30th Annual Southern California Alzheimer's Disease Research Conference to be held on Friday, October 25, 2019

30 Years of Discovery: Hope on the Horizon

GIFTED BRAINS YIELD PRICELESS GAINS

Julie A. Schneider, M.D. M.S.

The Deborah R. And Edgar D. Jannotta Presidential Professor of Pathology (Neuropathology) and Neurological Sciences

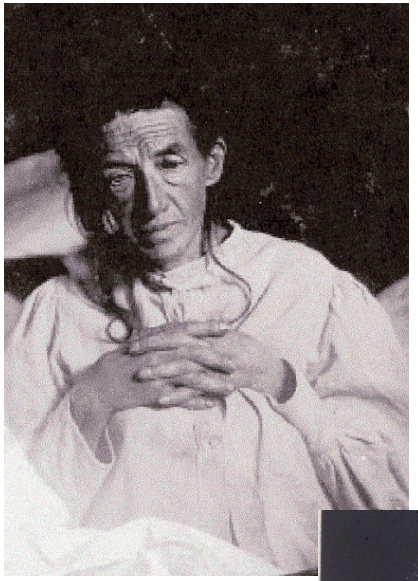
Associate Director, Rush Alzheimer's Disease Center, Rush University Medical Center

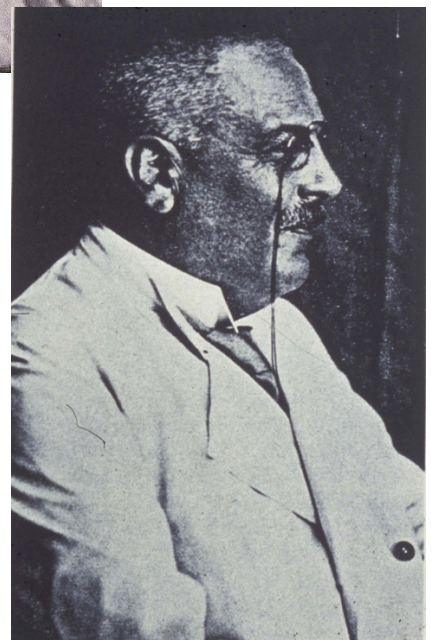
What are we learning from the precious gift of brain donation from older persons?

- Alzheimer's disease pathology is often mixed with other pathologies (mixed pathology)
- Risk factors may work through increasing/decreasing pathology.
- Persons without cognitive impairment may have a lot of "subclinical" pathology
- There is pathologically unexplained cognitive change and risk factors

Auguste D & Alois Alzheimer

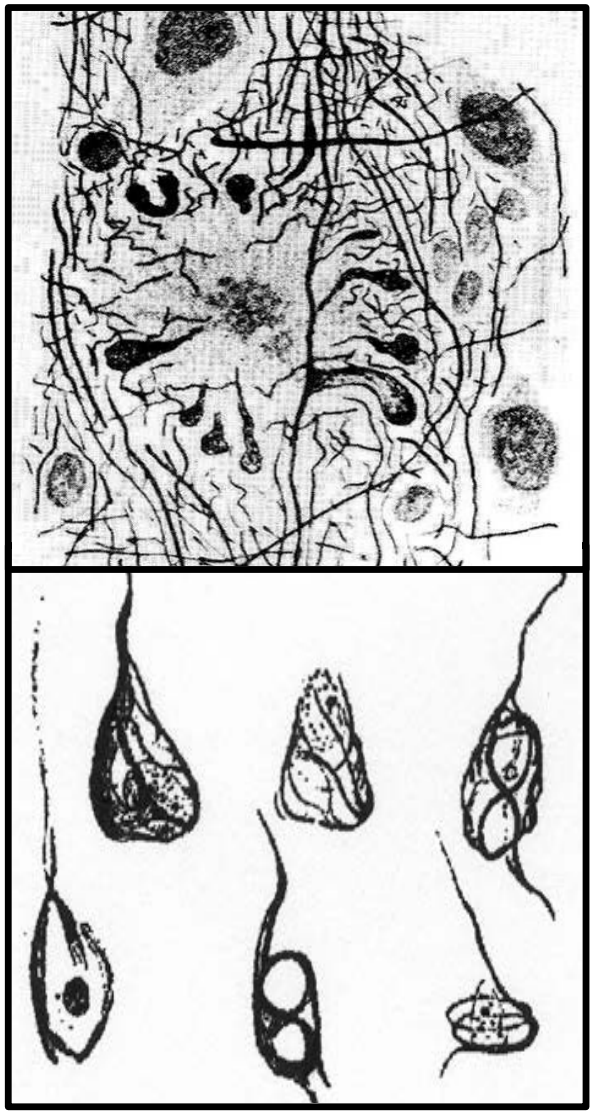
- First patient described - 1907
  - 51 year old woman
  - Memory impairment
  - Hallucinations, delusions, paranoia
  - Agitation
  - Disorientation
- Progression over 5 years
  - At end - fetal position, incontinent, unresponsive

