence is not as strong, other actions may promote cognitive health: be socially and intellectually active; continually seek opportunities to learn; get adequate sleep; and seek professional treatment for sleep disorders, if needed.

Health care systems and health care professionals will play a key role in educating patients and their families about cognitive aging and in implementing interventions to ensure optimal cognitive health across the life cycle. The committee noted the importance of programs to avoid delirium associated with medications or hospitalizations. Educating the patient and family members should include these clear messages: the brain ages, just like other parts of the body; cognitive aging is not a disease; cognitive aging is different for every individual (there is wide variability across persons of similar age); some cognitive functions improve with age and neurons are not dying as in Alzheimer disease (hence, realistic hope is inherent in cognitive aging); and patients can take certain steps to help protect their cognitive health.

Society can also contribute to cognitive health. The committee recommended that the US Food and Drug Administration and Federal Trade Commission should determine the appropriate regulatory review, policies, and guidelines for products advertised to consumers to improve cognitive health, such as medications, nutritional supplements, and cognitive training. Many medications and brain-stimulating

activities are being marketed directly to the public. Even though the committee did not evaluate each of these separately, it did find that overall the evidence for their effectiveness, especially the transfer of cognitive gains to real-life situations and the long-term benefit of the interventions, remains to be clearly demonstrated. Nevertheless, new data will undoubtedly emerge and could allow better evaluation of these interventions.

Cognitive aging is not a disease, but it is a major public health issue. Despite the public health importance of cognitive aging, there is limited research available on this process, especially research into basic biological mechanisms leading to cognitive aging and research into potential interventions through controlled clinical trials. The activities of multiple groups—advocacy groups, research organizations, government agencies, communities, health care professionals, senior centers, financial institutions, and departments of transportation—will be necessary for society to both better understand cognitive aging and promote cognitive health in later life. Patients are already concerned. The time has come for physicians, other health care professionals, and researchers to enter the conversation with them.

## ARTICLE INFORMATION

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## Clinical & Research News

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# Antipsychotics for Elderly Vary in Mortality Risk

Leslie Sinclair,

Nursing-home patients are typically excluded from randomized clinical trials, but a cohort study of antipsychotics in this population reveals frightening results.

Do elderly residents who receive antipsychotic drugs in nursing homes have a greater risk of dying than their non-medicated neighbors? Yes, and the severity of the risk depends on which drug they are taking.

That's the conclusion of researchers at Brigham and Women's Hospital and Harvard Medical School, who published their study in the February 23 *BMJ.*

**Krista Huybrechts, Ph.D.**

Led by Krista Huybrechts, Ph.D., an Instructor in Medicine in the Division of Pharmacoepidemiology and Pharmacoeconomics at the hospital, the team of researchers performed a population-based cohort study with linked data from Medicaid, Medicare, the Minimum Data Set, the National Death Index, and a national assessment of nursing-home quality. **The participants were 75,445 new users of antipsychotic drugs (haloperidol, aripiprazole, olanzapine, quetiapine, risperidone, and ziprasidone**; other antipsychotics were excluded because they were used by too few patients**). All participants were aged 65 or older, eligible for Medicaid, and living in a nursing home during 2001 to 2005.**

"The appropriate use of prescription medications in older patients is an important public-health concern," Huybrechts explained to *Psychiatric News* when asked to describe the impetus for the project. "**Older patients are more vulnerable to the side effects of all drugs, and psychotropics in particular, because of age-related changes in pharmacodynamic and pharmacokinetic processes. Because of polypharmacy, the chance that an older individual will be taking more than one medication with similar side effects increases, as does the risk of adverse drug interactions. The continued high use of antipsychotic medications in nursing-home residents, despite the FDA health advisories, motivated me to examine more closely the comparative safety of these agents."**

Huybrechts is referring to the Food and Drug Administration's (FDA) 2005 Public Health Advisory in which the agency said that it had determined the treatment of behavioral disorders in elderly patients with dementia with atypical (second generation) antipsychotic medications is associated with increased mortality. That advisory led to black-box warnings being added to the labels of all atypical antipsychotics. Subsequent studies found risks at least as high among users of conventional antipsychotics, and the FDA issued a similar warning for such drugs in 2008.

In their report, Huybrechts and colleagues cited a recent audit by the Department of Health and Human Services that showed continued growth in the number of people with dementia. That increase, along with the perceived need for some type of intervention in patients with severe persistent symptoms, and a paucity of effective alternative pharmacological or behavioral approaches, means the use of antipsychotic drugs in nursing homes is likely to remain substantial.

