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2021 Brock Institute Glennan Lecture

Virtual Presentation:

"An Approach to the Management of Cognitive Disfunction"

John Morley, MD, Professor of Medicine,
St. Louis University, St. Louis, MO

November 16, 2021

6:00 – 7:30 pm

The Brock Institute Glennan Lecture established by the Cooke Fund of the Hampton Roads Community Foundation

EVMS
GLENNAN CENTER
FOR GERIATRICS
AND GERONTOLOGY

25TH ANNIVERSARY

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M. FOSCUE BROCK
INSTITUTE FOR COMMUNITY
AND GLOBAL HEALTH

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M. Foscue Brock Institute for Community & Global Health

M. Foscue Brock, MD, was a tuberculosis specialist in charge of Norfolk's Grandy Sanitorium for 29 years before he entered private practice. Dr. Brock volunteered at the public health center in Norfolk throughout his career and was a popular family doctor. It was Dr. Brock's involvement with the community that inspired Dr. Brock's son, Macon F. Brock Jr., co-founder and chairman of Dollar Tree, Inc., and Macon's wife, Joan, to establish the M. Foscue Brock Institute for Community and Global Health at EVMS.

M. Foscue Brock, MD

The M. Foscue Brock Institute for Community and Global Health honors the values that led Dr. Brock in his life and career, aligning seamlessly with EVMS' values: excellence, collegiality and integrity. The vision of the institute is to be a focal point for integrating EVMS' clinical, education and research programs to fulfill its vision of becoming the most community-oriented school of medicine and health professions in the nation.

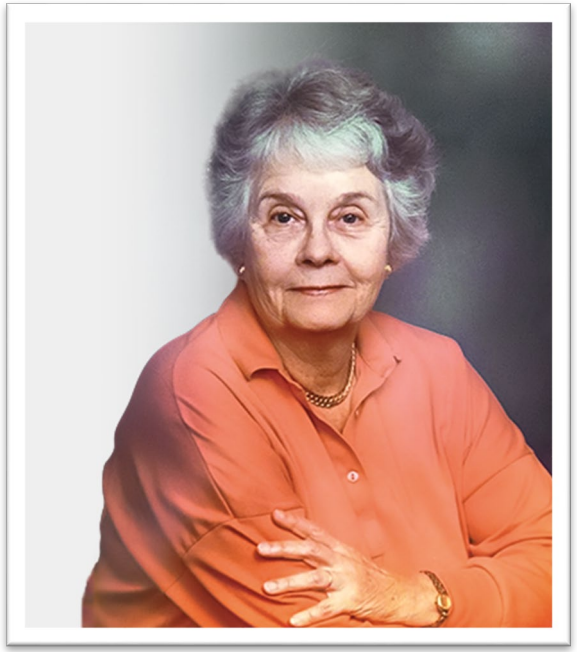
In accordance with its vision and mission, the institute invites scholars from around the country whose work inspires innovative ways to decrease health disparities and build cultural competency.

Glennan Center

The Glennan Center for Geriatrics and Gerontology was established in 1995 through a generous gift from Virginia Glennan Ferguson in honor of her father and grandfather.

The Glennan Center's mission is to integrate, coordinate and disseminate all age-related endeavors at EVMS.

The center's ultimate goals are to promote the health, well-being, independence, and quality of life of older adults; and to enhance the knowledge base and standards of practice in geriatrics and gerontology through clinical practice, education, research and advocacy on behalf of older adults and their caregivers.



Virginia Glennan Ferguson

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Brock Institute Glennan Lecture

Established in 2015 through *The Cooke Fund of the Hampton Roads Community Foundation* to highlight the latest in geriatric academic research. Every year lecture series has brought world-renowned leaders in geriatric care to EVMS to share their knowledge with the students, faculty, community physicians and leaders in healthcare throughout Hampton Roads.

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Disclosure of Relevant Relationships with Relevant Commercial Companies/Organizations

Eastern Virginia Medical School endorses the Standards for Commercial Support of the Accreditation Council for Continuing Medical Education and the Guidelines of the Association of American Medical Colleges that the sponsors of continuing medical education activities and the speakers at these activities disclose relevant relationships with commercial companies whose products or services are discussed in educational presentations.

For sponsors, relevant relationships include large research grants, institutional agreements for joint initiatives, substantial gifts, or other relationships that benefit the institution. For speakers, relevant relationships include receiving from a commercial company research grants, consultancies, honoraria and travel, other benefits, or having a self-managed equity interest in a company.

John Morley, MD disclosed he is a consultant for Merck, Behringer, and Ingelheim. All potential relevant financial relationships have been mitigated.

Marissa Galicia-Castillo, MD disclosed she receives financial/material support from Senior Medical Consultants, LLC. All potential relevant financial relationships have been mitigated.

The Planning Committee disclosed they have no relevant financial relationships.

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Continuing Medical Education

Accreditation

Eastern Virginia Medical School is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Credit Designation

Eastern Virginia Medical School designates this live activity for a maximum of ***1.5 AMA PRA Category 1 Credits***™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

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John Morley, MD

Professor of Medicine

St. Louis University

St. Louis, MO

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Dr. Morley's Presentation

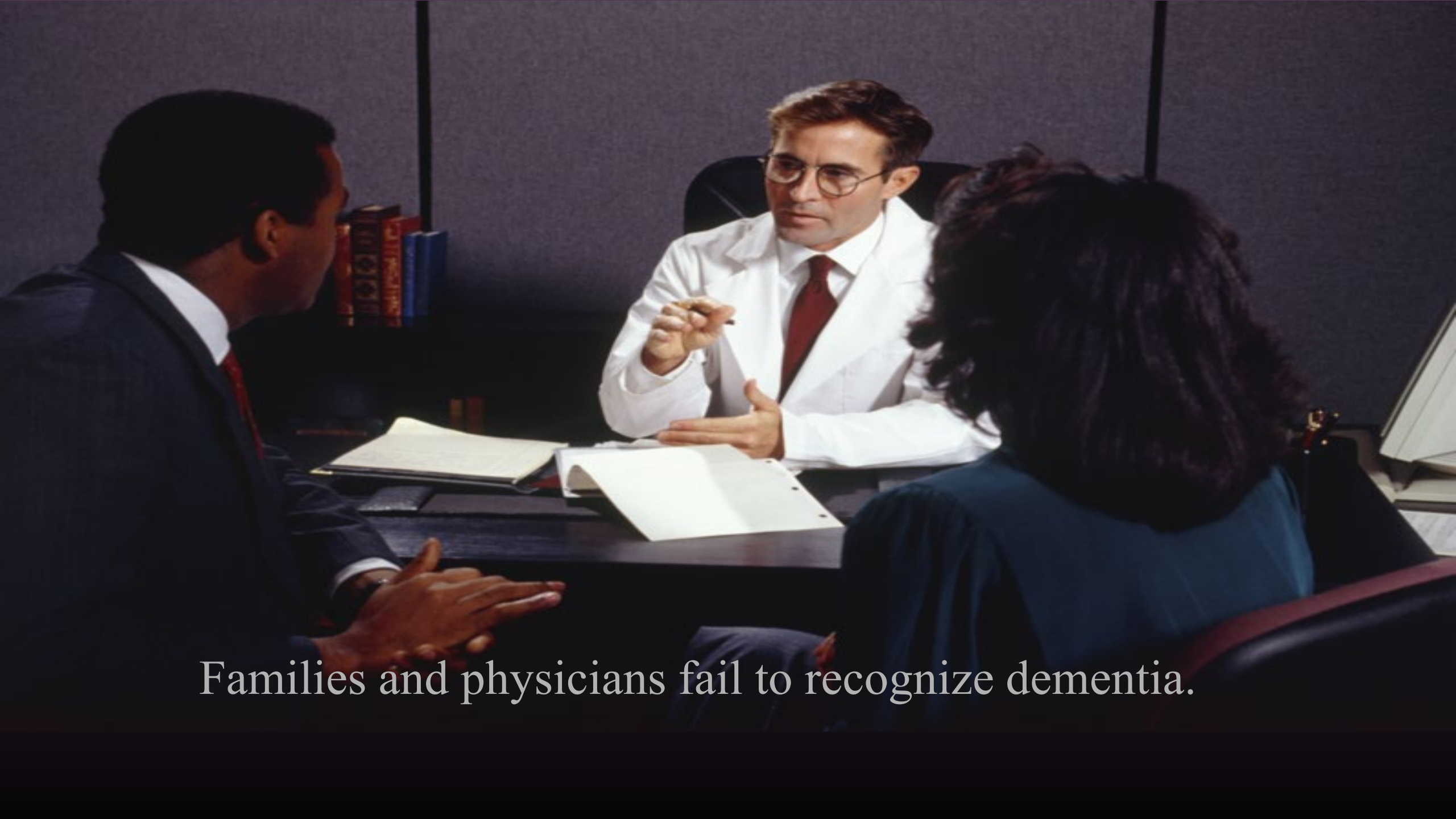
An Approach to the Management of Cognitive Disfunction

An Approach to Cognitive Dysfunction

Gateway Geriatric Education Center

Saint Louis University
Division of Geriatric Medicine


“Memory is a passion
no less powerful or pervasive
than love.”
Elie Wiesel
“All Rivers Run to the Sea”

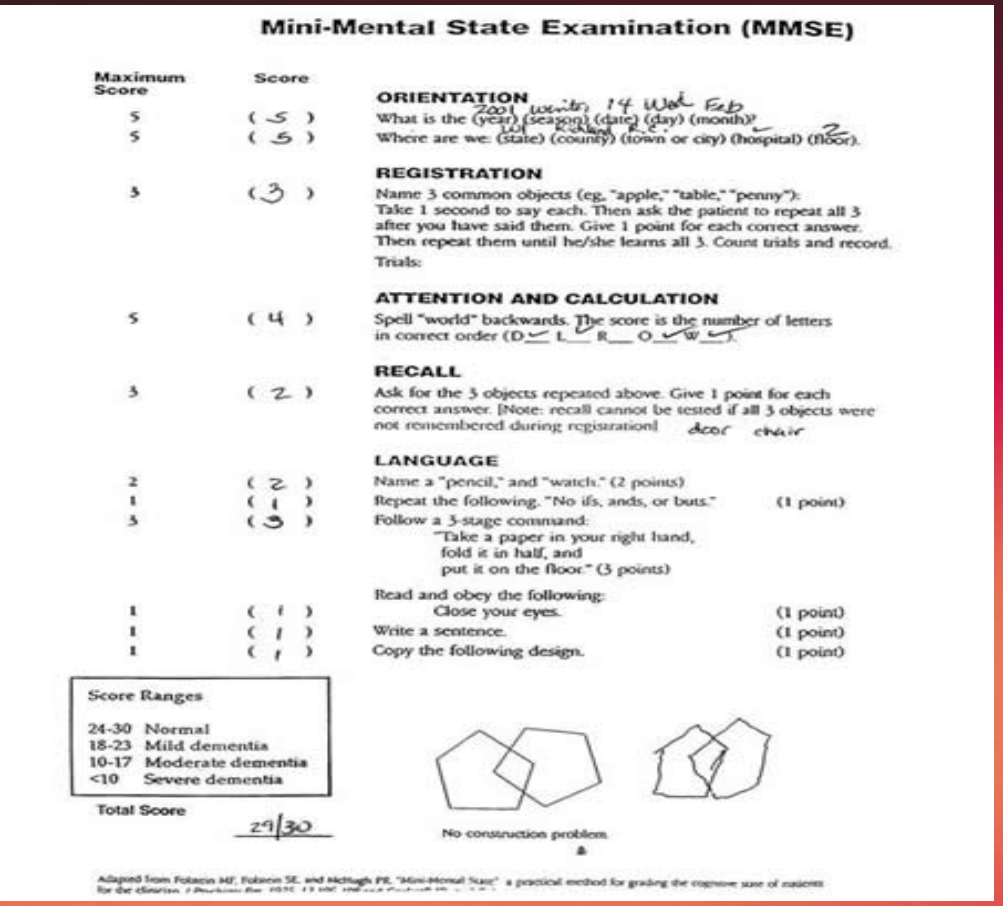


Families and physicians fail to recognize dementia.

Mini-Mental Status Examination

Folstein *et al.* 1975

1. Educationally dependent
2. Both false positives and false negatives
3. Minimal testing of visuospatial system



Mini-Mental State Examination (MMSE)

Maximum Score	Score	
		ORIENTATION
5	(5)	What is the (year) (season) (date) (day) (month)?
5	(5)	Where are we: (state) (county) (town or city) (hospital) (floor).
		REGISTRATION
3	(3)	Name 3 common objects (eg, "apple," "table," "penny"): Take 1 second to say each. Then ask the patient to repeat all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until he/she learns all 3. Count trials and record. Trials:
		ATTENTION AND CALCULATION
5	(4)	Spell "world" backwards. The score is the number of letters in correct order (D L R O W)
		RECALL
3	(2)	Ask for the 3 objects repeated above. Give 1 point for each correct answer. [Note: recall cannot be tested if all 3 objects were not remembered during registration]
		LANGUAGE
2	(2)	Name a "pencil," and "watch." (2 points)
1	(1)	Repeat the following. "No ifs, ands, or buts." (1 point)
3	(3)	Follow a 3-stage command: "Take a paper in your right hand, fold it in half, and put it on the floor." (3 points)
1	(1)	Read and obey the following: Close your eyes. (1 point)
1	(1)	Write a sentence. (1 point)
1	(1)	Copy the following design. (1 point)

Score Ranges	
24-30	Normal
18-23	Mild dementia
10-17	Moderate dementia
<10	Severe dementia

Total Score 29/30

No construction problem

Adapted from Folstein MF, Folstein SE, and McHugh PR, "Mini-Mental State," a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-198.

VAMC
SLUMS EXAMINATION

Questions about this assessment tool? E-mail aging@slu.edu

ame_____ Age_____

the patient alert?_____ Level of education_____

_/1 (1) 1. What day of the week is it?

_/1 (1) 2. What is the year?

_/1 (1) 3. What state are we in?

4. Please remember these five objects. I will ask you what they are later.
Apple Pen Tie House Car

5. You have $100 and you go to the store and buy a dozen apples for $3 and a tricycle for $20
(1) How much did you spend?
_/3 (2) How much do you have left?

6. Please name as many animals as you can in one minute.
_/3 (0) 0-4 animals (1) 5-9 animals (2) 10-14 animals (3) 15+ animals

_/5 7. What were the five objects I asked you to remember? 1 point for each one correct.

8. I am going to give you a series of numbers and I would like you to give them to me backwards. For example, if I say 42, you would say 24.
_/2 (0) 87 (1) 648 (1) 8537

9. This is a clock face. Please put in the hour markers and the time at ten minutes to eleven o'clock.
(2) Hour markers okay
_/4 (2) Time correct

(1) 10. Please place an X in the triangle.

_/2 (1) Which of the above figures is largest?

11. I am going to tell you a story. Please listen carefully because afterwards, I'm going to ask you some questions about it.
Jill was a very successful stockbroker. She made a lot of money on the stock market. She then met Jack, a devastatingly handsome man. She married him and had three children. They live in Chicago. She then stopped work and stayed at home to bring up her children. When they w teenagers, she went back to work. She and Jack lived happily ever after.
_/8 (2) What was the female's name? (2) What work did she do?
(2) When did she go back to work? (2) What state did she live in?

_____ TOTAL SCORE

SCORING

High School Education		Less than High School Education
27-30	Normal	25-30
21-26	Mild Neurocognitive Disorder	20-24
1-20	Dementia	1-19

Am J Geriatr Psychiatry. 2006;14:900-910

VAMC(退伍軍人事務醫療中心)
聖路易斯大學心理狀態檢驗

對這份評估問卷有疑問嗎？電郵地址 aging@slu.edu.

姓名_____ 年齡_____

病人是否思維反應迅速和靈敏？_____ 教育程度_____

_/1 (1) 1. 今日係星期幾？

_/1 (1) 2. 今年係乜嘢年份？

_/1 3. 我哋喺邊一區？

4. 請記住呢五種嘢。稍後我會問你佢哋係乜。
蘋果 筆 領呔 房屋 汽車

5. 你有 100 蚊，你去商店買咗一個 3 蚊嘅蘋果，同埋用 20 蚊買咗一個杯。
(1) 你用咗幾多錢？
_/3 (2) 你剩翻幾多錢？

6. 請喺一分鐘內講出盡可能多嘅不同動物名稱。
_/3 (0) 0-4 隻動物 (1) 5-9 隻動物 (2) 10-14 隻動物 (3) 15 或以上隻動物

_/5 7. 我要你記住嘅 5 種嘢係乜？答對一種得 1 分。

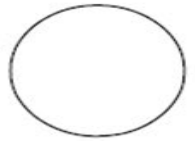
8. 我將會同你講一連串數字，我想請你倒轉咁講一次畀我聽。
例如，如果我講 42 ，你就講 24 。
_/2 (0) 87 (1) 648 (1) 8537

9. 呢個係一個鐘嘅表面。請畫小時標記同埋時分指針放喺十點五十分。
(2) 小時標記正確
_/4 (2) 時間正確

(1) 10. 請喺三角形內畫一個 X。

_/2 (1) 以上圖形邊一個最大？

11. 我將會對你講一個故事。請小心聆聽，因為稍後我會問你一啲相關嘅問題。
美琪係一位十分成功嘅股票經紀。佢喺股市上賺咗好多錢。之後佢遇到志明，一個極之英俊嘅男仔。佢嫁畀志明有三個仔女。佢哋住係跑馬地。之後佢唔再工作，留喺家中照顧佢嘅仔女。當佢哋成長到少年時，佢又返出去工作。佢同志明此後一直過住幸福嘅生活。
_/8 (2) 個女人叫乜嘢名？ (2) 佢做乜嘢工作？
(2) 佢幾時返出去工作？ (2) 佢住邊一區？