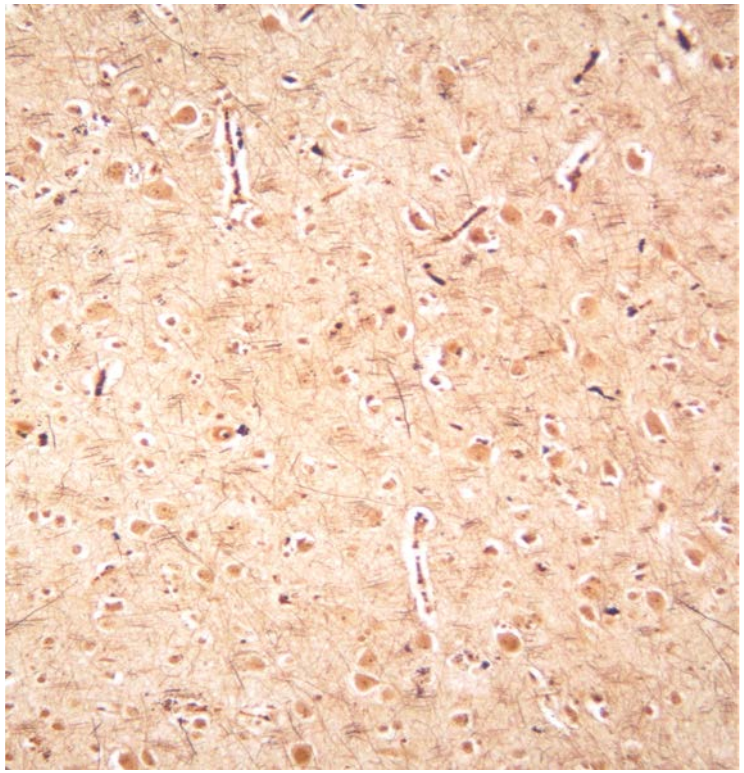


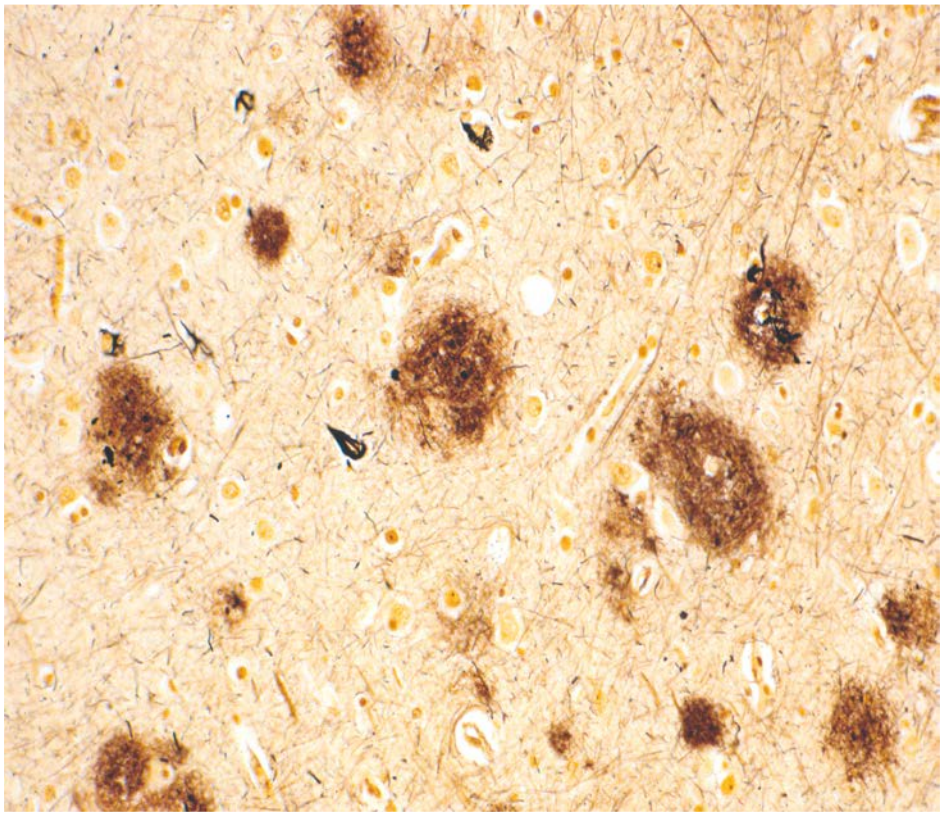


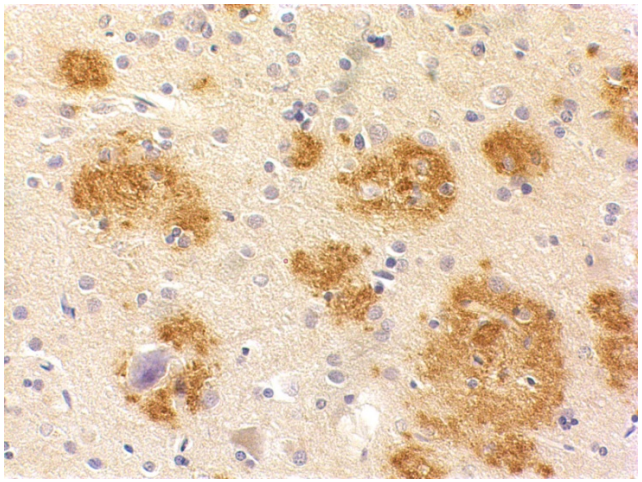
Autopsy brain examination

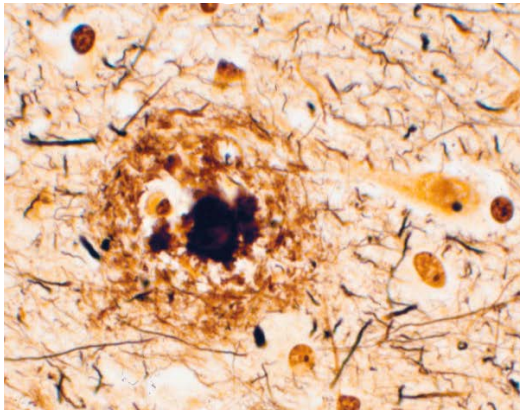
- Grossly atrophic
- Microscopic exam:
  - Neuronal loss
  - Neuritic plaques
  - Neurofibrillary tangles