**Their results were daunting, with Huybrechts and her colleagues finding that there is a variation in the risk of death according to the type of drug used in elderly residents receiving antipsychotics in nursing homes.** Compared with risperidone users, for example, haloperidol users had double the risk of mortality within 180 days, and quetiapine users had a decreased risk. **The effects were strongest shortly after the start of treatment and remained after adjustment for dose**. No clinically meaningful differences were observed for the other drugs. There was no evidence that the treatment effect differed

for patients with a diagnosis of dementia or behavioral disturbances. **A dose-response relationship was observed for all drugs except quetiapine.**

The findings about haloperidol were especially concerning, but consistent with those of previous observational studies, and Huybrechts believes they have clinical importance. "**The current FDA advisories for antipsychotics do not distinguish between individual agents and therefore offer no guidance to clinicians who have decided to proceed with drug treatment for severe and refractory behavioral problems,**" she told *Psychiatric News.* "Our hope is that clinicians who are currently prescribing haloperidol to manage behavioral problems associated with dementia will reconsider this practice … and will consider prescribing an alternative agent instead if they feel that pharmacologic treatment is indicated."

Huybrechts said the evidence provided by the study reinforces the risks associated with the use of antipsychotics and underscores the need to try alternative means of dealing with behavioral problems in elderly patients with dementia. "**While our findings cannot tackle the efficacy-safety tradeoff involved in the decision to proceed with drug treatment for severe and refractory behavioral problems, they can contribute to decision making regarding treatment," she said**.

Huybrechts and her colleagues are completing a companion study that evaluates antipsychotic agents in community-dwelling elderly individuals, as opposed to nursing-home residents.

This study was supported by awards from the Agency for Healthcare Research and Quality, and researchers Huybrechts and Sebastian Schneeweiss, M.D., were partially funded by the National Institute of Mental Health. ■

***"Differential Risk of Death in Older Residents in Nursing Homes Prescribed Specific Antipsychotic Drugs: Population-Based Cohort Study" is posted at www.bmj.com/content/344/bmj.e977 .***

# Experts Recommend New Approach for Treating Neuropsychiatric Symptoms of Dementia

A panel of neurocognitive experts from the University of Michigan and Johns Hopkins University proposed in an articlein the *Journal of the American Geriatrics Society*, an alternative method to help reduce unfavorable neuropsychiatric symptoms such as agitation—that are often associated with dementia.

“Often, more than memory loss, behavioral symptoms of dementia are among the most difficult aspects of caring for people with dementia,” said **Helen Kales, M.D**., lead author and an assistant professor of psychiatry at Michigan. “These symptoms are experienced almost universally… [They] are often associated with poor outcomes including early nursing home placement, hospital stays, caregiver stress and depression, and reduced caregiver employment.”

The approach, dubbed DICE—presented this week at APA’s annual meeting—focuses on the implementation of environmental modifications and other interventions, such as exercise, as a first-line method to alleviate neuropsychiatric symptoms.

Briefly described, the components are:

•**D**: Describe - Asking the caregiver, and the patient if possible, to describe the "who, what, when, and where" of situations in which problem behaviors occur and the physical and social context for them. These observations will be shared with caregivers.

•**I**: Investigate – Having the health provider look into all aspects of the patient's health, including dementia symptoms and current medications and sleep habits, that might be combining with physical, social, and caregiver-related factors to produce the behavior.

•**C**: Create – Working together, the patient's caregiver and health providers develop a plan to prevent and respond to behavioral issues, including everything from changing the patient's activities and environment to educating and supporting the caregiver.

•**E**: Evaluate – Giving the provider responsibility for assessing how well the plan is being followed and how it's working, or what might need to be changed.

In an interview with *Psychiatric News*, Kales said, “Innovative approaches are needed to support and train the front-line providers for older populations with behavioral symptoms of dementia. We believe that the DICE approach offers clinicians an evidence-informed structured clinical reasoning process that can be integrated into diverse practice settings.”

To see read more about nonpharmacological therapies for treating symptoms of neurocognitive disorders, see the *Psychiatric News* article, "Mindful Exercises and Meditation: Neurobiological Effects." Also, watch a *Psychiatric News*interview with Kales here.

**From the President**

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## Mindful Exercises and Meditation: Neurobiological Effects

Dilip Jeste, M.D.

There is a tendency to divide psychiatric interventions into two distinct groups: pharmacological/biological and psychosocial/behavioral. Such a classification implies that pharmaceuticals work through biologic mechanisms, while psychosocial ones act through mental/behavioral processes. This notion is simplistic and erroneous. Many studies have shown that at least a part of the effect of medications is probably placebo effect by virtue of a patient's expectations that a drug prescribed by an expert physician must be effective.

At the same time, a growing number of investigations have demonstrated biological changes, not just in function but also in the structure of the brain, produced by psychotherapeutic and social interventions. For example, cognition enhancement therapy has been shown to increase gray matter in specific regions of the brain on MRIs in people with schizophrenia. Similar research has recently expanded to integrative medicine—formerly called complementary and alternative medicine. Interventions such as meditation, Tai Chi, and yoga, which once were considered unscientific, have been found to be useful in some people with mental illness and to have significant effects on brain-based as well as blood-based biomarkers.