_____ 總分

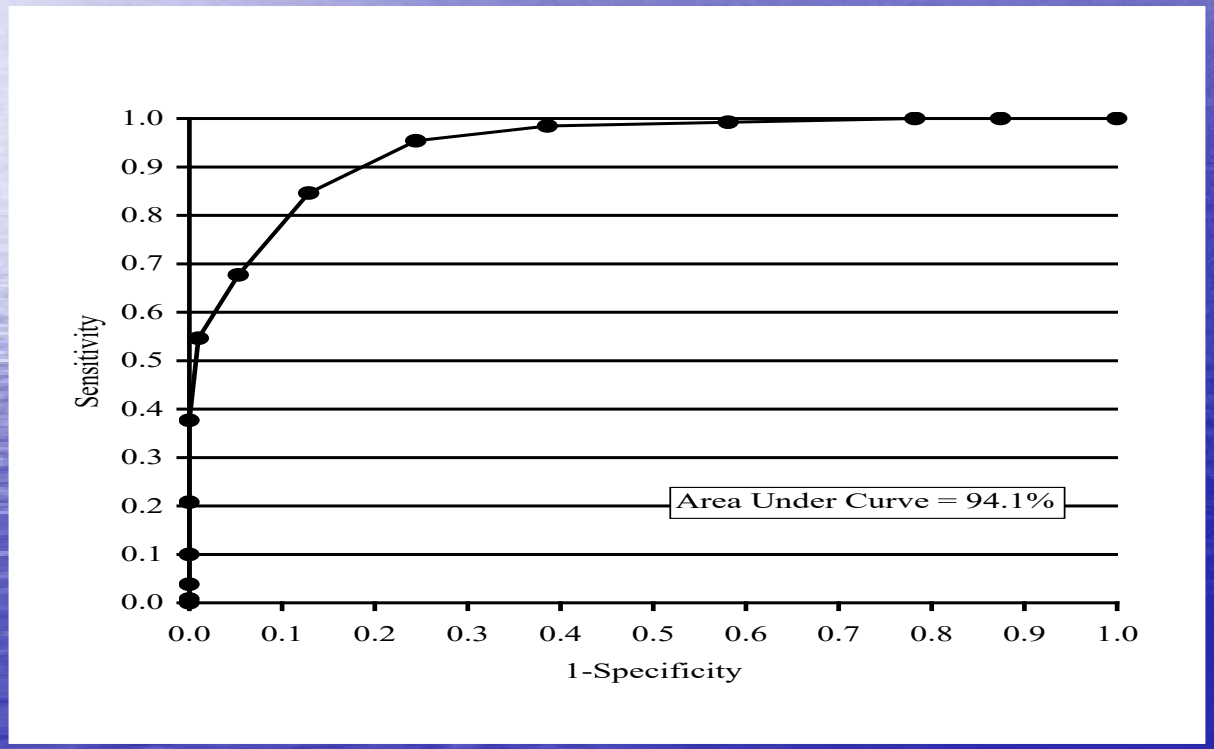
計分

高中教育程度		高中以下教育程度
27-30	正常	25-30
21-26	輕微神經認知障礙	20-24
1-20	癡呆	1-19

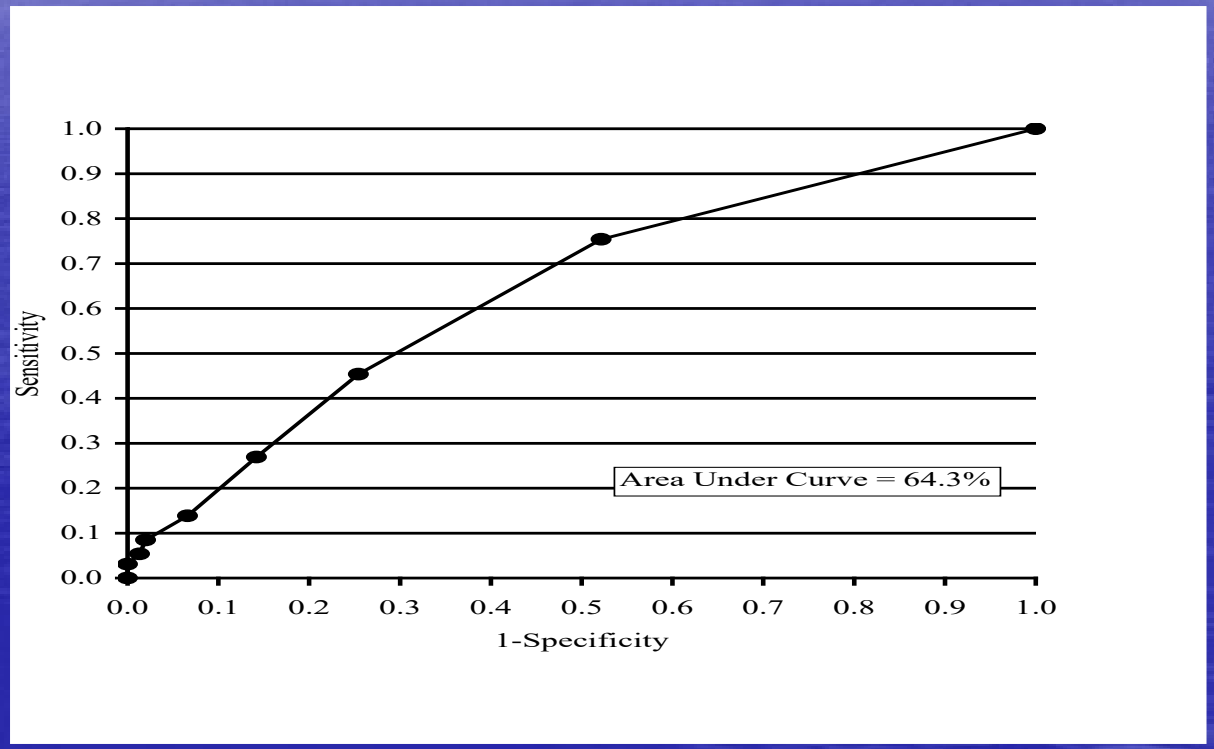
臨床醫護人員簽署 日期 時間

SH Tariq, N Tumosa, JT Chibnall, HM Perry III, and JE Morley. The Saint Louis University Mental Status (SLUMS) Examination for detecting mild cognitive impairment and dementia is more sensitive than the Mini-Mental Status Examination (MMSE) - A pilot study. *Am J Geriatr Psych* 14:900-10, 2006.

ROCs For SLUMS &MMSE for MCI ≥ HS Education



SLUMS



MMSE

Rapid Cognitive Screen (RCS)

Figure 1: Rapid Cognitive Screen (RCS), Page 1

Name_____ Age_____

Is the patient alert?_____ Level of education_____

1. **Please remember these five objects. I will ask you what they are later.**
   [Read each object to patient using approximately 1 second intervals.]

   Apple Pen Tie House Car

   Please repeat the objects for me. [If patient does not repeat all 5 objects correctly, repeat until all objects are recalled correctly or up to a maximum of 2 times.]

2. [Give patient pencil and the blank sheet with clock face.]
   This is a clock face. Please put in the hour markers and the time at ten minutes to eleven o'clock.

   ____/2 (points) Hour markers okay
   ____/2 (points) Time correct

   [When scoring, give full credit for all 12 numbers. If the patient puts only ticks on the circle, prompt them once to put numbers next to those ticks for full credit. Do not repeat the time. When scoring the correct time, make sure that the minute hand points at the 10 and the hour hand points at the 11.]

3. **What were the five objects I asked you to remember?**

   ____/1 (point) Apple
   ____/1 (point) Pen
   ____/1 (point) Tie
   ____/1 (point) House
   ____/1 (point) Car

4. **I'm going to tell you a story. Please listen carefully because afterwards, I'm going to ask you about it.**

   Jill was a very successful stockbroker. She made a lot of money on the stock market. She then met Jack, a devastatingly handsome man. She married him and had three children. They lived in Chicago. She then stopped work and stayed at home to bring up her children. When they were teenagers, she went back to work. She and Jack lived happily ever after.

   What state did she live in?

   ____/1 (point) Illinois

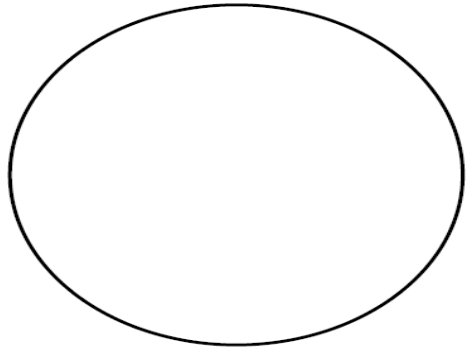
   [Do not repeat the story but do make sure the patient is paying attention the first time you read it to them. Do not prompt or give hints. The answer of "Chicago" as the state she lives in gets no credit but you may prompt them once by repeating the question when "Chicago" is given as the answer.]

_____ Total Score [0-10 points]

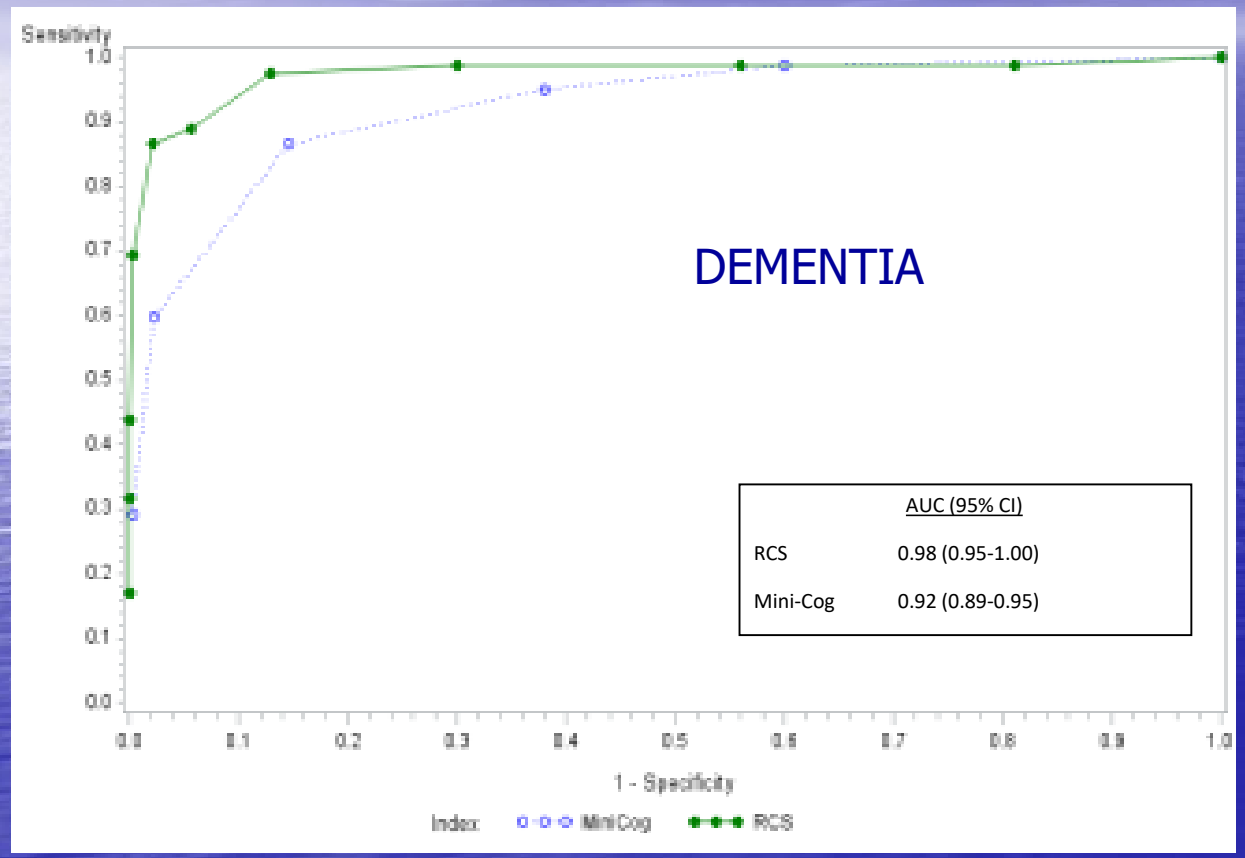
SCORING	
8-10.....	Normal
6-7.....	Mild Cognitive Impairment
0-5.....	Dementia

_____ _____ _____
CLINICIAN'S SIGNATURE DATE TIME

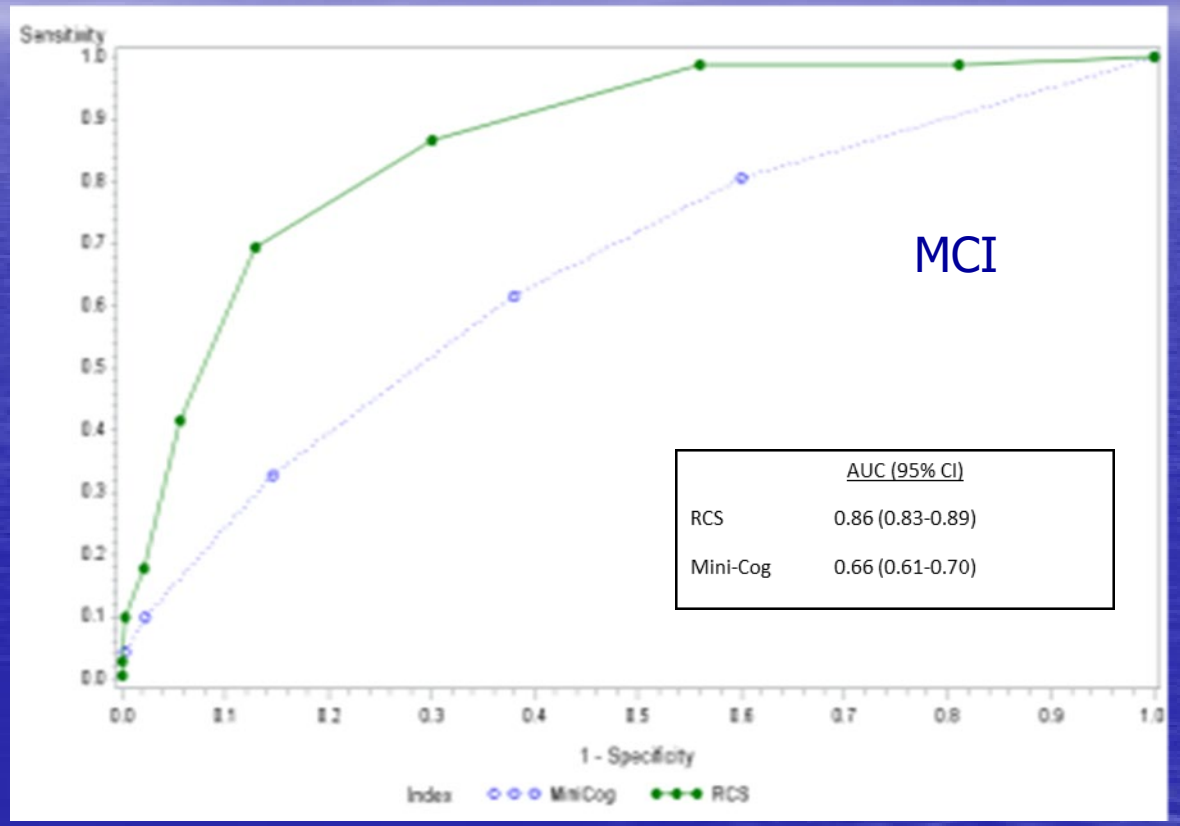
Figure 1 [Continued]: Rapid Cognitive Screen (RCS), Page 2



Rapid Cognitive Screen vs MiniCog

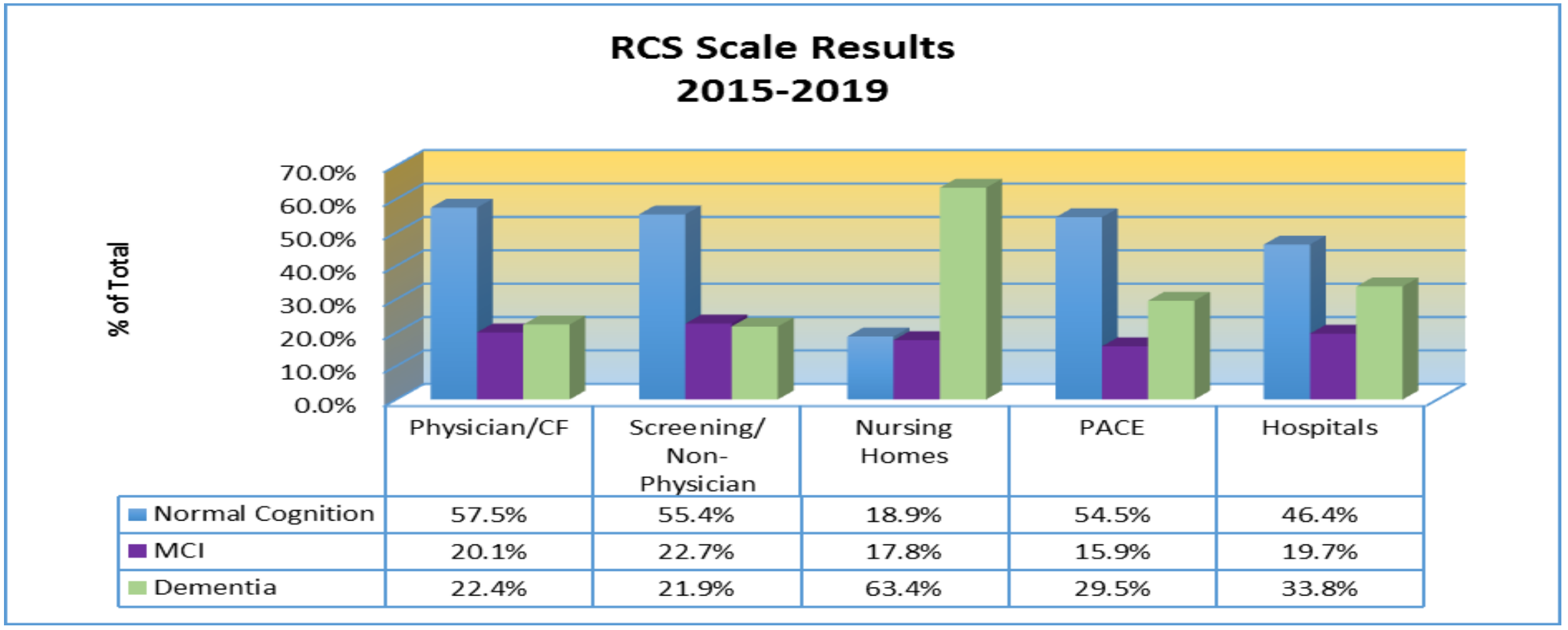


Dementia
Scores ≤ 5 Sen=0.89, Spc=0.94



MCI
Scores ≤ 7 Sen=0.87, Spc=0.70)

Screening for MCI and Dementia



	Physician/CF	Screening/ Non-Physician	Nursing Homes	PACE	Hospitals
Normal Cognition	57.5%	55.4%	18.9%	54.5%	46.4%
MCI	20.1%	22.7%	17.8%	15.9%	19.7%
Dementia	22.4%	21.9%	63.4%	29.5%	33.8%

From: **A Comparison of the Prevalence of Dementia in the United States in 2000 and 2012**

JAMA Intern Med. 2017;177(1):51-58. doi:10.1001/jamainternmed.2016.6807

Table 3. Cognitive Function, by Age Range, 2000 and 2012 Cohorts

Cognitive Function	No. (%) [95% CI][a]							
	65-74 y		75-84 y		≥85 y		Total (Age >65 y)	
	2000 (n = 5566)	2012 (n = 4983)	2000 (n = 3668)	2012 (n = 3991)	2000 (n = 1312)	2012 (n = 1537)	2000 (n = 10 546)	2012 (n = 10 511)
Normal	4320 (78.1) [76.5-79.7]	3931 (82.8) [81.1-84.4]	2231 (62.0) [60.1-64.0]	2603 (67.5) [65.6-69.3]	415 (32.8) [30.3-35.4]	580 (40.8) [38.0-43.6]	6966 (67.2) [65.8-68.6]	7114 (72.4) [71.1-73.6]
CIND	942 (16.5) [15.2-17.8]	837 (14.0) [12.7-15.4]	924 (24.4) [23.0-25.9]	936 (22.6) [20.9-24.3]	427 (32.9) [29.5-36.5]	451 (29.9) [27.4-32.6]	2293 (21.2) [20.1-22.3]	2224 (18.8) [17.8-19.9]
Dementia	304 (5.4) [4.7-6.3]	215 (3.2) [2.7-3.8]	513 (13.6) [12.1-15.1]	452 (9.9) [9.0-10.9]	470 (34.4) [31.2-37.6]	506 (29.3) [26.9-31.8]	1287 (11.6) [10.7-12.7]	1173 (8.8) [8.2-9.4]
Age- and Sex-Standardized to 2000 Population								
Normal	4320 (78.1) [76.5-79.7]	3931 **(82.9)** [81.1-84.4]	2231 (62.0) [60.1-64.0]	2603 **(67.6)** [65.6-69.3]	415 (32.8) [30.3-35.4]	580 **(40.7)** [38.0-43.6]	6966 (67.2) [65.8-68.6]	7114 **(72.6)** **[71.2-73.7]**
CIND	942 (16.5) [15.2-17.8]	837 (14.0) [12.7-15.4]	924 (24.4) [23.0-25.9]	936 **(22.5)** [20.9-24.3]	427 (32.9) [29.5-36.5]	451 **(29.7)** [27.4-32.6]	2293 (21.2) [20.1-22.3]	2224 (18.8) [17.8-19.9]
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Abbreviations: CIND, cognitive impairment—no dementia; HRS, Health and Retirement Study.[16]

[a] Values in parentheses are weighted percentages (95% CIs) derived using the HRS sampling weights to adjust for the complex design of the HRS survey.