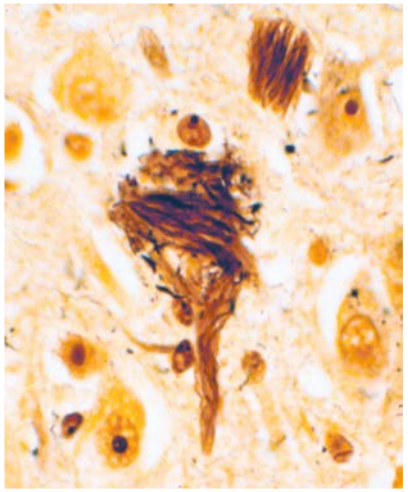






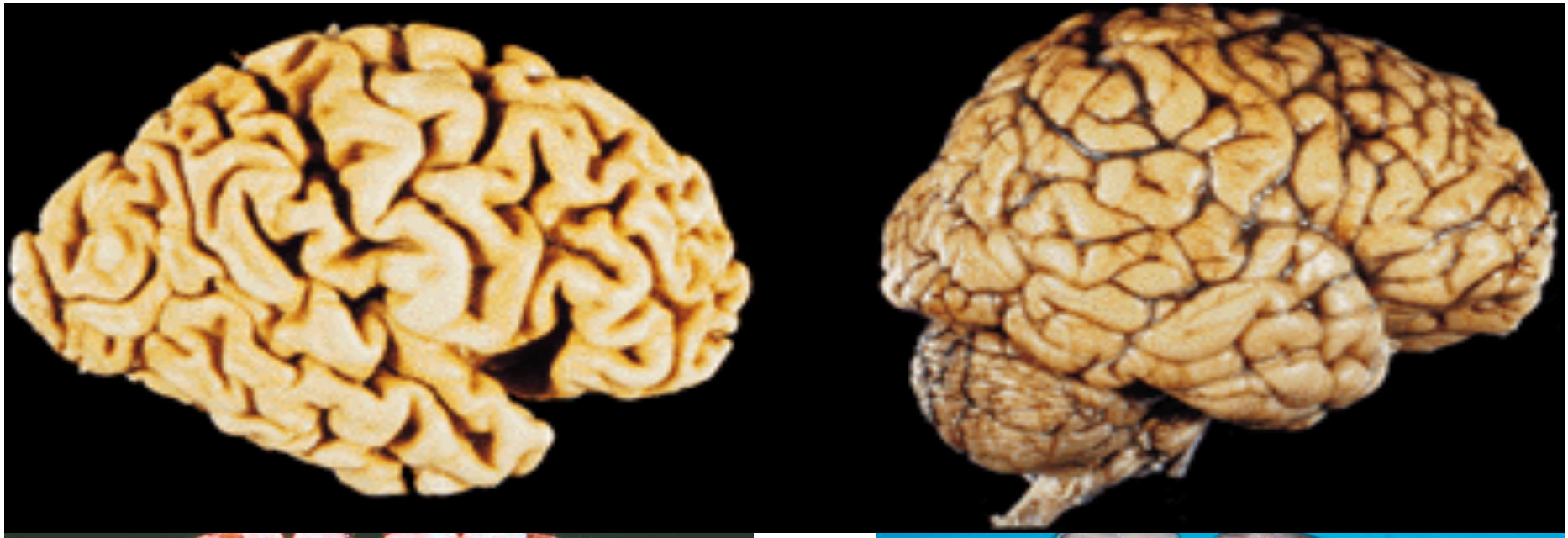


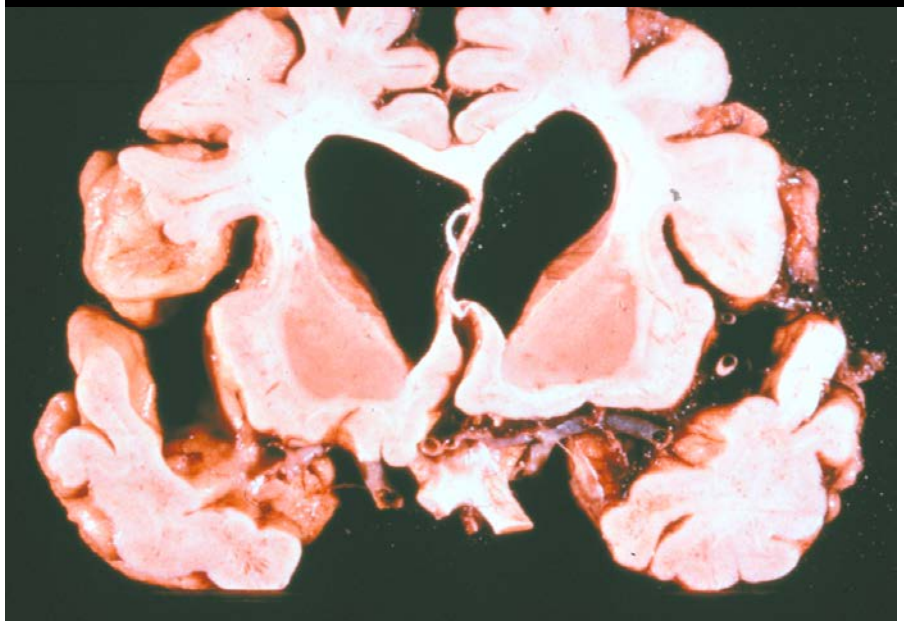


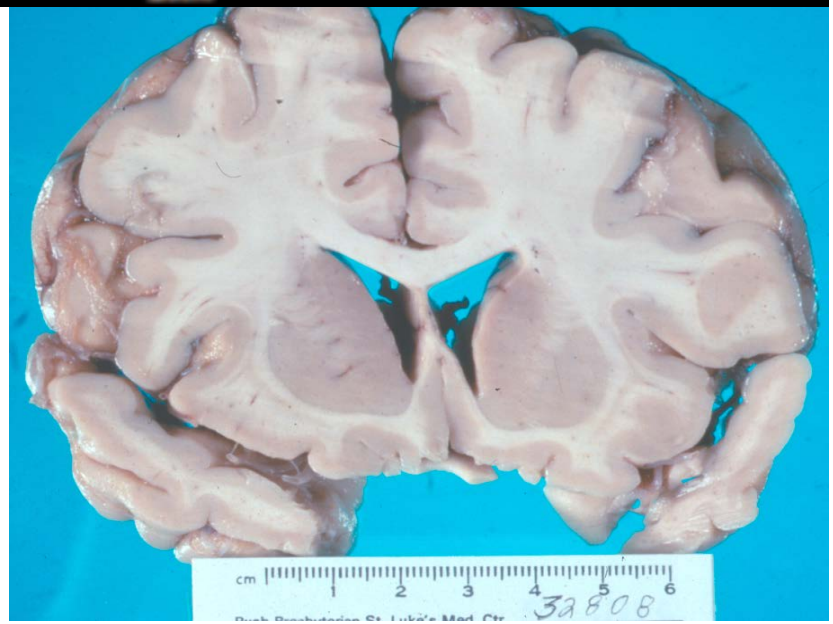


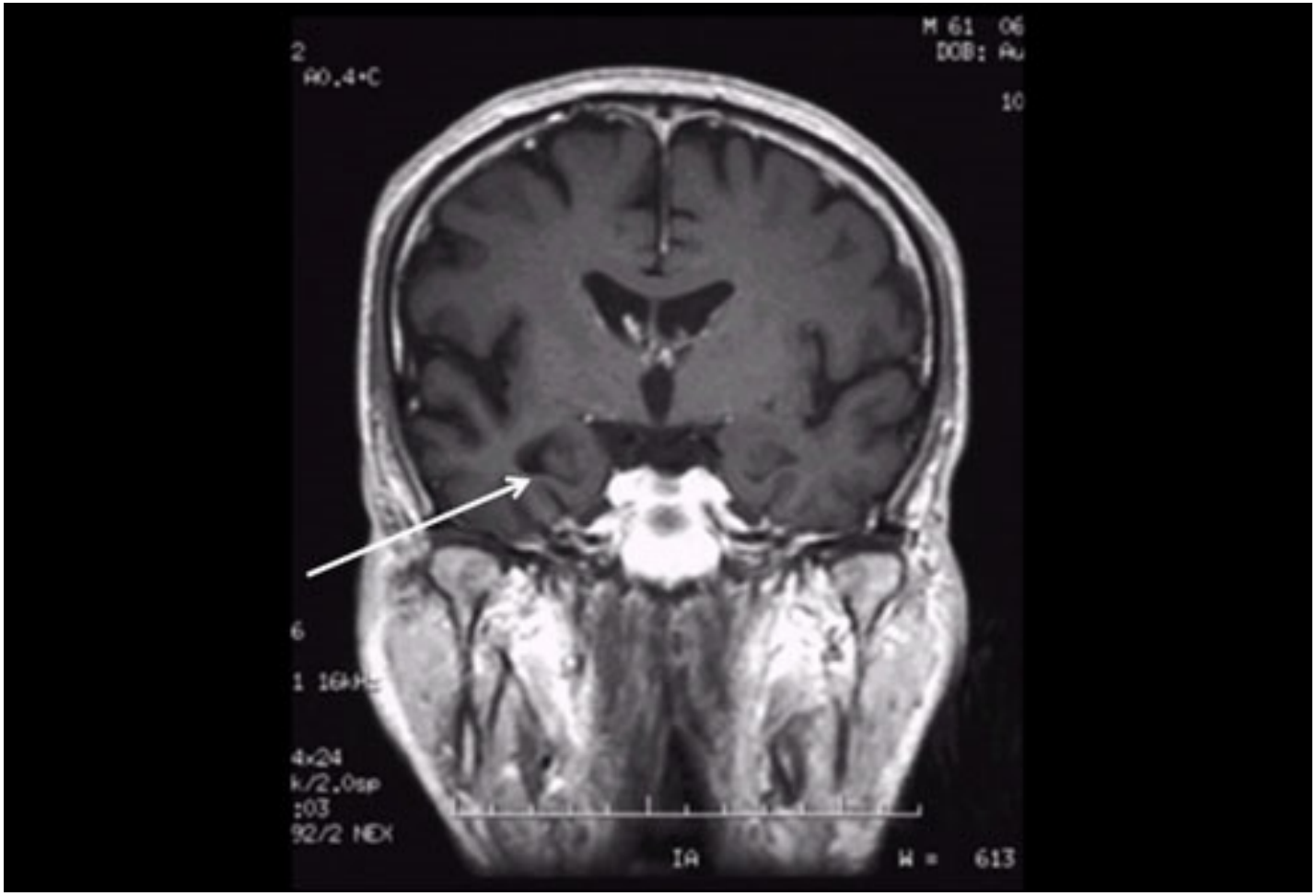
Alzheimer's disease

Normal brain





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IA
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The Religious Orders Study

Began in 1993

- Older nuns, priests, and brothers without known dementia from across the U.S.
- All agreed to annual cognitive testing
- All agreed to brain donation at the time of death

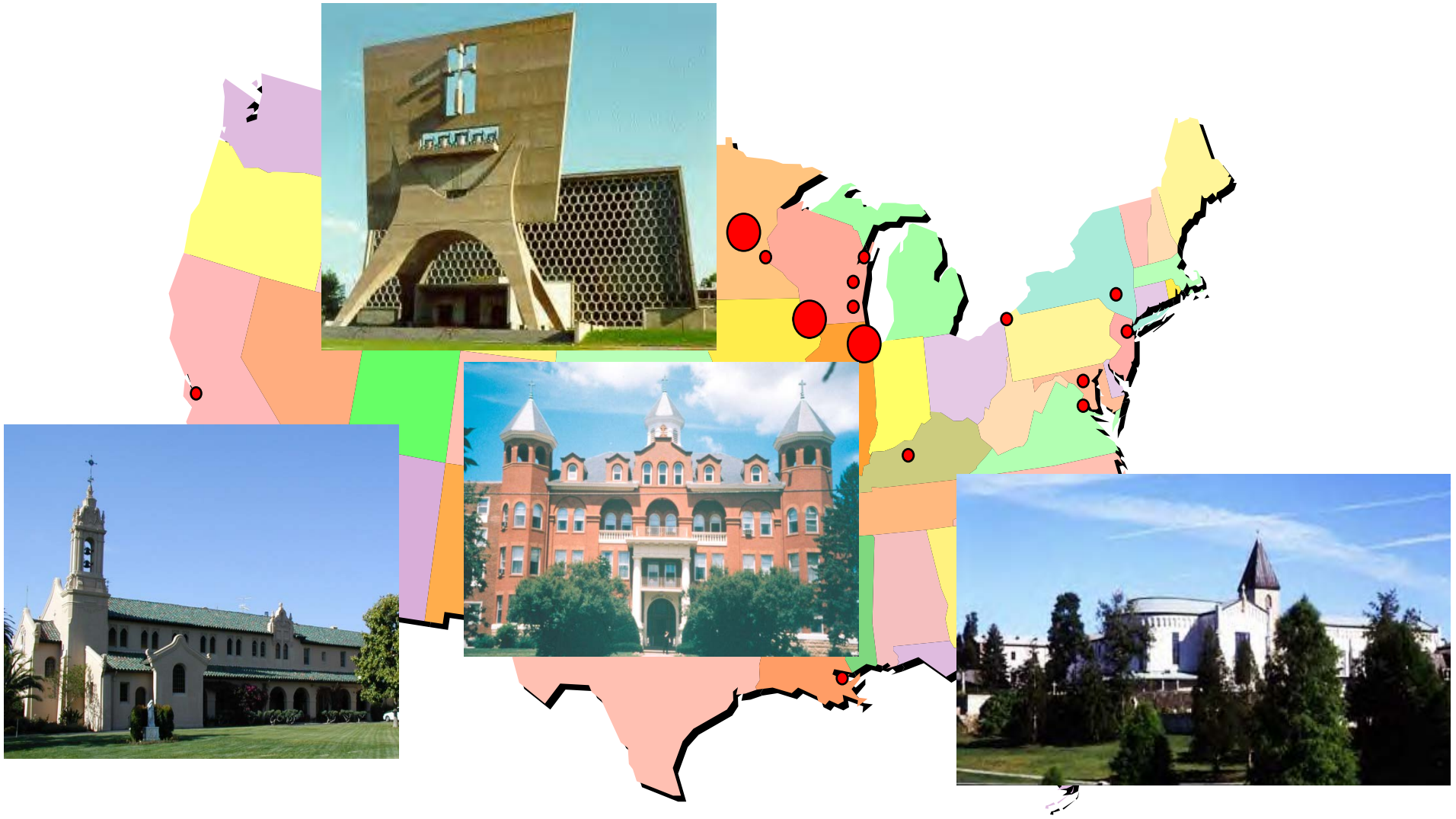
The Rush Memory and Aging Project

Began in 1997

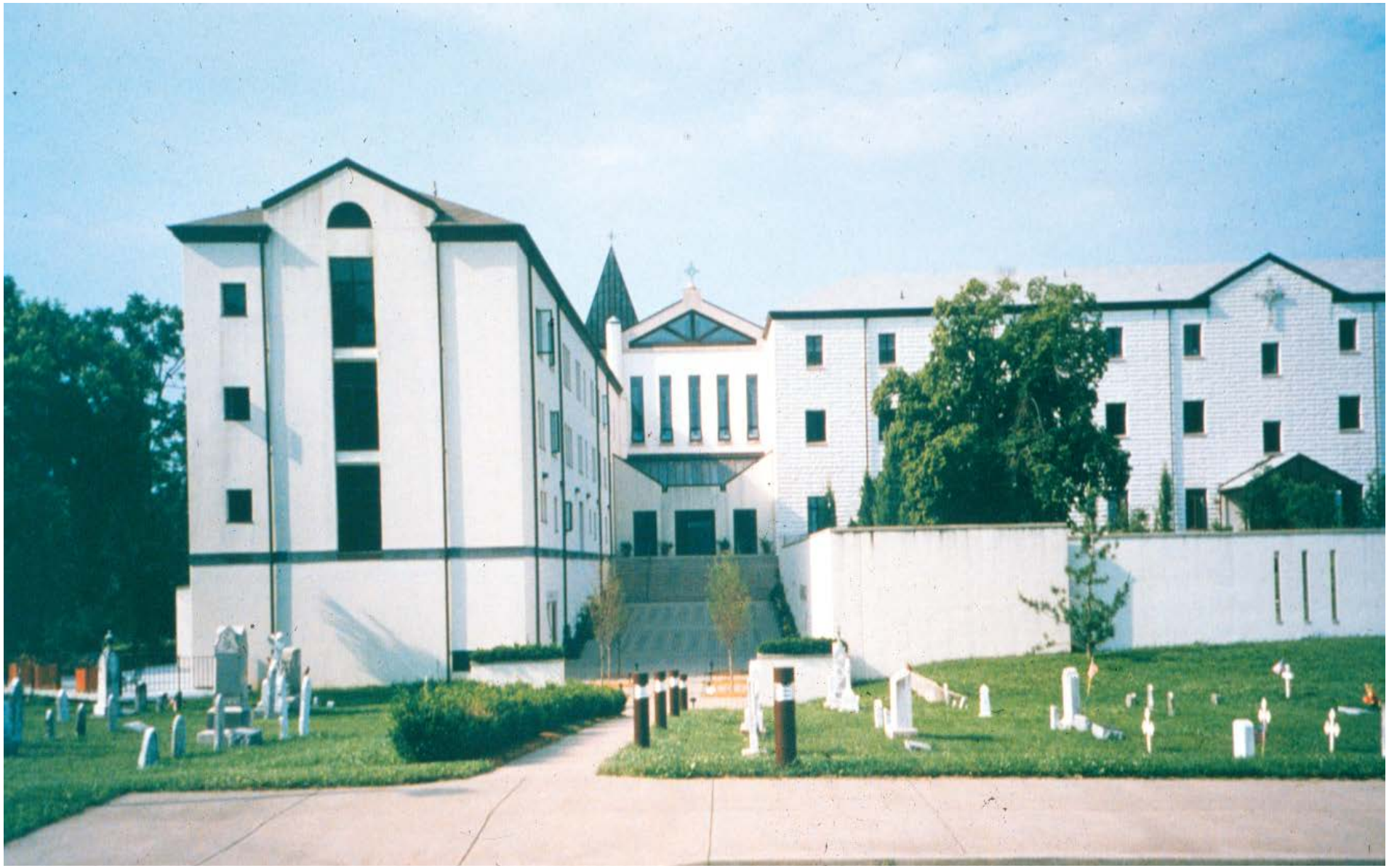
- Study with similar methods but lay population more reflective of general population - from about 40 retirement communities and senior housing
- All agreed to annual cognitive/motor testing, blood draws