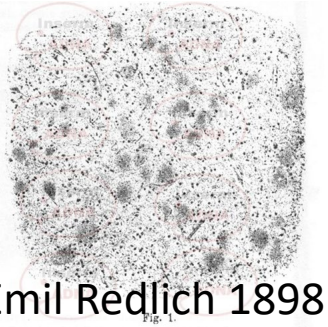
Values for 2012 weighted percentages in the lower half of the table are age- and sex-standardized to the 2000 population using direct standardization. Boldface values differ from those in the non–age- and sex-standardized data.

DEMENTIA is DECREASING in the United States

Seattle-based Adult Changes in Thought study

- Alzheimer's disease……. 45%
- Vascular based lesions……. 33%
- Lewy Body Dementia…… 10%

Solomon Carter Fuller, 1906

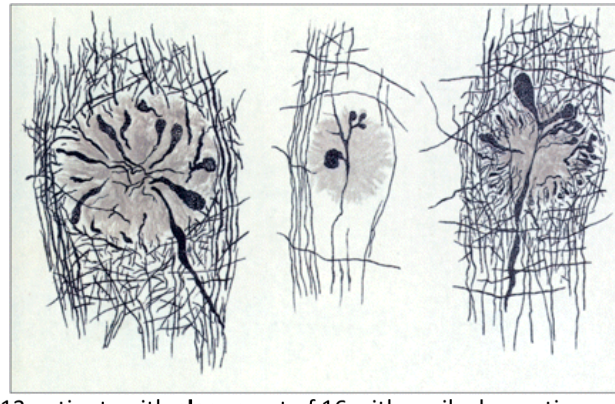


Emil Redlich 1898

What's in a name?

Paul Blocq 1882

Miyake 1906



12 patients with **plaque** out of 16 with senile dementia

10 controls, 10 psychosis,45 neurosyphilis – NO PLAQUES

Oskar Fischer, 1907

Aloysius Alzheimer,1906/7

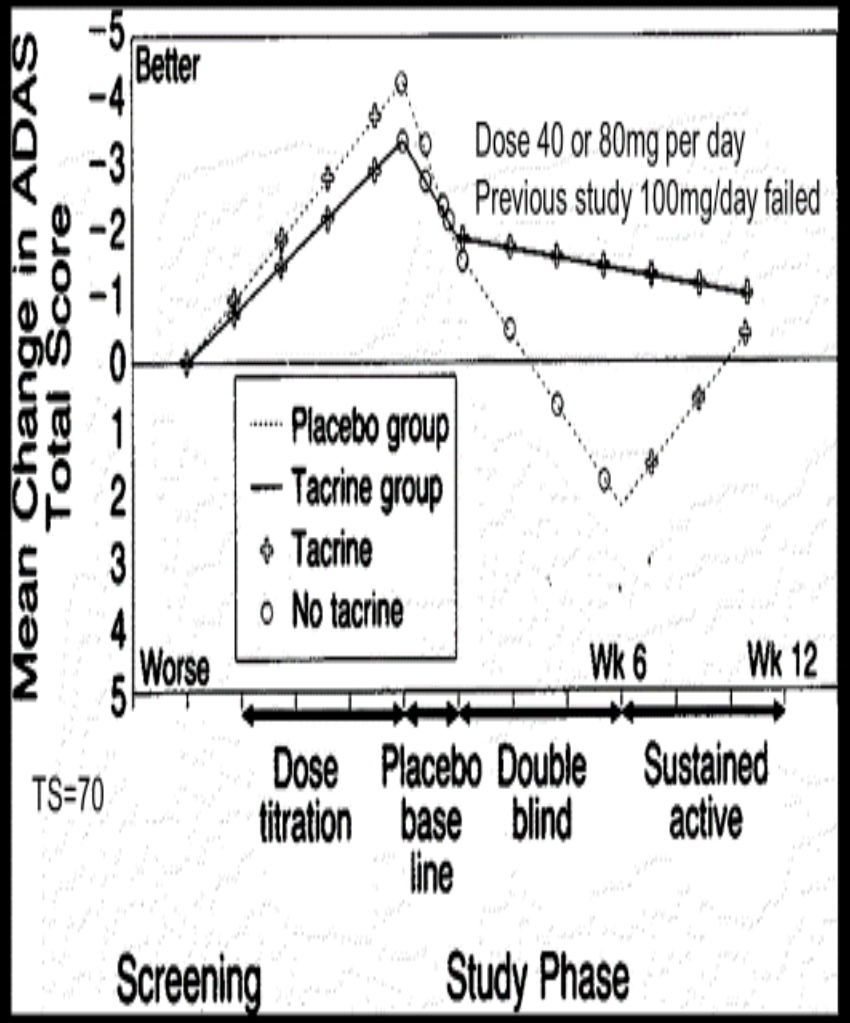
Auguste Deter

The Cholinergic Hypothesis

David Bowen

Peter Whitehouse

Mean Change in ADAS Total Score during the Phases of the Study.



Davis KL et al. N Engl J Med 1992;327:1253-1259.

The NEW ENGLAND JOURNAL of MEDICINE

Drugs Aging. 2015 Jun;32(6):453-67. doi: 10.1007/s40266-015-0266-9.

A Risk-Benefit Assessment of Dementia Medications: Systematic Review of the Evidence.

Buckley JS[1], Salpeter SR.

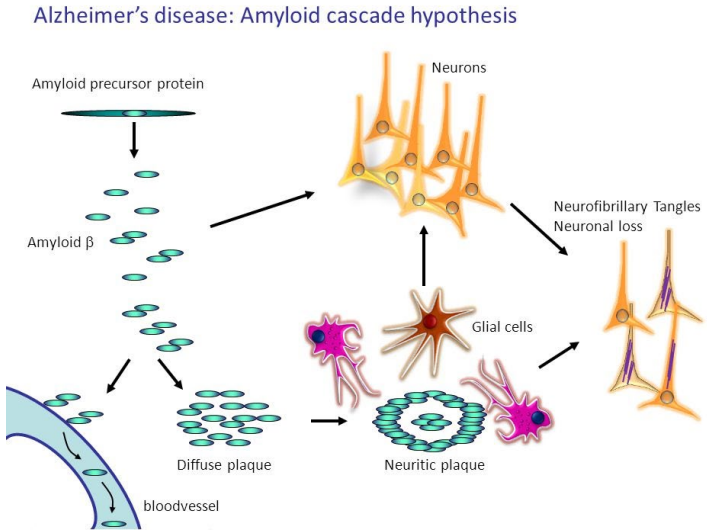
- 257 were included in the systematic review.
- In pooled trial data,cholinesterase inhibitors (ChEIs) produce small improvements in cognitive, functional, and global benefits in patients with mild to moderate Alzheimer's and Lewy body dementia, **but the clinical significance of these effects are unclear.**
- The efficacy of ChEI treatment appears to wane over time, with minimal benefit seen after 1 year.
- There is no evidence for benefit for those with advanced disease or those aged over 85 years.
- Adverse effects are significantly increased with ChEIs, in a dose-dependent manner. A two- to fivefold increased risk for gastrointestinal, neurological, and cardiovascular side effects is related to cholinergic stimulation, **the most serious being weight loss, debility, and syncope.**
- Those aged over 85 years have double the risk of adverse events compared with younger patients.

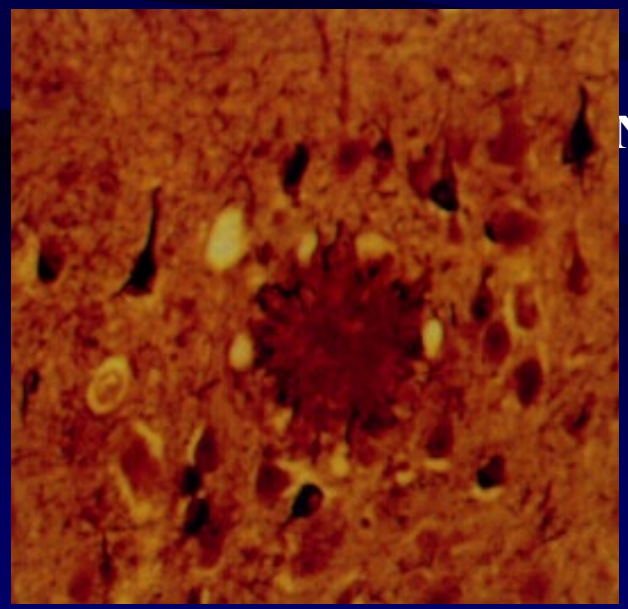
Amyloid Cascade Hypothesis

George and Joy Glenner
AD is an amyloidosis;1984
Down's Syndrome

John Hardy
1992

Dennis Selkoe





APP

Overproduction

TNF

IL-6

DECREASED MEMORY

ACh

LRP

Amyloid-B

Mitochond

Amyloid Oligomer (soluble)

GSK-3

TAU

Phosphorylation

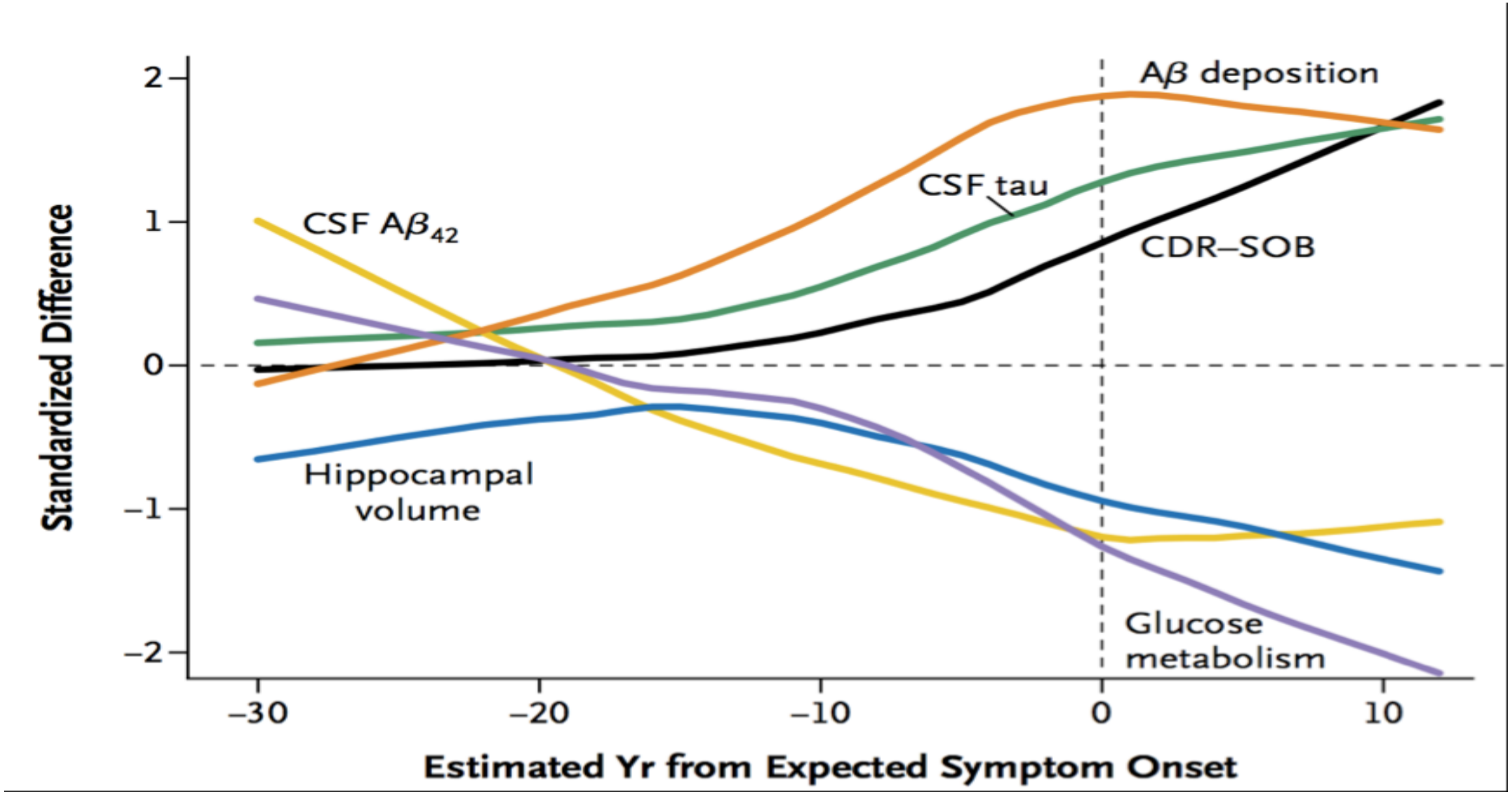
OXIDATIVE DAMAGE

AMYLOID PLAQUES

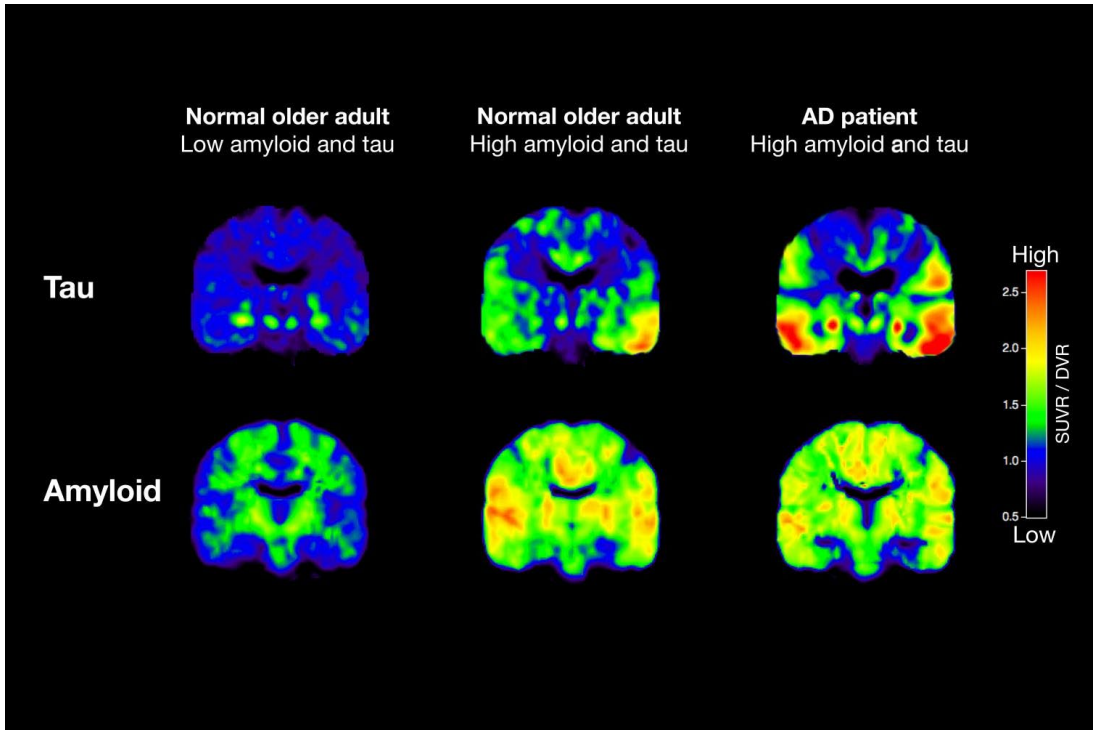
APOPTOSIS

NEUROFIBRILLARY TANGLES

BAPtist THEORY


Standardized Difference
2
1
0
−1
−2
−30
−20
−10
0
10
Estimated Yr from Expected Symptom Onset
Aβ deposition
CSF tau
CSF Aβ42
CDR–SOB
Hippocampal volume
Glucose metabolism

Normal older persons have amyloid-beta plaques



- Ann Neurol. 1988 Feb;23(2):138-44.
- **Clinical, pathological, and neurochemical changes in dementia: a subgroup with preserved mental status and numerous neocortical plaques.**
- Katzman R[1], Terry R, DeTeresa R, Brown T, Davies P, Fuld P, Renbing X, Peck A.
- Postmortem examination was performed on 137 residents (average age 85.5 years) of a skilled nursing facility whose mental status, memory, and functional status had been evaluated during life.
- **Ten subjects** whose functional and **cognitive performance was in the upper quintile** of the nursing home residents, as good as or better than the performance of the upper quintile of residents without brain pathology (control subjects), showed the pathological features of mild Alzheimer's disease, with **many neocortical plaques**. Plaque counts were 80% of those of demented patients with Alzheimer's disease.
- The unexpected findings in these subjects were higher brain weights and greater number of neurons (greater than 90 micron 2 in a cross-sectional area in cerebral cortex) as compared to age-matched nursing home control subjects.

What is the physiological role of amyloid beta protein?