- All agreed to donate brain, spinal cord, muscle, nerve at the time of death
- *F/U rates over 90% Autopsy Rates 80%*

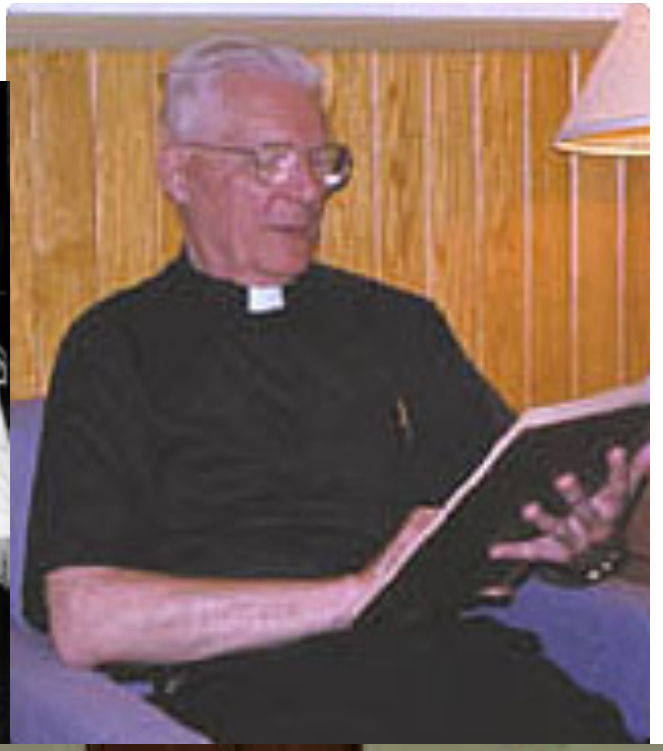
Both studies on going for 20+ years • >3,000 older persons enrolled without [known] dementia from across the USA, over 1500 autopsies

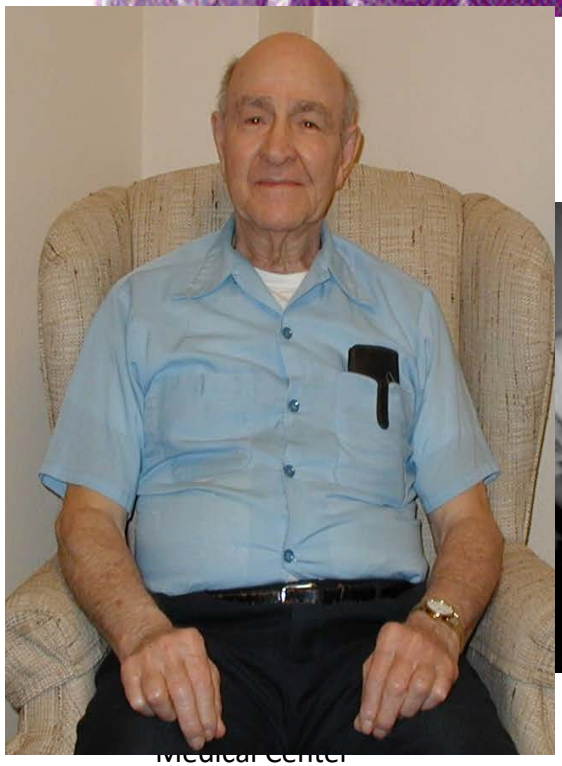
Religious Orders Study Sites



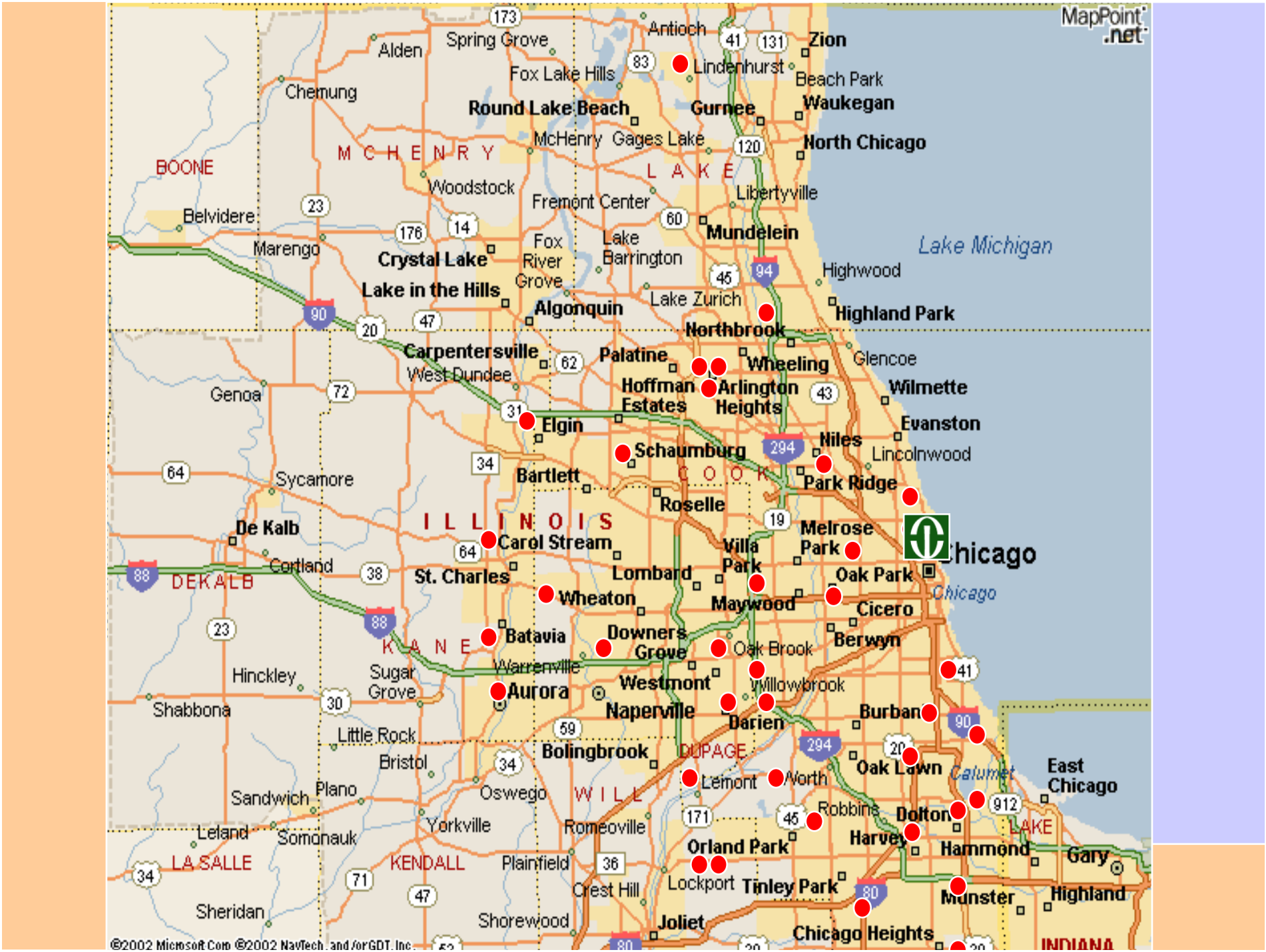
Religious Orders Study: Participating Sites







Medical Center


MapPoint.net
Antioch
Zion
Lindenhurst
Beach Park
Waukegan
Gurnee
Round Lake Beach
Fox Lake Hills
Spring Grove
Alden
Chemung
McHenry
Gages Lake
North Chicago
MCHENRY
LAKE
BOONE
Woodstock
Fremont Center
Libertyville
Belvidere
Mundelein
Marengo
Crystal Lake
Fox River Grove
Lake Barrington
Lake Michigan
Highwood
Lake in the Hills
Algonquin
Lake Zurich
Highland Park
Northbrook
Carpentersville
West Dundee
Palatine
Wheeling
Glencoe
Hoffman Estates
Arlington Heights
Wilmette
Genoa
Elgin
Evanston
Schaumburg
Niles
Lincolnwood
Sycamore
Bartlett
COOK
Park Ridge
Roselle
ILLINOIS
De Kalb
Carol Stream
Melrose Park
Villa Park
Chicago
Cortland
St. Charles
Lombard
Oak Park
DEKALB
Wheaton
Maywood
Cicero
Batavia
Downers Grove
Oak Brook
Berwyn
KANE
Hinckley
Sugar Grove
Warrenville
Westmont
Willowbrook
Aurora
Naperville
Burbank
Shabbona
Darien
Little Rock
Bolingbrook
DUPAGE
Oak Lawn
Calumet
East Chicago
Bristol
Lemont
Worth
Sandwich
Plano
Oswego
WILL
Robbins
Dolton
Yorkville
Romeoville
Harvey
Hammond
Gary
Leland
Somonauk
Orland Park
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Highland
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Medical Center

Medical Center

What are we learning from the precious gift of brain donation from older persons?