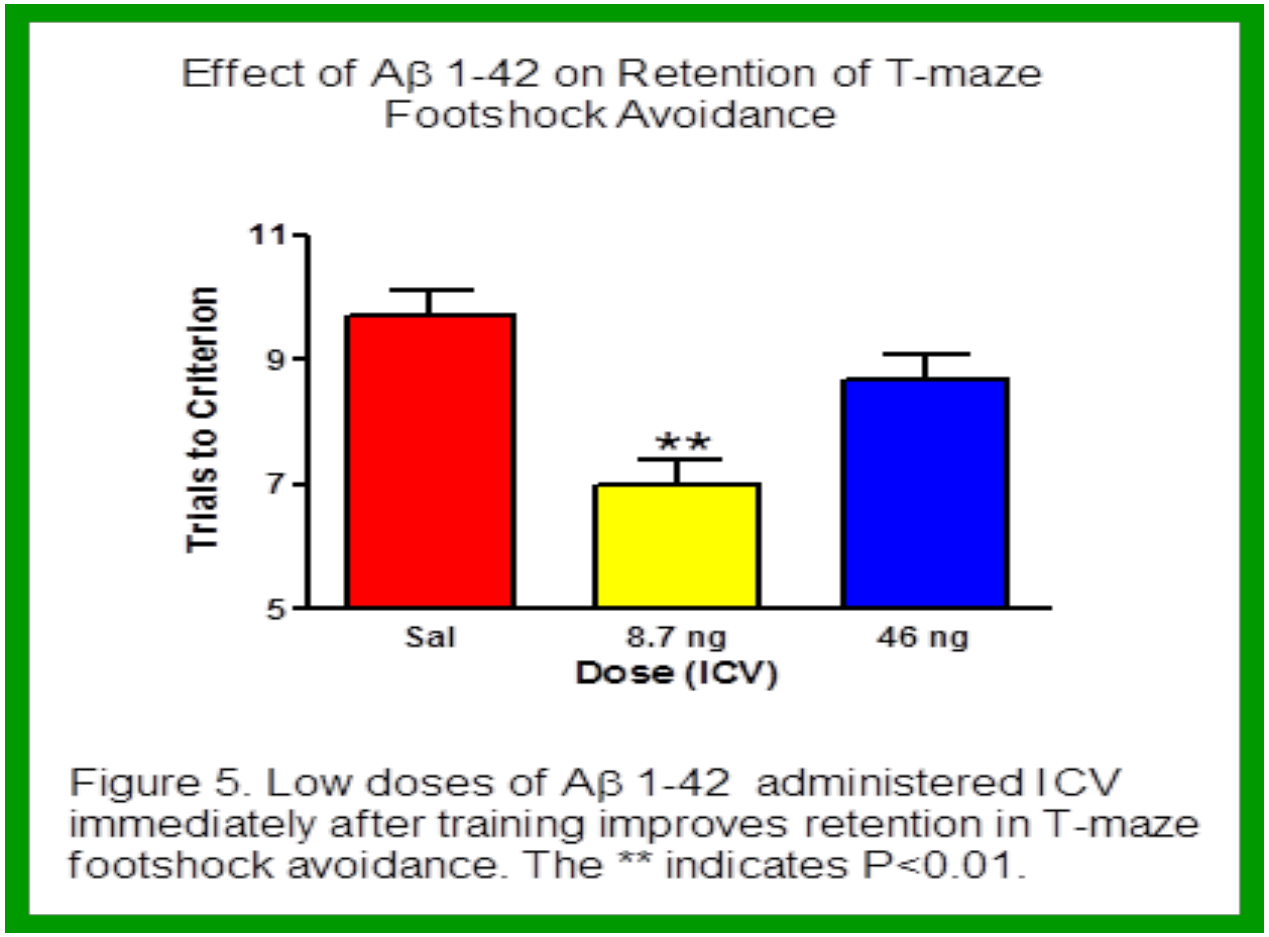
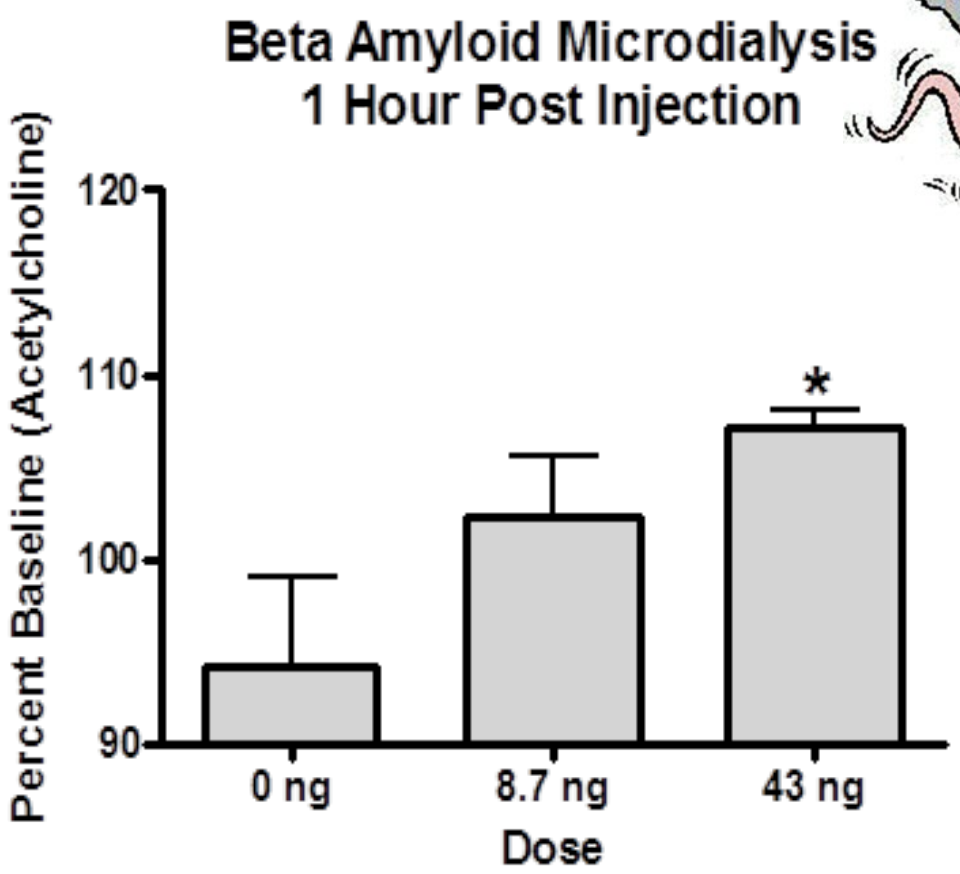
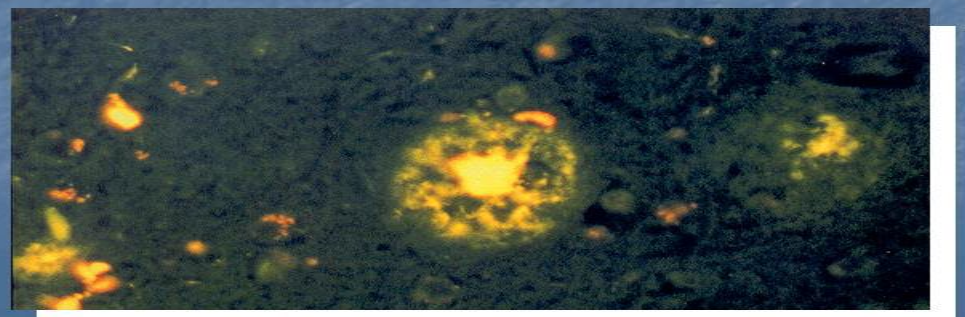
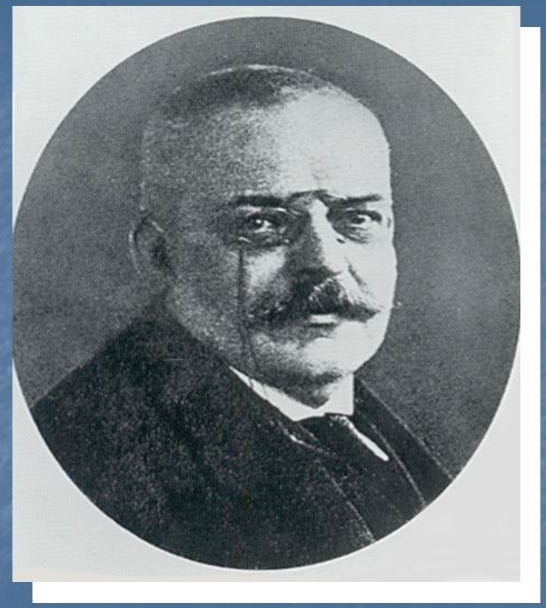


Figure 5. Low doses of Aβ 1-42 administered ICV immediately after training improves retention in T-maze footshock avoidance. The ** indicates P<0.01.



Antisense to APP reverses memory deficits, oxidative damage and delayed AB clearance in mice models of Alzheimer's disease. It can be administered intranasally.





Alois Alzheimer

Amyloid Beta and Memory

(APP = Amyloid Precursor Protein; BBB = Blood Brain Barrier

Inflammation (Cytokines)

Genes

Early onset hyperamyloidosis
Type I
(Presinilin 1 and 2; APP)

Late Onset Hyperamyloidosis
Type II
(ApoE4 and 33 other genes)

Vascular damage
Infections
Traumatic Brain Injury

APP

↓

Amyloid-beta

Physiological

Increase Acetylcholine

↓

Increase Memory

\+ \+

Pathological Increase

Plaques without Memory Impairment

Plaques with Memory Impairment

Impaired Cognition

↑GSKβ

↓

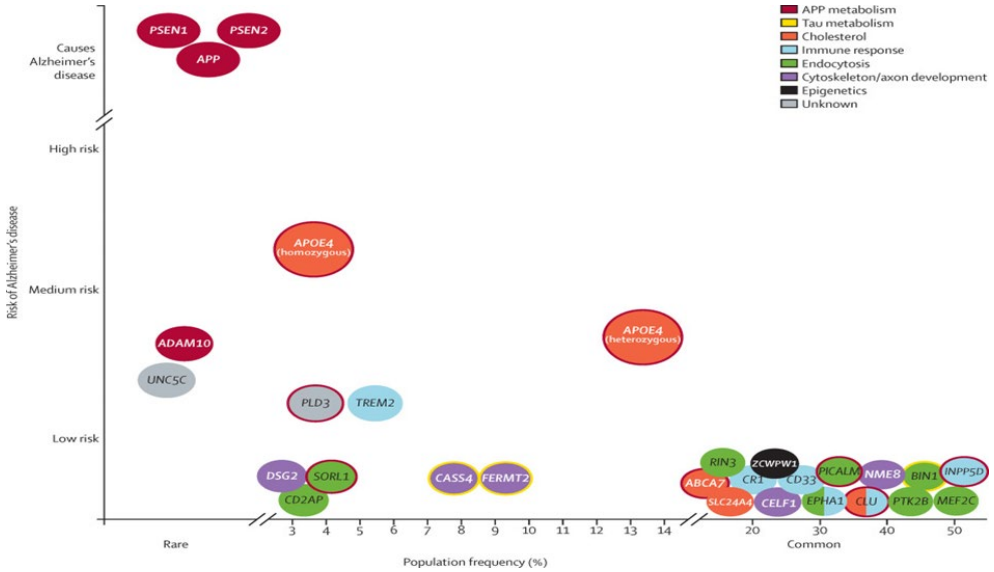
Tau phosphorylation

↓

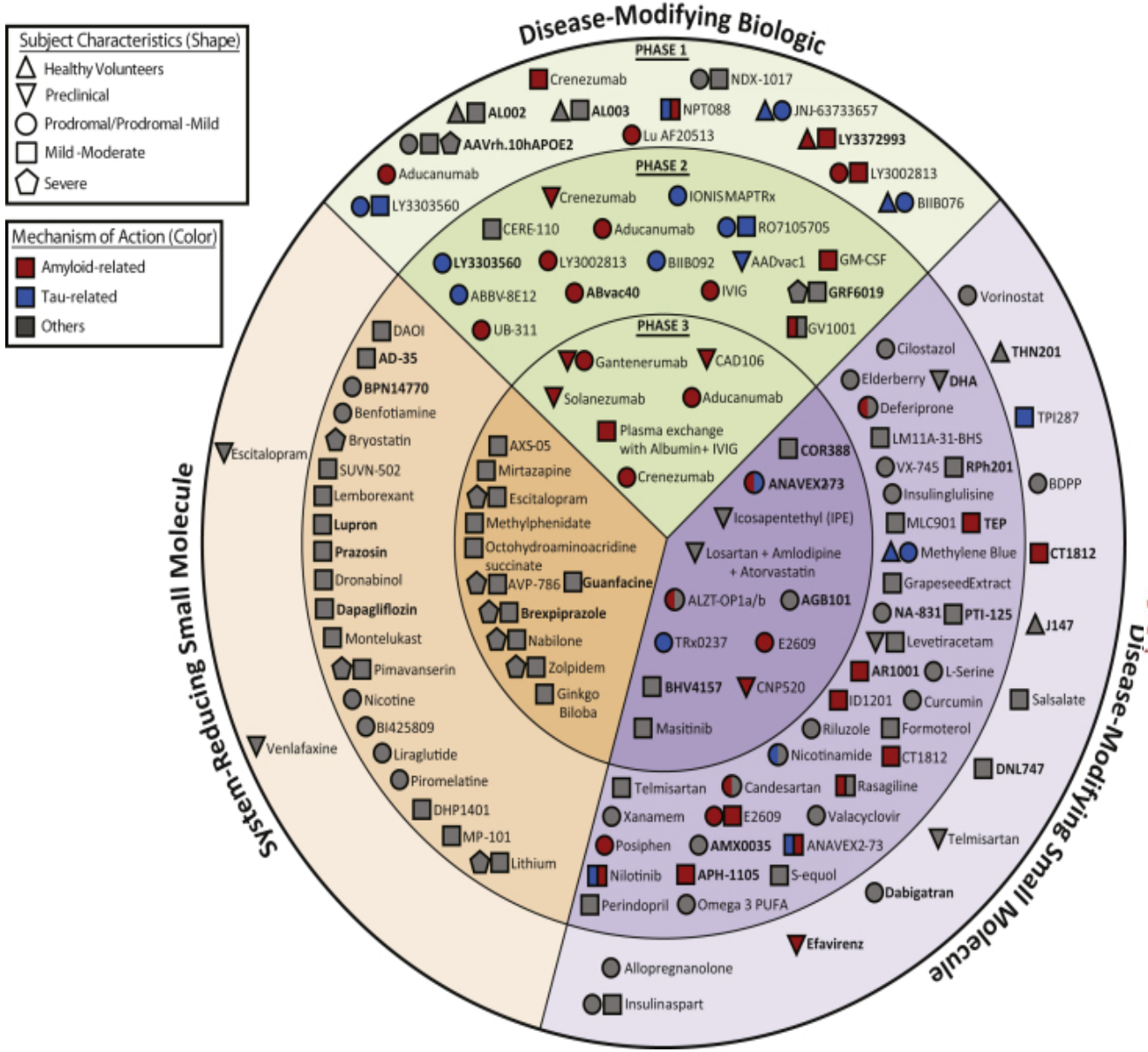
Neurofibrillary Tangles

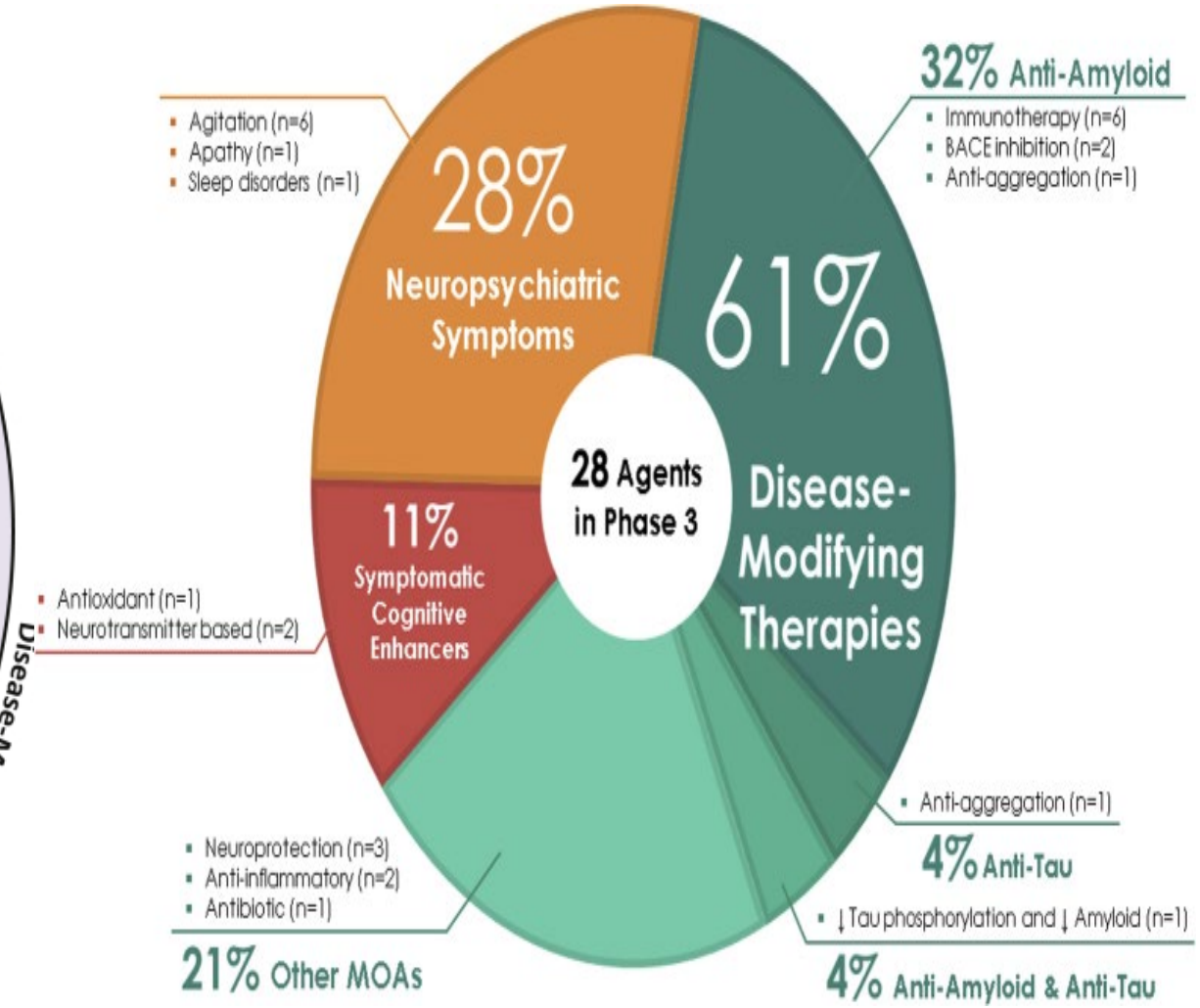
Brain Oxidative Damage

Damaged BBB



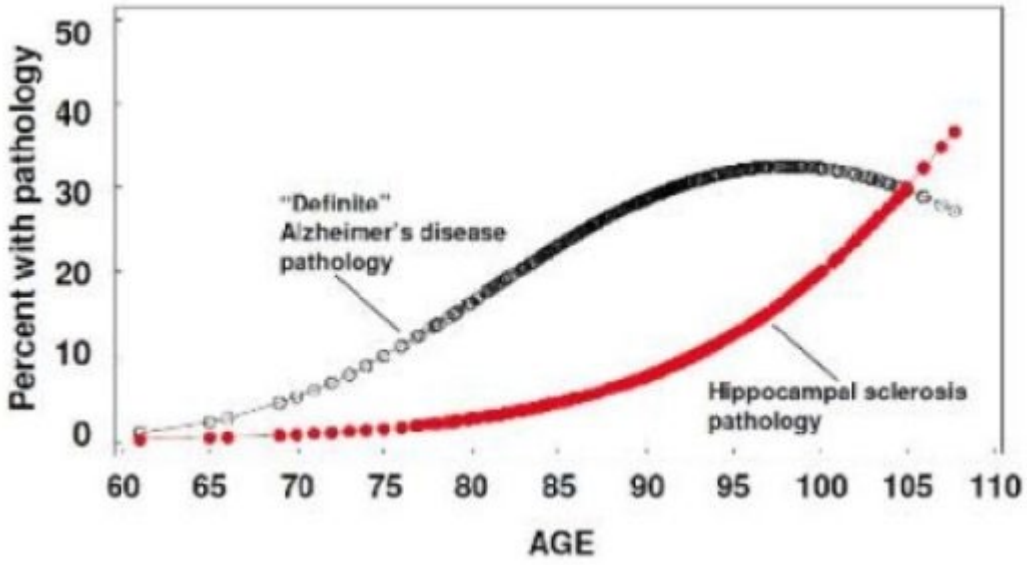
2019 Alzheimer's Drug Development Pipeline



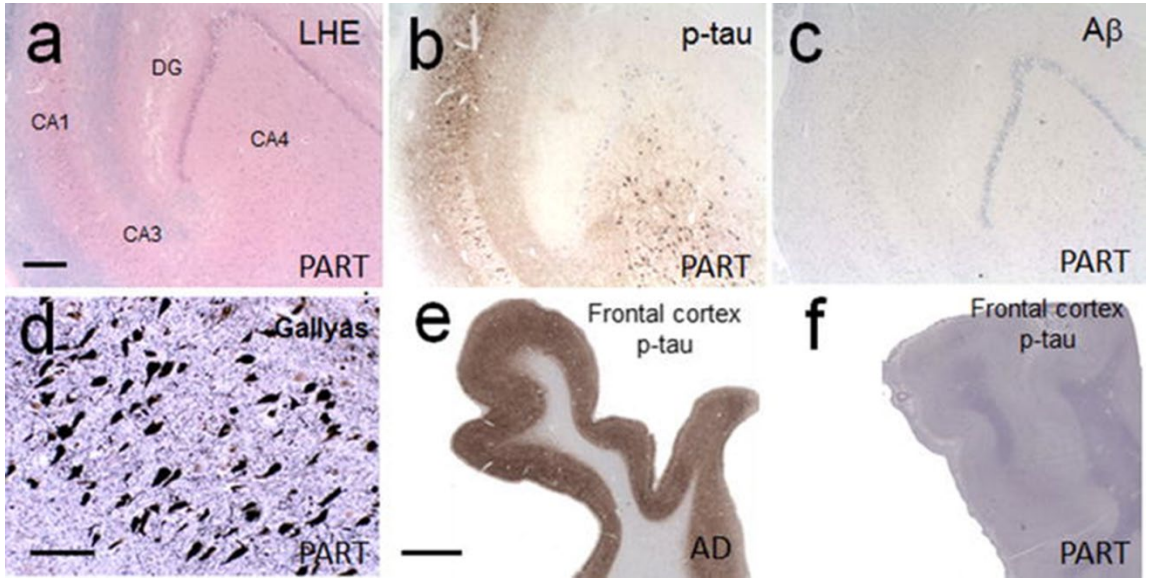


Common Dementias in Older Persons

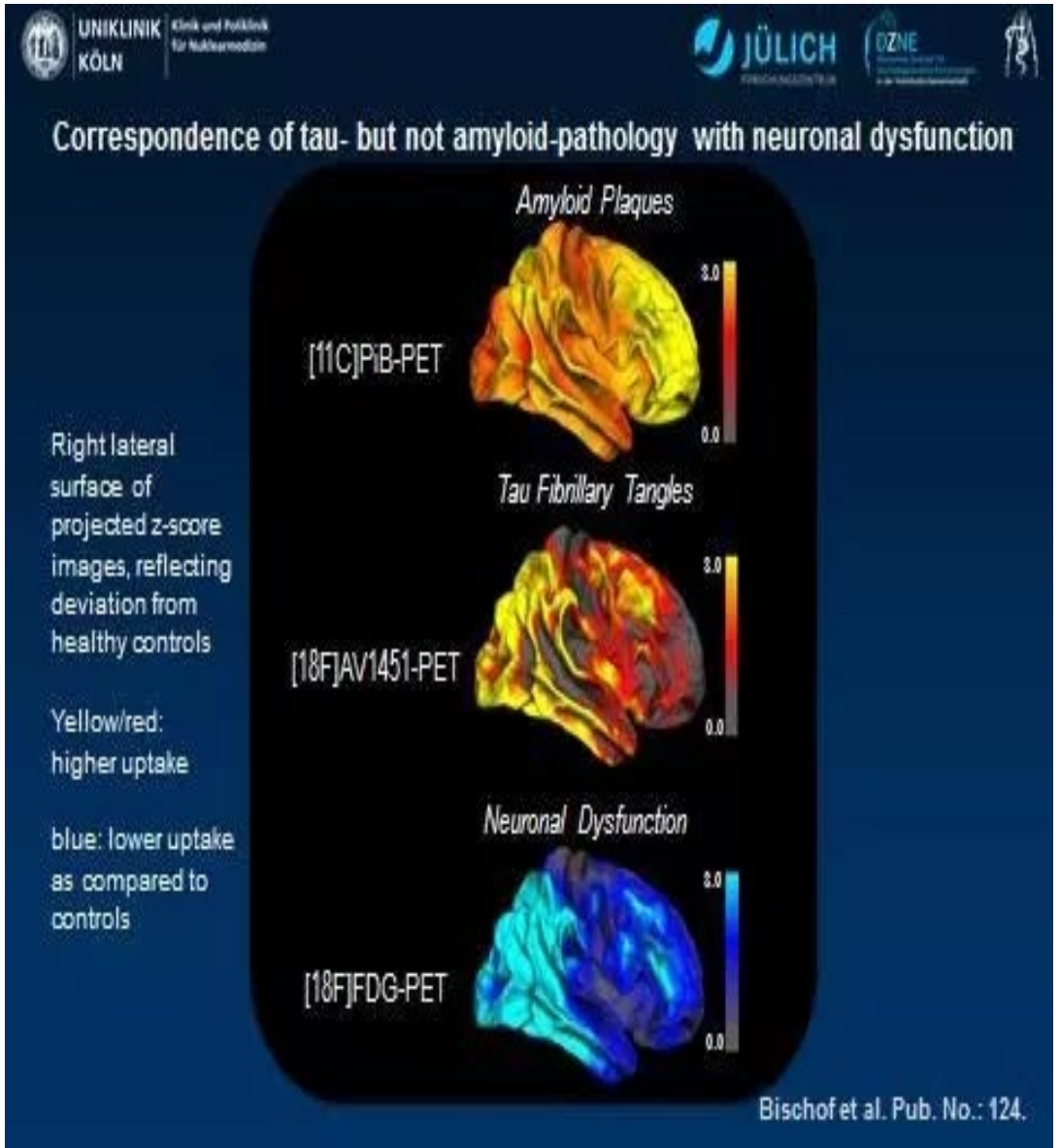
- Primary age-related tauopathy (PART)
- Hippocampal sclerosis of aging
- Vascular dementia
- Lewy body dementia
- Dementia of Diabetes
- Alzheimer's disease



Primary Age Related Tauopathy



Tau inhibitors?



Hachinski score

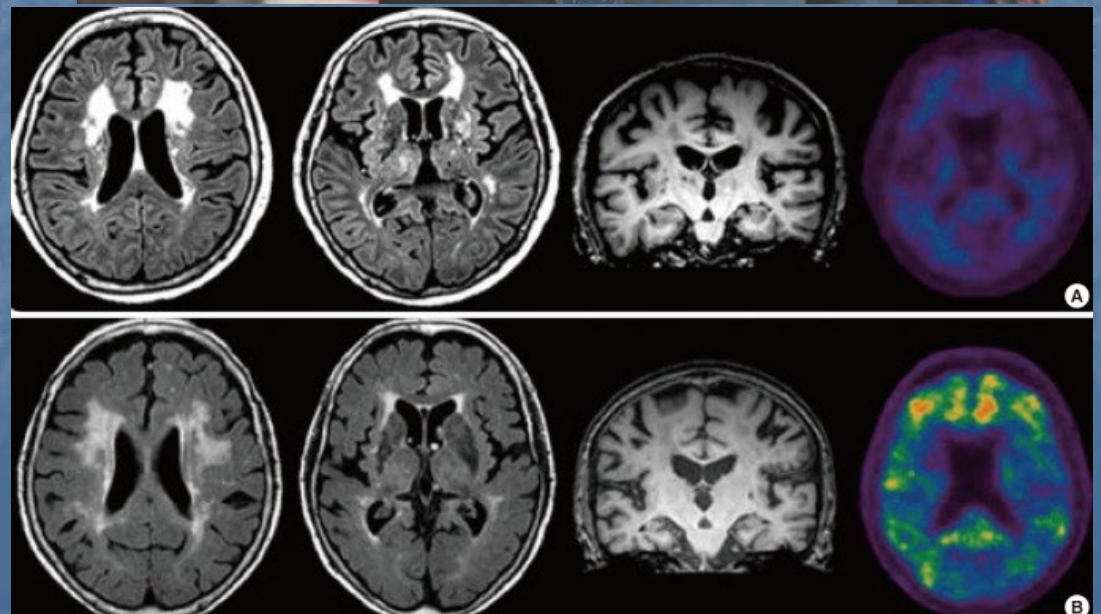
Clinical feature	Score
Abrupt onset	2
Stepwise deterioration	1
Fluctuating course	2
Nocturnal confusion	1
Relative preservation of personality	1
Depression	1
Somatic complaints	1
Emotional incontinence	1
History of hypertension	1
History of stroke	2
Clinical evidence of atherosclerosis	1
Focal neurologic symptoms	2
Focal neurologic signs	2

from Hachinski et al, Arch Neurol 32; 1975: 632

A total score of 4 or less is suggestive of a degenerative cause of dementia such as Alzheimer's disease

A score of 7 or more is suggestive of vascular dementia

Vascular Dementia



Binswanger O
Die Abgrenzung der allgemeinen progressiven Paralyse. Berl Klin Wochenschr 1894;31:1180–

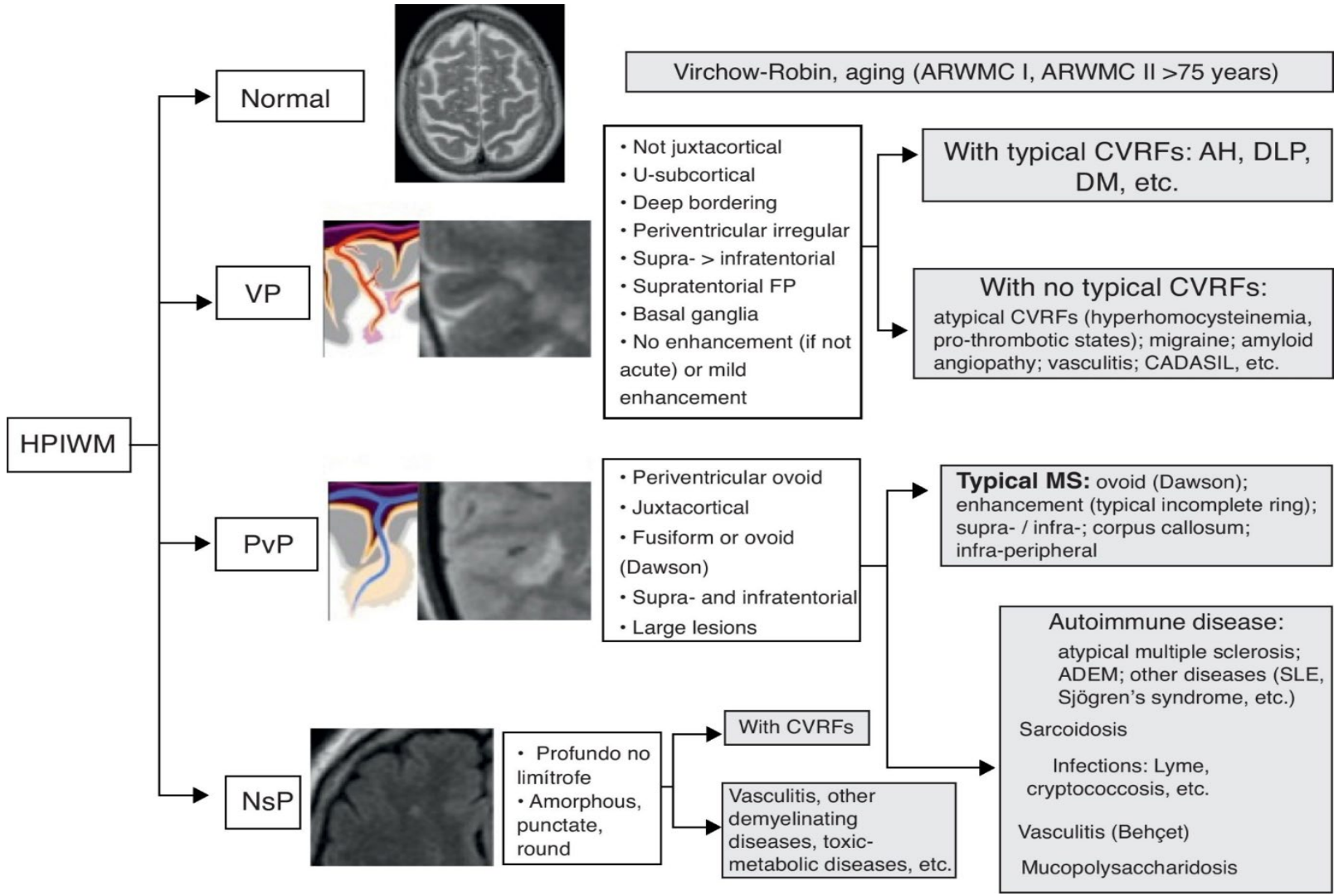
Alzheimer A
Die Seelenstörung auf arteriosklerotischer Grundlage. Allg Z Psychiat1902;59:695–701.

Leukoaraiosis
(White Matter Hyperintensities)

Rotterdam Study
Prevalence of Leukoaraiosis
Age 65-84 : 27%
Age 80-84 : 54%

Causes

Hypertension
Hyperlipidemia
Diabetes
Atrial fib



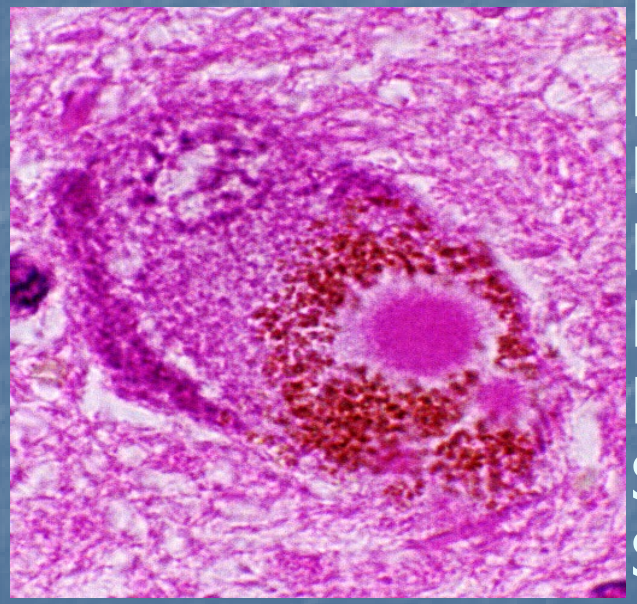
Differential Diagnosis of Dementia

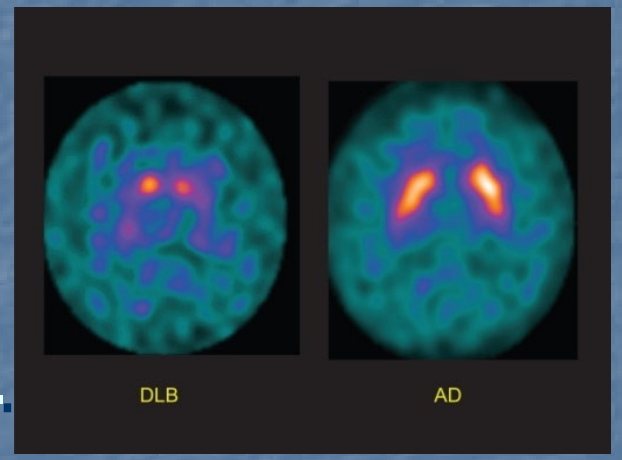
Lewy-Body Dementia

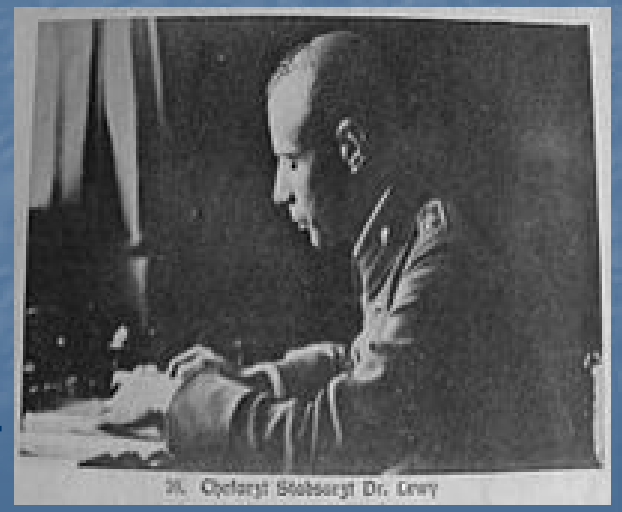
Onset: Insidious.

Progression: Progressive and more rapid.

Clinical features: Interferes early with social functions.
Memory impairment may be late.
Prominent attention and visuospatial defects.
Fluctuating levels of alertness.
Recurrent visual hallucinations.
Parkinsonism.
Repeated falls.
Systemized delusions.
Syncope.

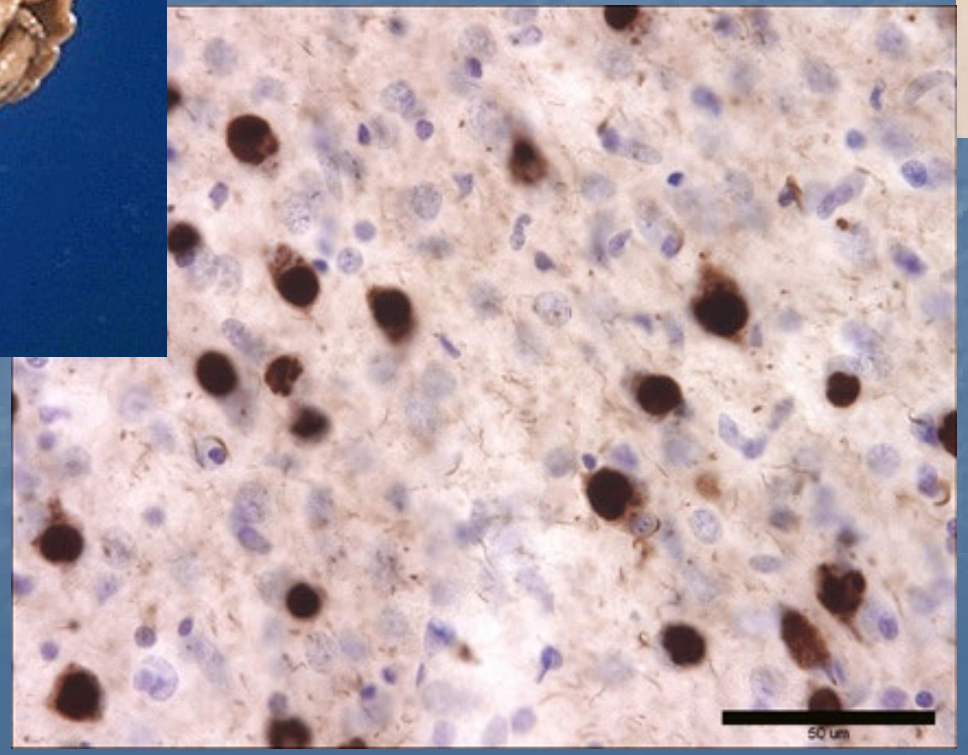




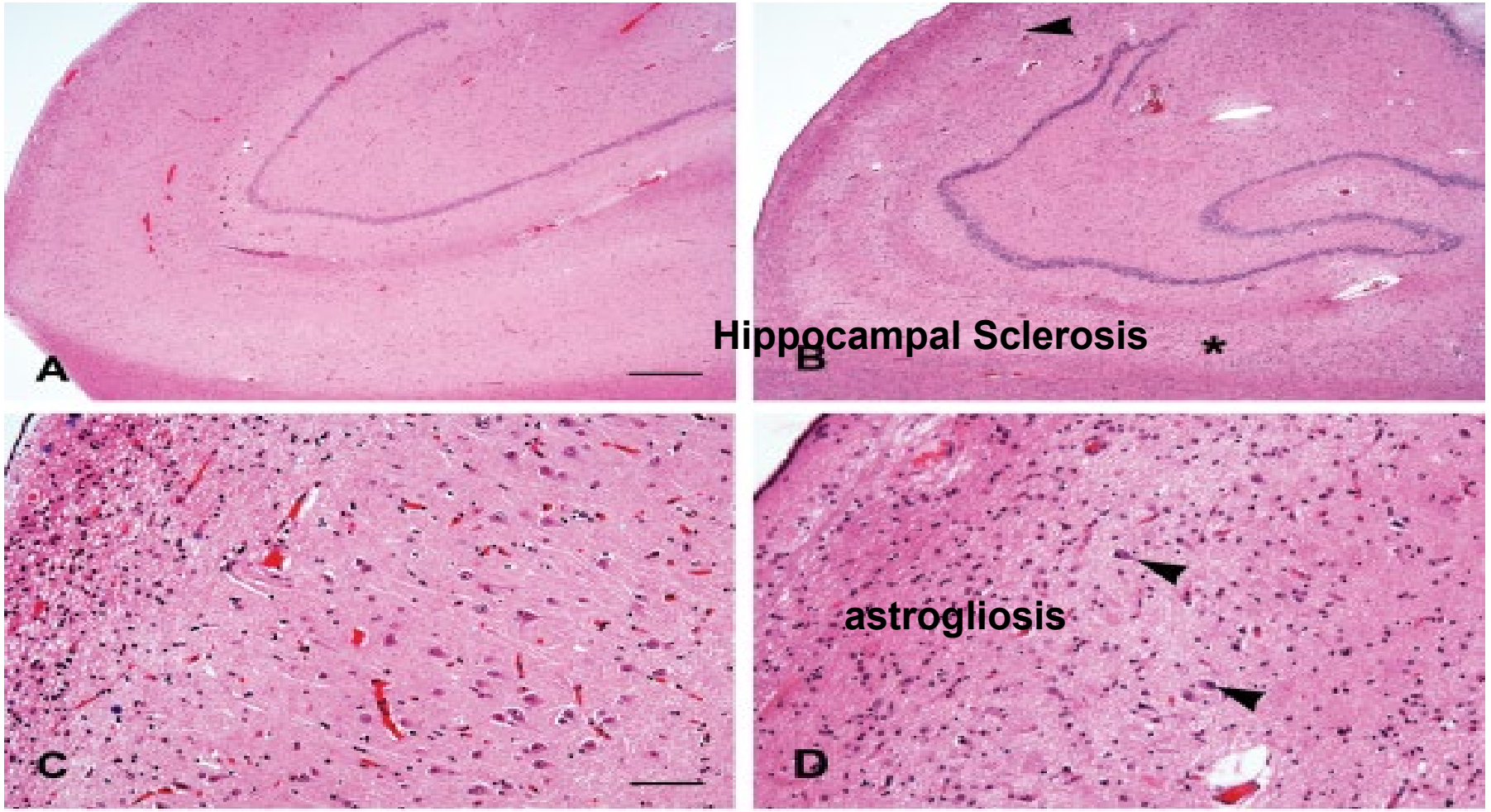


Neuroimaging: Lack of dopamine receptor uptake on SPECT

Pick's Disease
Fronto-temporal dementia



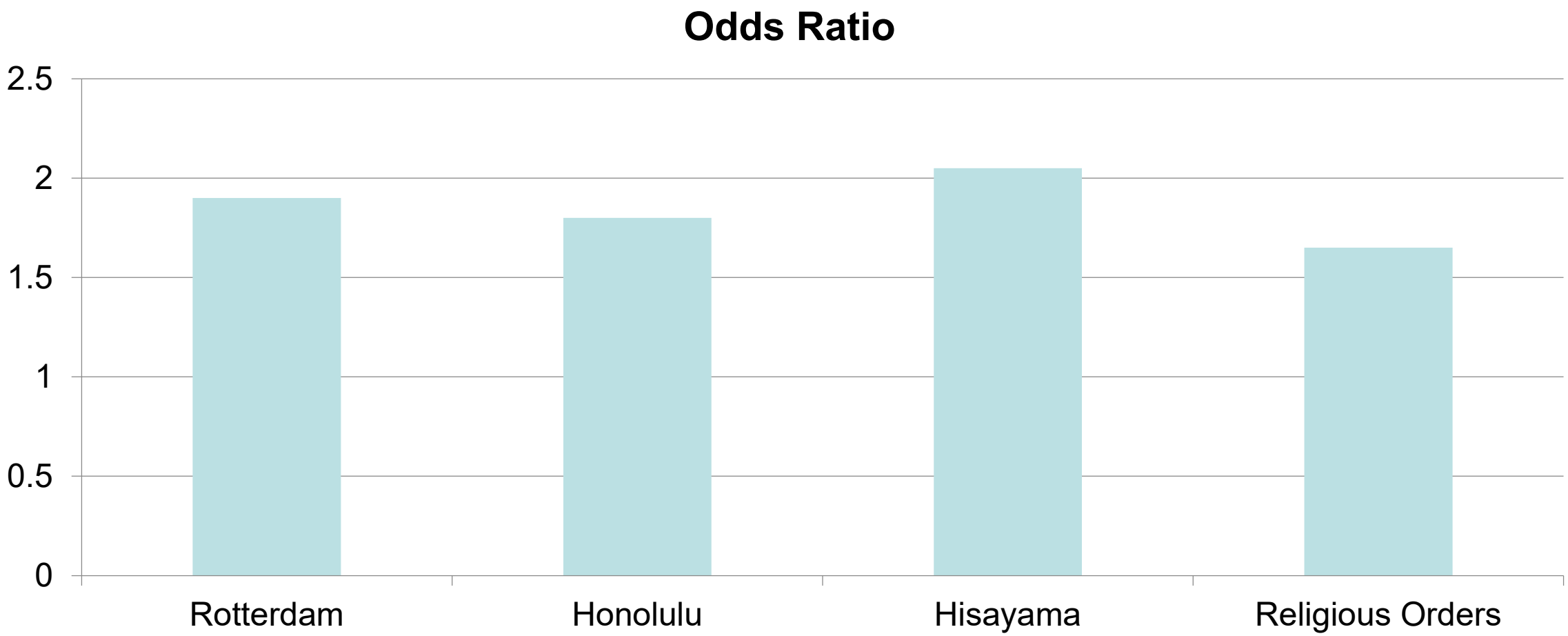
Hippocampal sclerosis and TDP-43 pathology in aging and Alzheimer disease
ABCC9 - sulfonylurea receptor



Annals of Neurology
Volume 77, Issue 6, pages 942-952, 22 APR 2015 DOI: 10.1002/ana.24388
http://onlinelibrary.wiley.com/doi/10.1002/ana.24388/full#ana24388-fig-0001

Alzheimer's Disease :Epidemiological Studies

Clin Interv Aging. 2014 Jun 28;9:1011-9. **Type 2 diabetes as a risk factor for cognitive impairment: current insights.**
Umegaki H[1].



‚Diabetes is NOT related to Alzheimer's Pathology

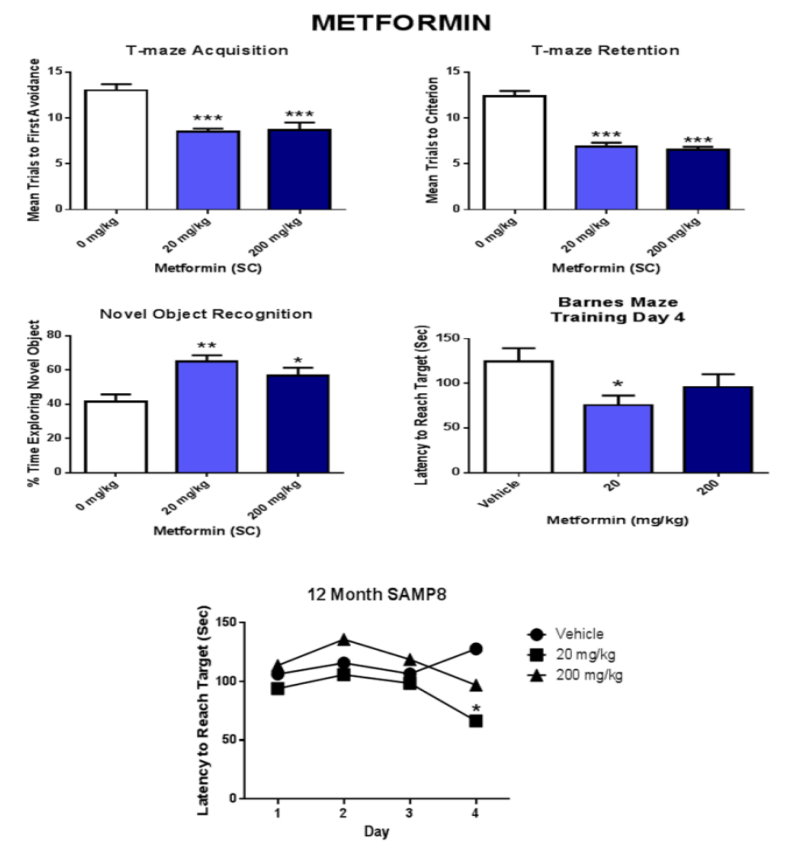
- 2365 autopsied persons.
- Diabetes increased odds of **brain infarcts** (odds ratio [OR] = 1.57, P < .0001), specifically lacunes (OR = 1.71, P < .0001), but **NOT Alzheimer's disease neuropathology**
- .
- Alzheimers Dement. 2016
  Diabetes is associated with cerebrovascular but not Alzheimer's disease neuropathology.
  Abner EL[1]

Individuals with diabetes were **less likely** to have **β-amyloid** (hazard ratio [HR] [95% confidence interval (CI)] was 0.48 [0.23–0.98]) and **tangles** (HR [95% CI] 0.72 [0.39–1.33]) but **more likely** to have **cerebral infarcts** (HR [95% CI] 1.88 [1.06–3.34])

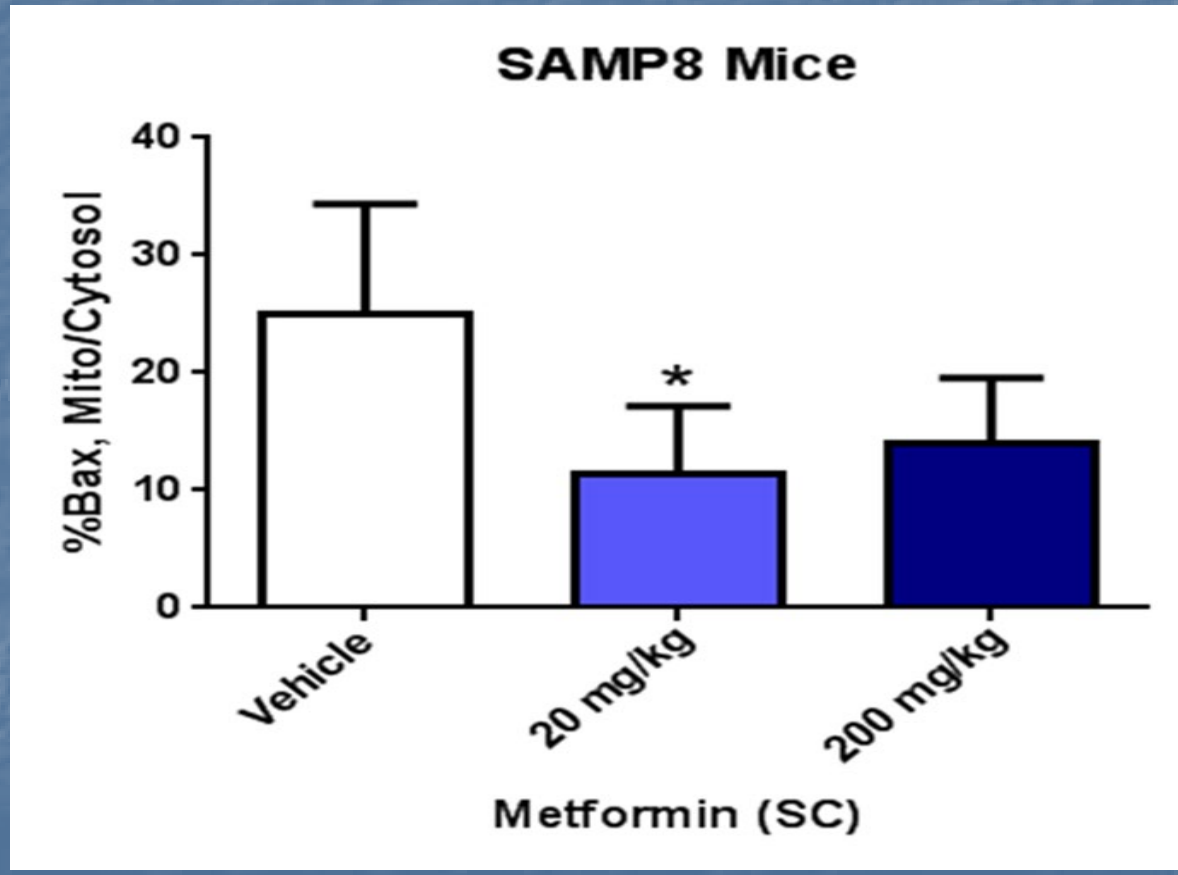
Diabetes is related to cerebral infarction but not to AD pathology in older persons
Z. Arvanitakis, MD

Diabetes (present in 15% subjects) was associated with **an increased odds of infarction** (OR = 2.47, 95% CI: 1.16, 5.24). Diabetes was **not related to global AD pathology** score, or to specific measures of neuritic plaques, diffuse plaques or tangles, or to amyloid burden or tangle density

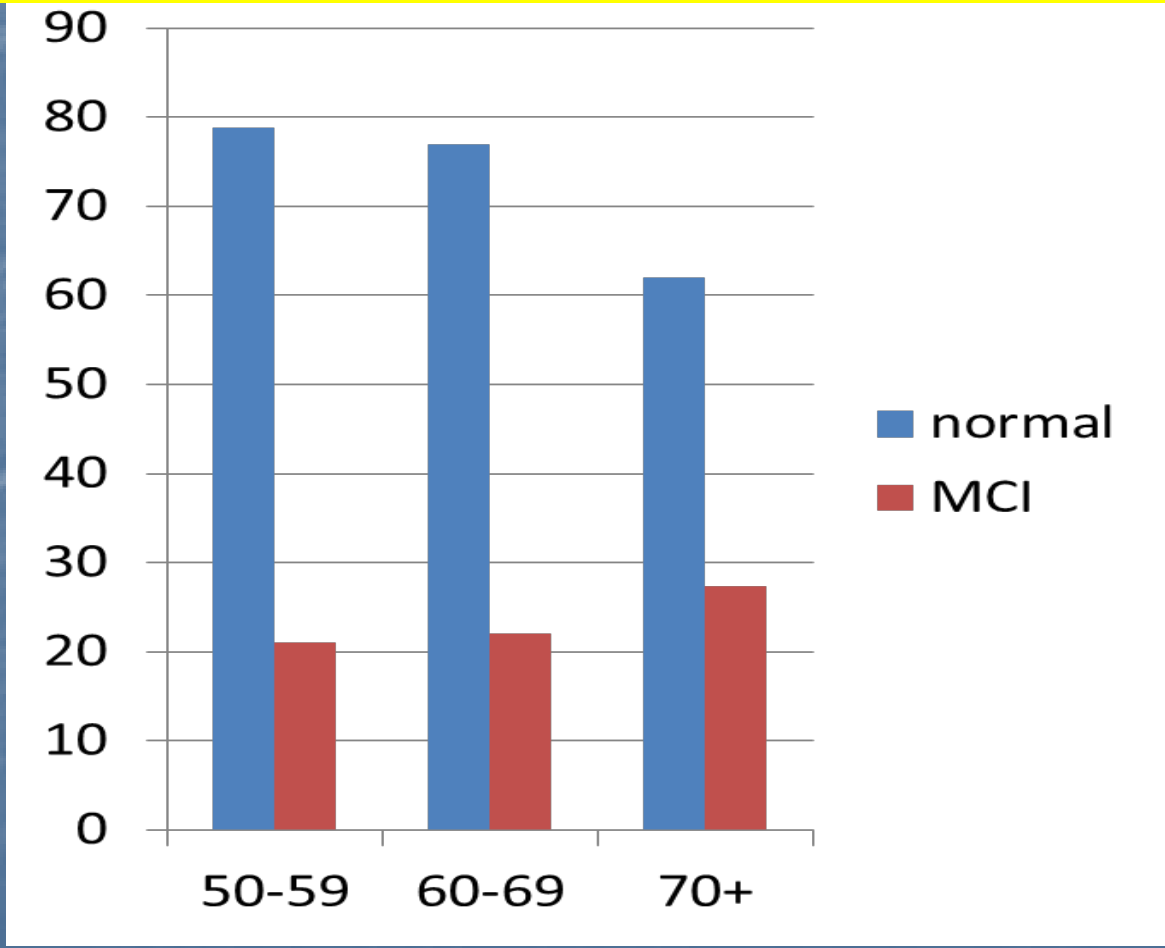
Metformin improves memory in SAMP8



Metformin prevents Bax translocation to nucleus



Metformin, Cognitive Dysfunction and Diabetics



OD in Diabetics Receiving Metformin

O.51 (0.22-0.99); P<.05

J Alzheimers Dis. 2014;41(1):61-8.

Long-term metformin usage and cognitive function among older adults with diabetes

Metformin use showed a significant inverse association with cognitive impairment in longitudinal analysis (OR = 0.49, 95% CI 0.25-0.95).

Dementia in Diabetes (VA)
11 year follow up, n=61010
HR for metformin 0.82

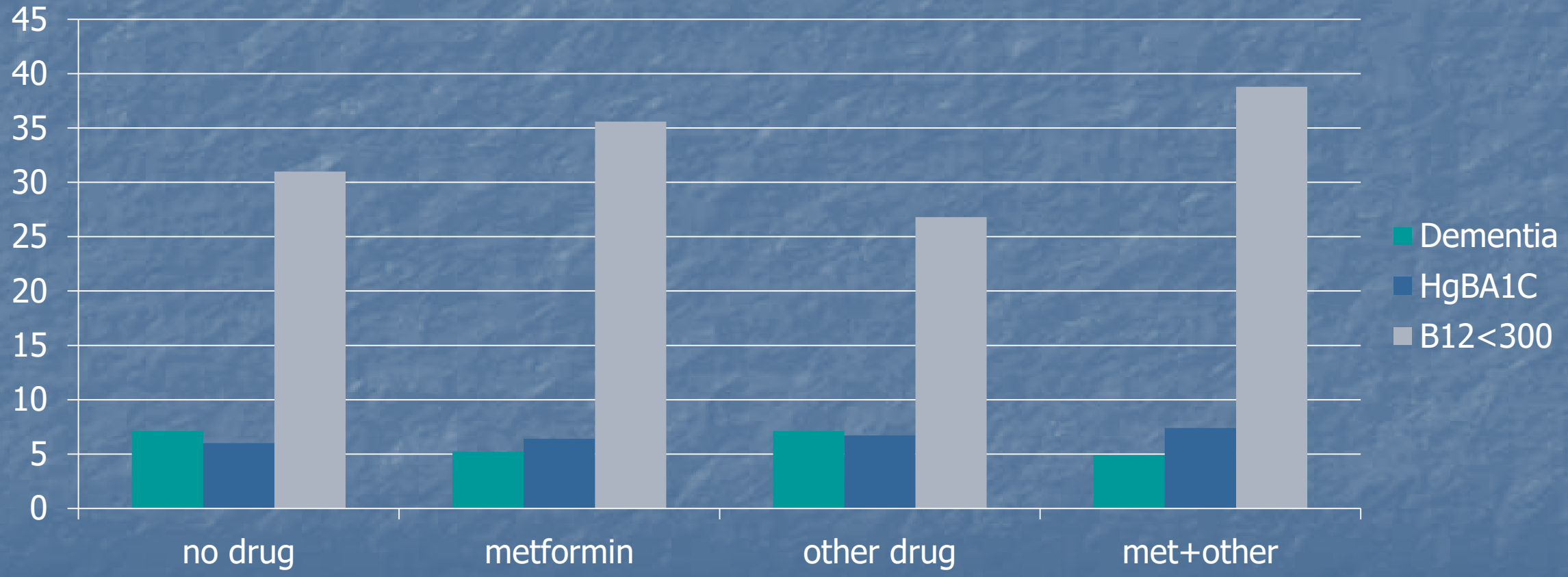
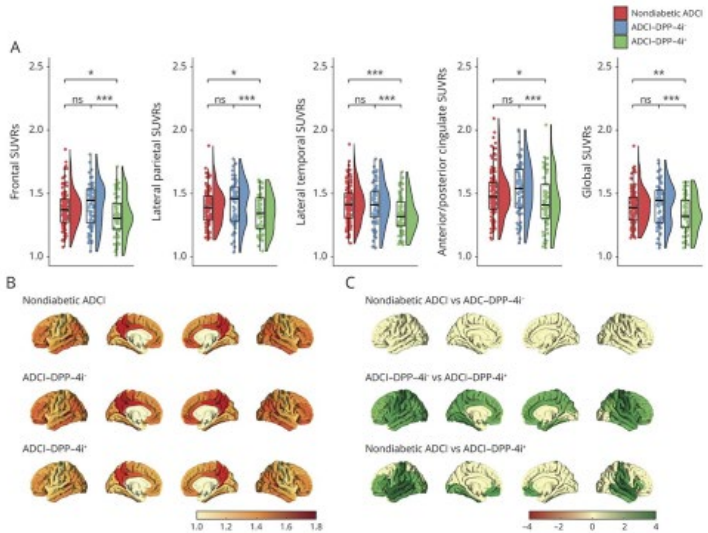
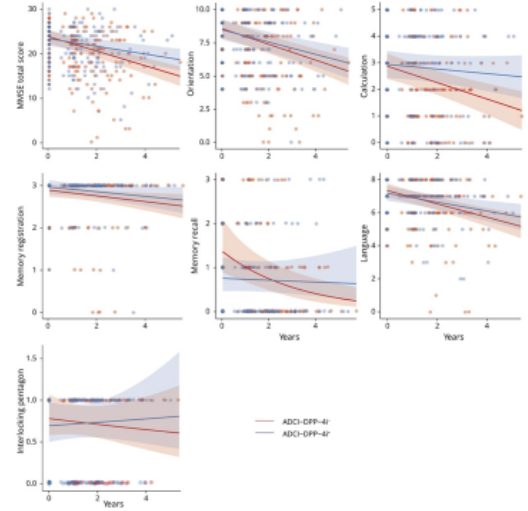


Figure 2 Group Comparison of Amyloid Retention



Seong Ho Jeong et al. Neurology 2021;97:e1110-e1122

Figure 3 Association Between Dipeptidyl Peptidase-4 Inhibitors (DPP-4i) Use and Mini-Mental State Examination (MMSE) Total and Subscores Over Time

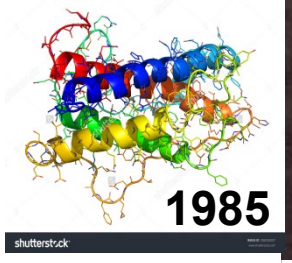


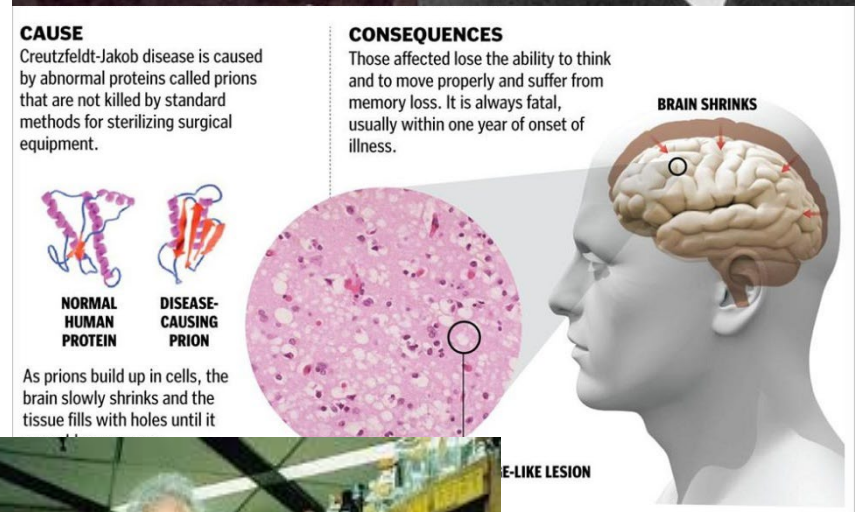
Seong Ho Jeong et al. Neurology 2021;97:e1110-e1122

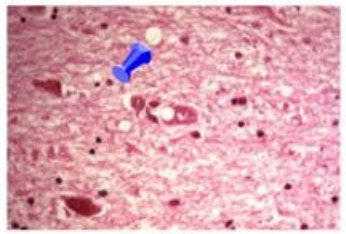
Association of Dipeptidyl Peptidase-4 Inhibitor Use and Amyloid Burden in Patients With Diabetes and AD-Related Cognitive Impairment

- (1) diabetic patients with ADCI treated with DPP-4i^{+} had significantly lower Aβ burden than those treated without DPP-4i^{-} and those without diabetes;
- (2) the ADCI-DPP-4i^{+} group had a slower longitudinal decline in cognitive performance than the ADCI-DPP-4i^{-} group.
- These findings suggest that DPP-4i may have beneficial effects on Aβ burden and long-term cognitive outcomes in diabetic patients with ADCI.

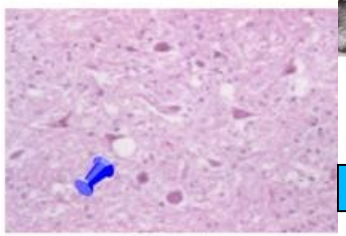
PRION DISEASES
(spongiform encephalopathies)



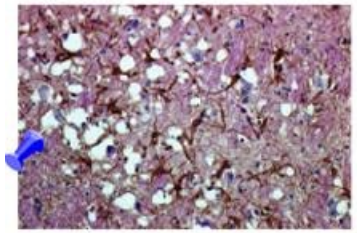




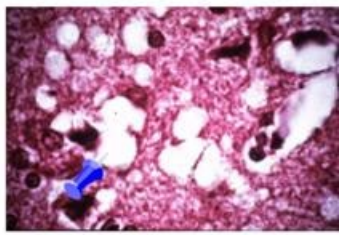
CJD



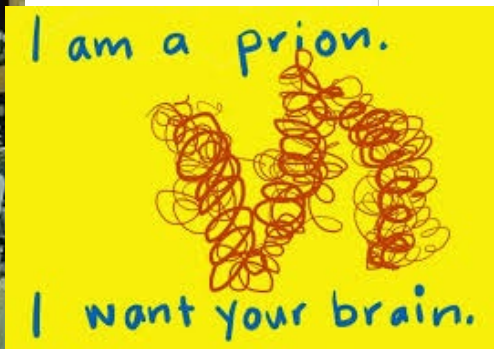
BSE



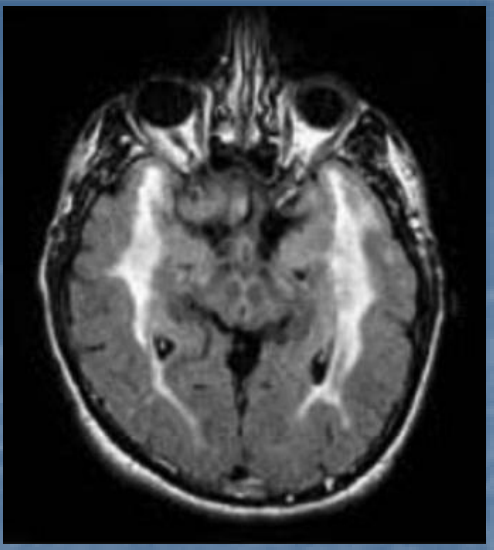
Scrapie



Kuru



Rare Dementias



- **CADASIL** (**"Cerebral Autosomal-Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy**") :Mutations on Notch 3 gene (Ch 19)
- Fragile X Syndrome (FMR1 gene : mental retardation) : essential tremor

Reversible Causes of MCI/Dementia

D rugs (digoxin, theophylline, cimetidine, anticholinergic

E motional (depression)

M etabolic (hypothyroidism,B12)

E yes and ears (sensory isolation)

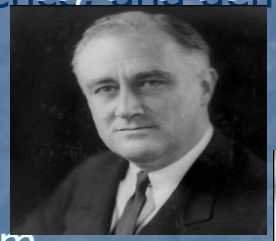
N ormal Pressure Hydrocephalus (ataxia, incontinence, and dementia)

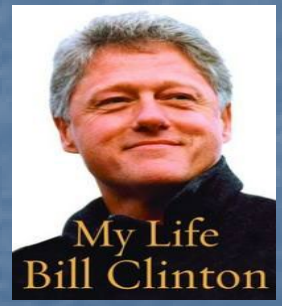
T umor or other space-occupying lesion

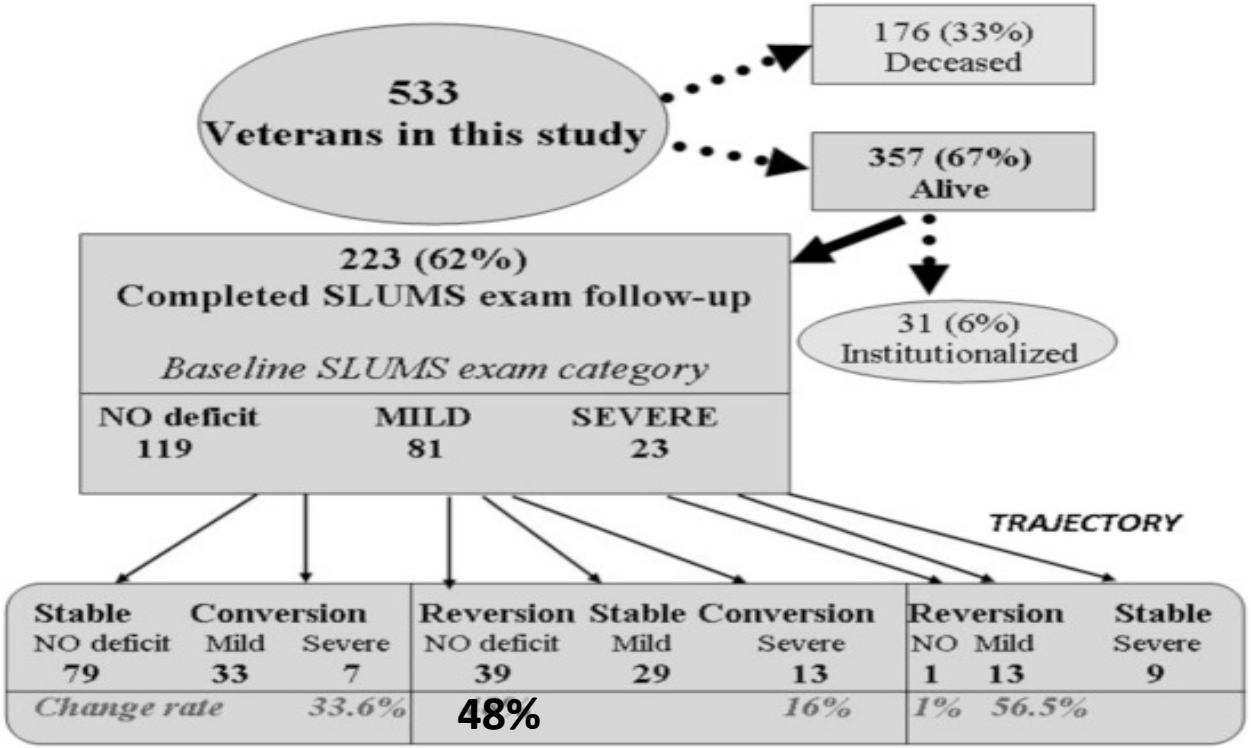
I nfection (syphilis, chronic infections)

A trial fibrillation (vitamin B12 deficiency)/Alcoholism

S leep Apnea







Correction of visual loss		
Stability	1 [Reference]	
Conversion	1.12 (0.27–4.71)	.877
Reversion	4.65 (1.58–13.70)	.005
Discontinuation of anticholinergic		
Stability	1 [Reference]	
Conversion	1.88 (0.69–5.13)	.218
Reversion	4.57 (1.87–11.18)	.001

Cognitive Deficit Reversal as Shown by Changes in the Veterans Affairs Saint Louis University Mental Status (SLUMS) Examination Scores 7.5 Years Later

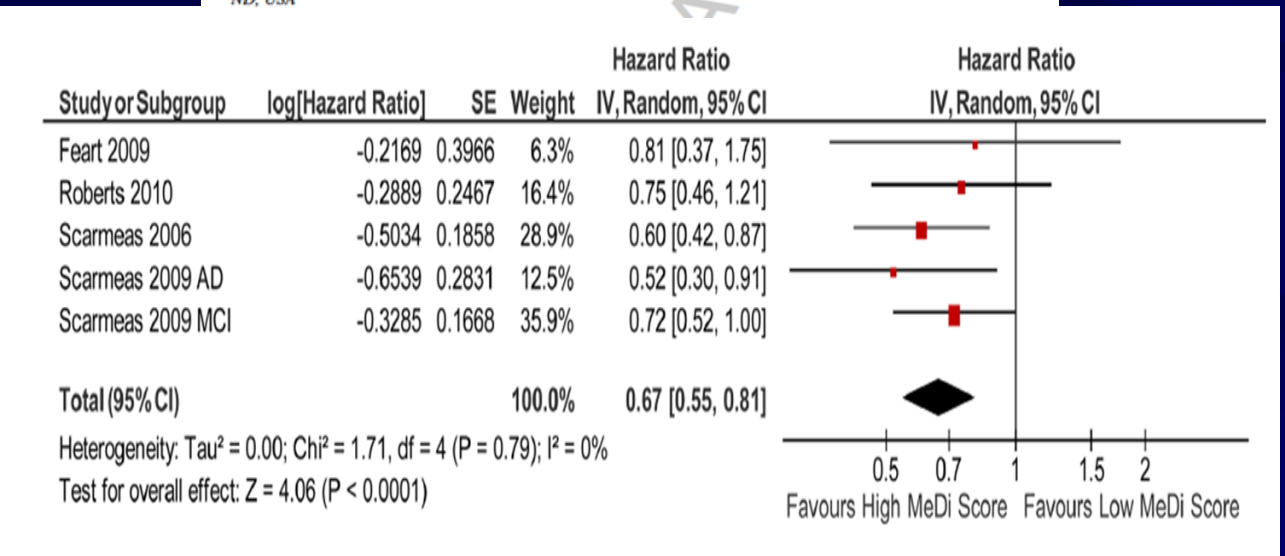
Journal of the American Medical Directors Association, Volume 15, Issue 9, 2014, 687.e5–687.e10

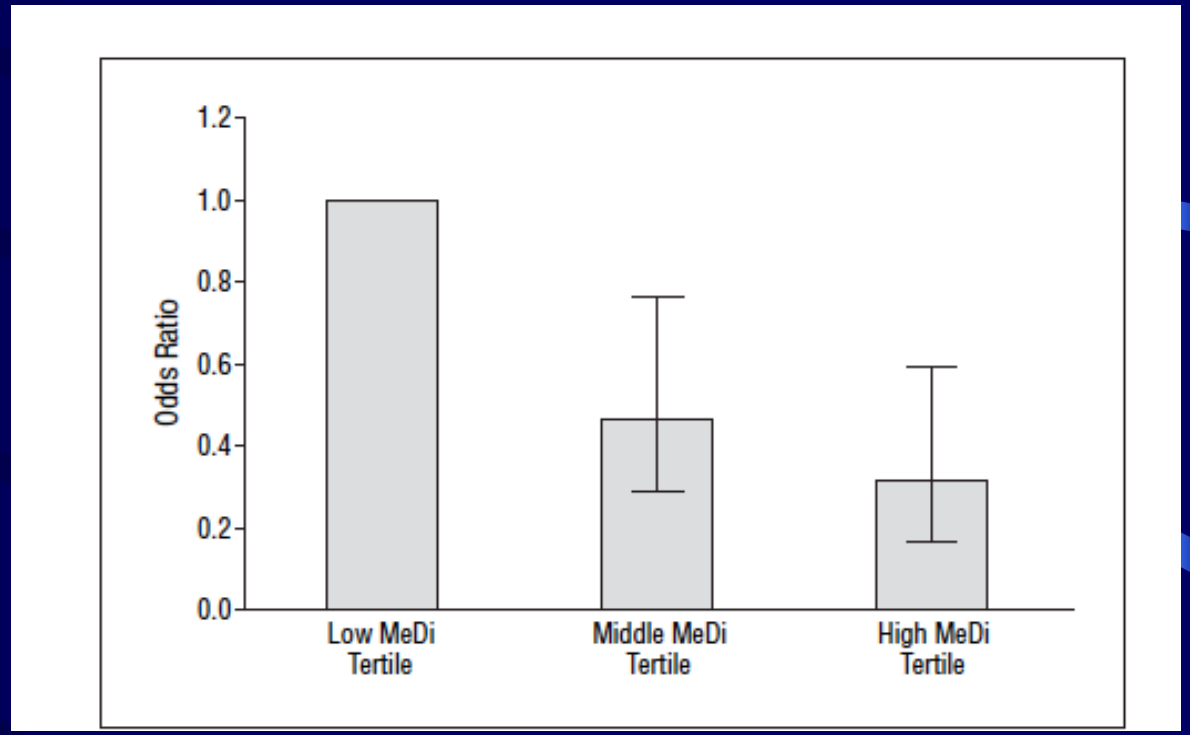
Mediterranean Diet associated with reduced risk of Alzheimer's Disease

Journal of Alzheimer's Disease xx (20xx) x–xx
DOI 10.3233/JAD-130830
IOS Press

Association of Mediterranean Diet with Mild Cognitive Impairment and Alzheimer's Disease: A Systematic Review and Meta-Analysis

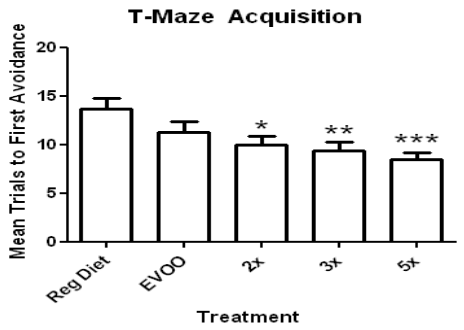
Balwinder Singh[a,d], Ajay K. Parsaik[a], Michelle M. Mielke[b], Patricia J. Erwin[c], David S. Knopman[a], Ronald C. Petersen[a,b] and Rosebud O. Roberts[a,b,*]
[a]*Department of Neurology, Department of Health Sciences Research, Mayo Clinic, Rochester, MN, USA*
[b]*Division of Epidemiology, Department of Health Sciences Research, Mayo Clinic, Rochester, MN, USA*
[c]*Mayo Medical Libraries, Mayo Clinic, Rochester, MN, USA*
[d]*Department of Clinical Neuroscience, University of North Dakota School of Medicine and Health Sciences, Fargo, ND, USA*



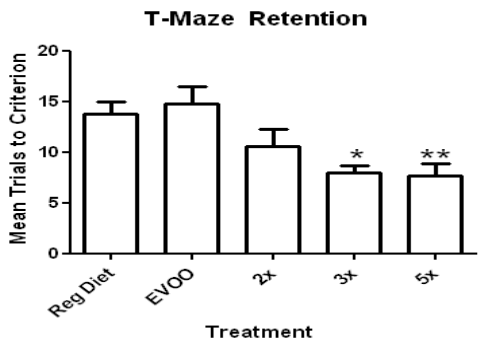


Extra Virgin Olive Oil Extracts

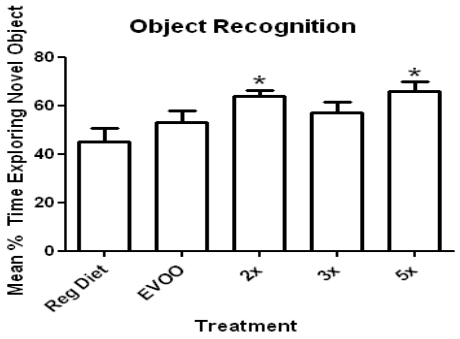
A



B



C



Polyphenyls block oxidative damage

RESEARCH PAPER

Mediterranean diet improves cognition: the PREDIMED-NAVARRA randomised trial

Elena H Martínez-Lapiscina,[1,2] Pedro Clavero,[3] Estefania Toledo,[1,4] Ramon Estruch,[4,5] Jordi Salas-Salvadó,[4,6] Beatriz San Julián,[1] Ana Sanchez-Tainta,[1] Emilio Ros,[4,7] Cinta Valls-Pedret,[4,7] Miguel Á Martinez-Gonzalez[1]

Table 4 Multivariable-adjusted means after a 6½-year follow-up and differences versus control (95% CIs) in each intervention group

	MedDiet+EVOO (n=224)		MedDiet+Nuts (n=166)		Control (low-fat diet) (n=132)
	Mean (95% CI)	p Value (vs control)	Mean (95% CI)	p Value (vs control)	Mean (95% CI)
MMSE	27.73 (27.27 to 28.19)		27.68 (27.20 to 28.16)		27.11 (26.61 to 27.61)
Adjusted diff. versus control (95% CI)	+0.62 (+0.18 to +1.05)	0.005	+0.57 (+0.11 to +1.03)	0.015	0 (reference)
CDT	5.31 (4.98–5.64)		5.13 (4.78–5.47)		4.80 (4.44–5.16)
Adjusted diff. versus control (95% CI)	+0.51 (+0.20 to +0.82)	0.001	+0.33 (+0.003 to +0.67)	0.048	0 (reference)

Exercise and the Brain

- Aerobic exercise for 6 months decreased brain atrophy…..

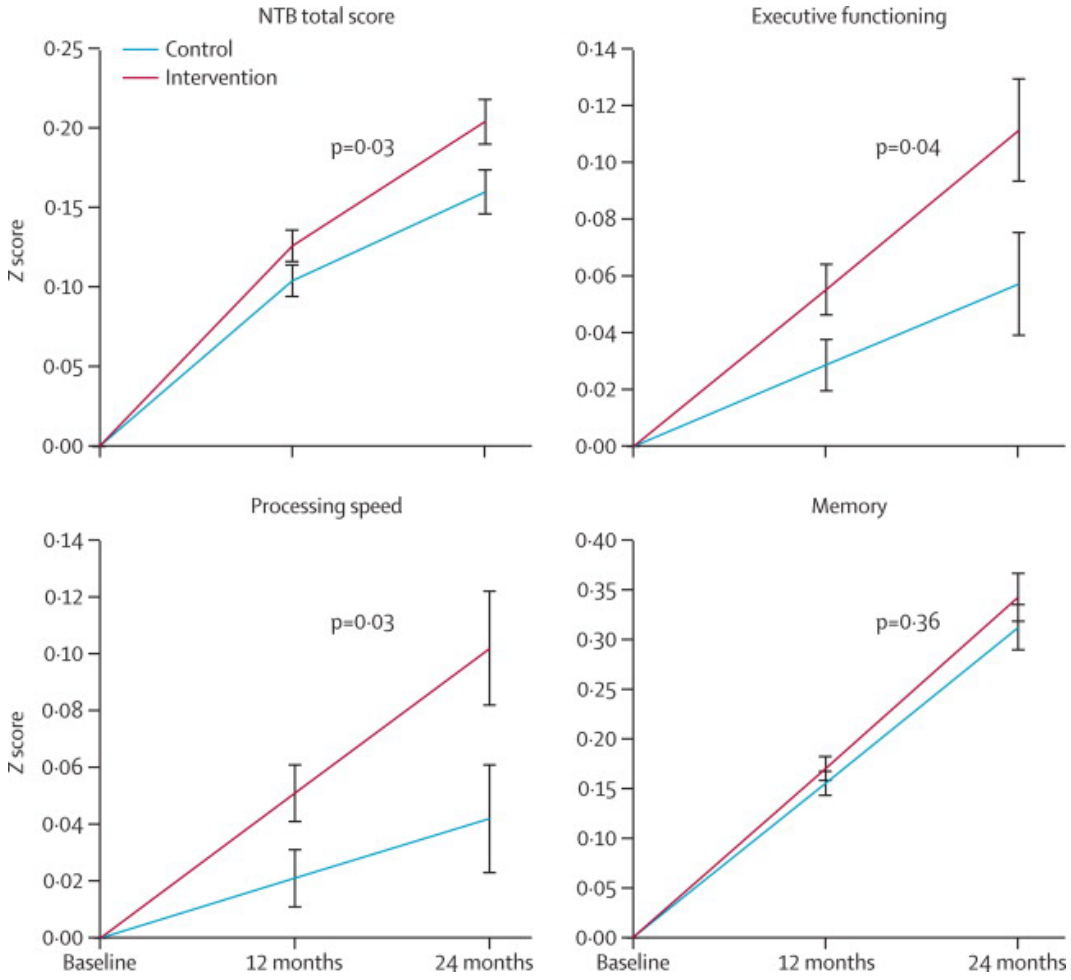
LIFE Study suggests need For HIGH DOSE exercise

Colcombe et al

J Gerontol A 2006; 61:1166

Increased cognition

Decreased dysphoria



FINGER STUDY

Aged 60-77 years recruited from previous national surveys.

A 2 year multidomain intervention (diet, exercise, cognitive training, vascular risk monitoring), or a control group (general health advice).

1260 to the intervention group (n=631) or control group (n=629).

A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial

Tiia Ngandu , Jenni Lehtisalo , Alina Solomon , Esko Levälahti , Satu Ahtiluoto , Riitta Antikainen , Lars Bäckma...

Improves Cognition

Making a difference

An evidence-based group programme
to offer cognitive stimulation therapy (CST)
to people with dementia

The manual for group leaders

Aimée Spector, Lene Thorgrimsen
Bob Woods, Martin Orrell

Published by **The Journal for Dementia Care**

Making a difference 2

An evidence-based group programme
to offer maintenance cognitive stimulation therapy
(CST) to people with dementia

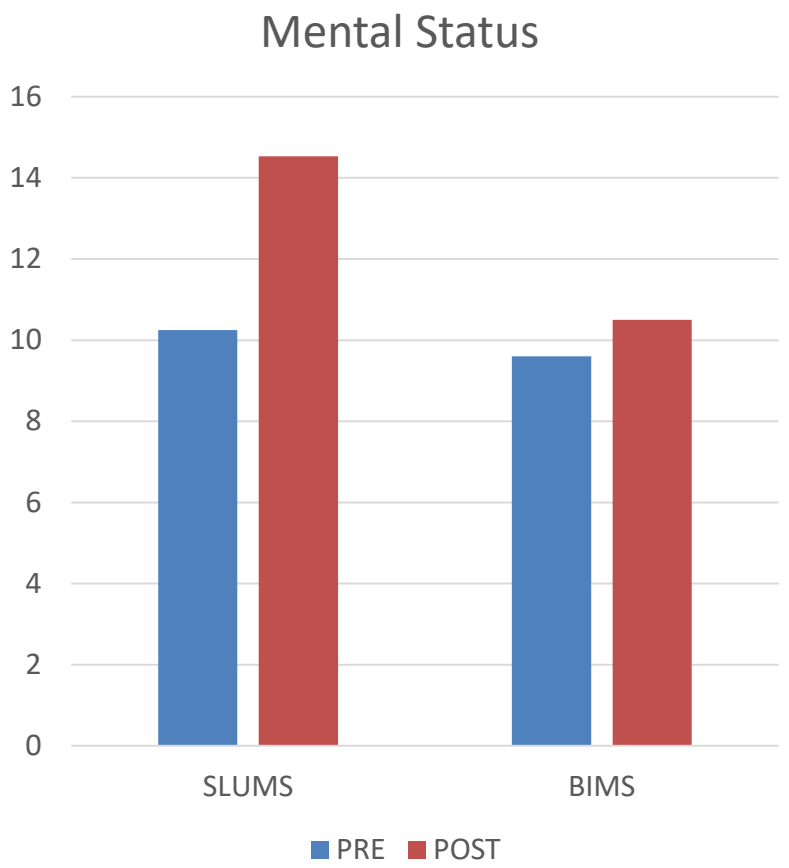
The manual for group leaders

VOLUME TWO

Elisa Aguirre, Aimée Spector, Amy Streater
Juanita Hoe, Bob Woods, Martin Orrell

Published by **The Journal of Dementia Care**

Cognitive Stimulation Therapy : NHC Nursing Home



Cardinals Reminiscence League

Unsafe behaviors in persons with dementia without a diagnosis of dementia

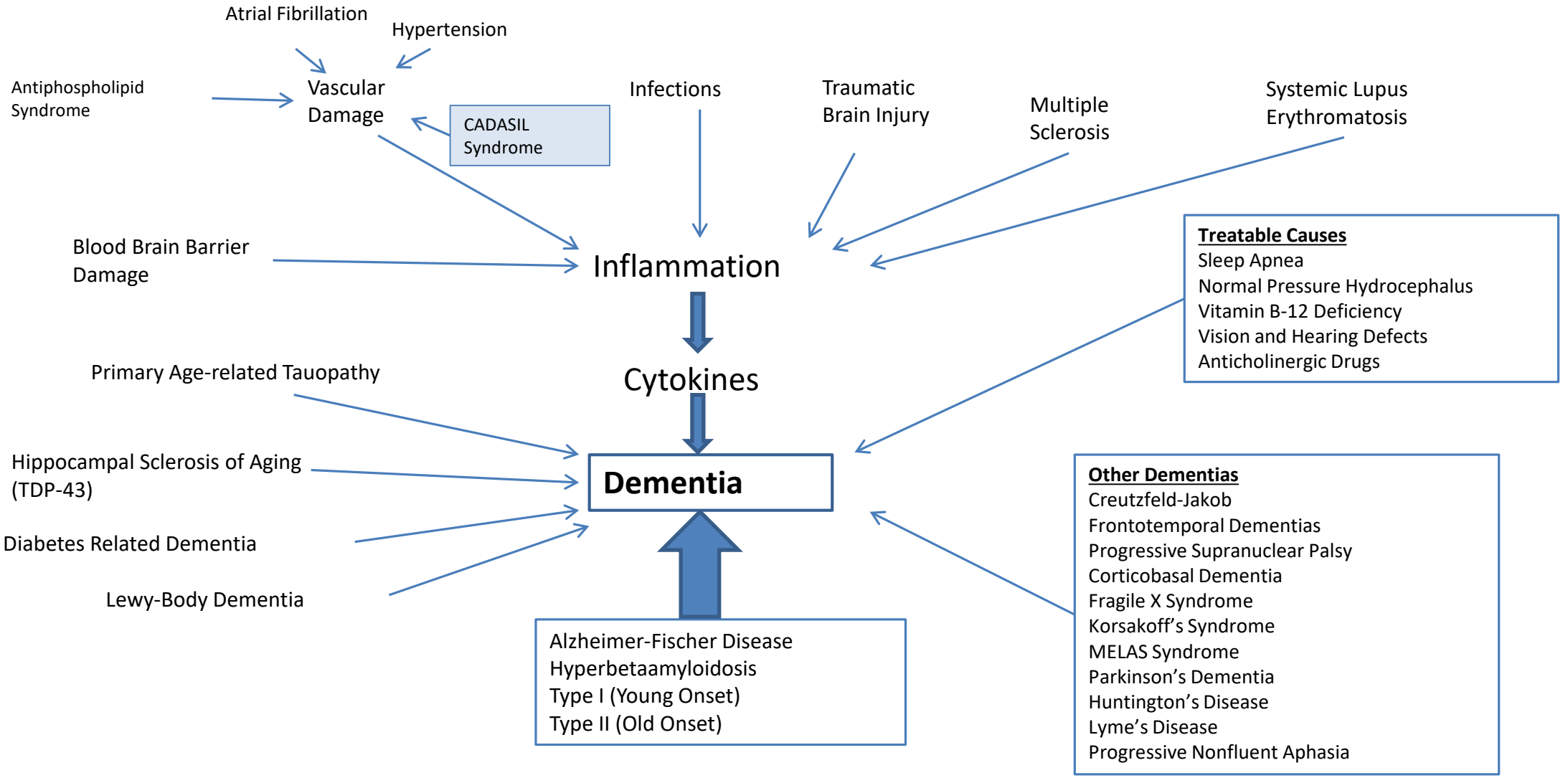
- Driving 23%
- Self medication management 49%
- Handling finances 29%
- Visiting doctor alone 29%

IAGG Brain Health Case Finding

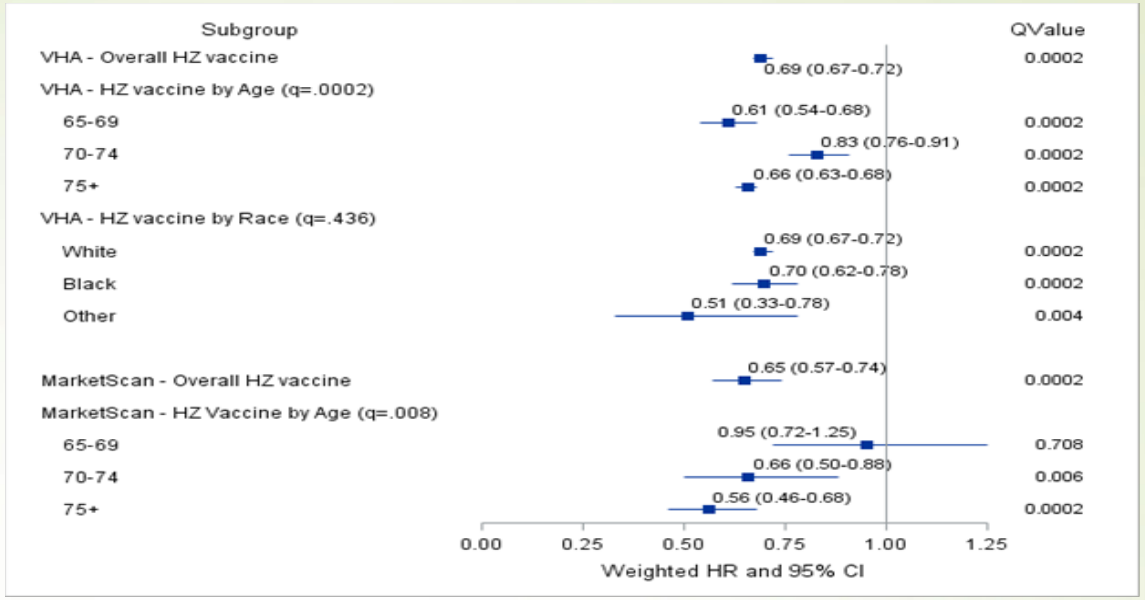
- Health Care Professionals need to know how well patients can follow instructions
- There are treatable causes of cognitive function
- Lifestyle interventions can slow the rate of cognitive dysfunction
- Early diagnosis allows development of advance directives

The Multiple Causes of Dementia

(CADASIL – Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy)



Herpes Zoster Vaccination and Dementia



Implications of all the available evidence: HZ and Tdap vaccinations in Veterans and civilians were associated with a reduction in new onset dementia.

Tdap Vaccination and Dementia

	Veterans Health Affairs Cohort		MarketScan Cohort	
Age group	**Crude**	**Weighted**	**Crude**	**Weighted**
All ages	0.53 (0.50–0.56)	0.58 (0.54–0.63)	0.58 (0.50–0.66)	0.58 (0.48–0.70)
Age 65–69	0.64 (0.55–0.73)	0.68 (0.57–0.81)	0.80 (0.61–1.05)	0.77 (0.58–1.03)
Age 70–74	0.59 (0.49–0.71)	0.45 (0.36–0.56)	0.74 (0.54–1.02)	0.58 (0.37–0.91)

Dementia : Best Practices

- Train health care professionals to use rapid screening test eg RCS
- Develop a computer assisted management algorhythm to help health care professionals recognize treatable causes
- Provide a lifesyle modification sheet to patient and family
- Check for caregiver stress in primary caregiver
- Provide CST programs

www.cstdementia.com and

www.aging.slu.edu

Thank You Dr. Morley!

EVMS

Eastern Virginia Medical School

Community Focus.
World Impact.