- Alzheimer's disease pathology is often mixed with other pathologies (mixed pathology)
- Risk factors may work through increasing/decreasing pathology.
- Persons without cognitive impairment may have a lot of "subclinical" pathology
- There is pathologically unexplained cognitive change and risk factors

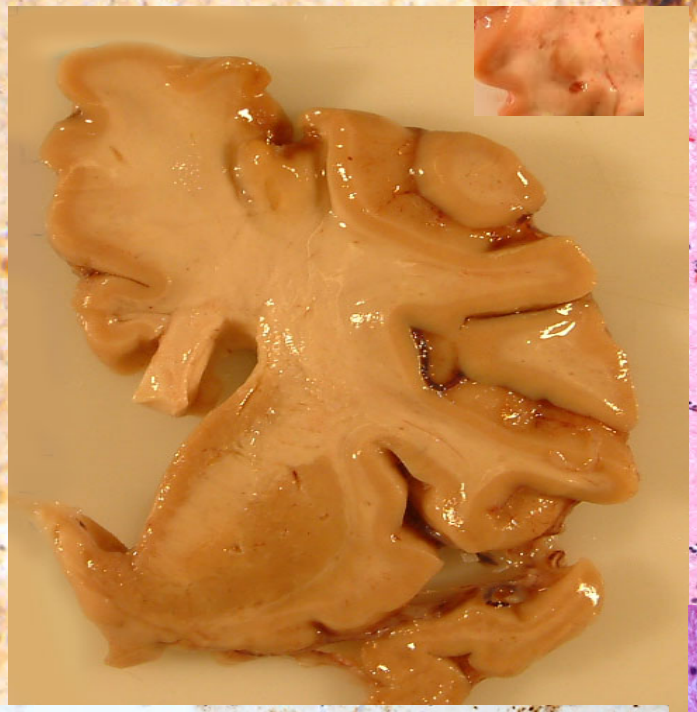
The pathologies of the aging brain

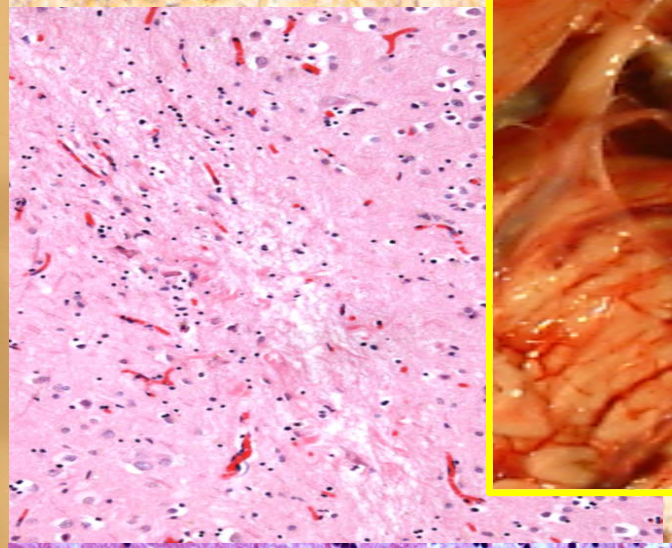
- NEURODEGENERATIVE
- Alzheimer's disease (plaques/tangle)
- Lewy body disease

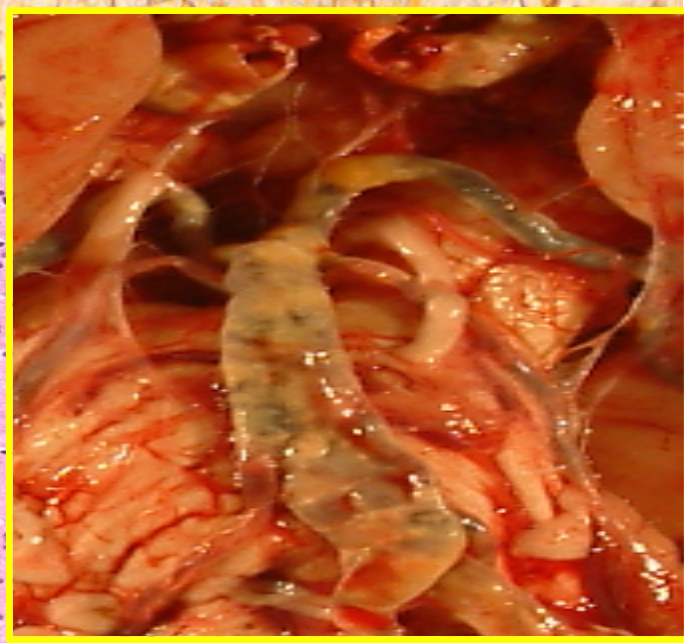
- **TDP-43 pathology**
- **Hippocampal sclerosis**

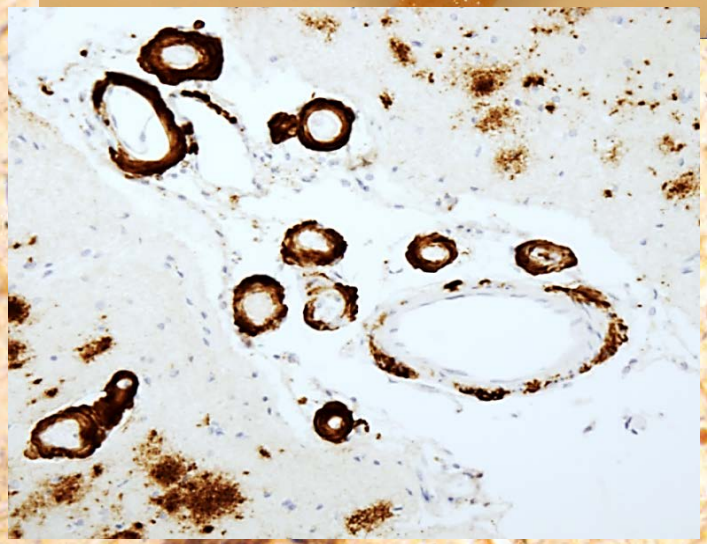
- VASCULAR
- Macroinfarcts (strokes)

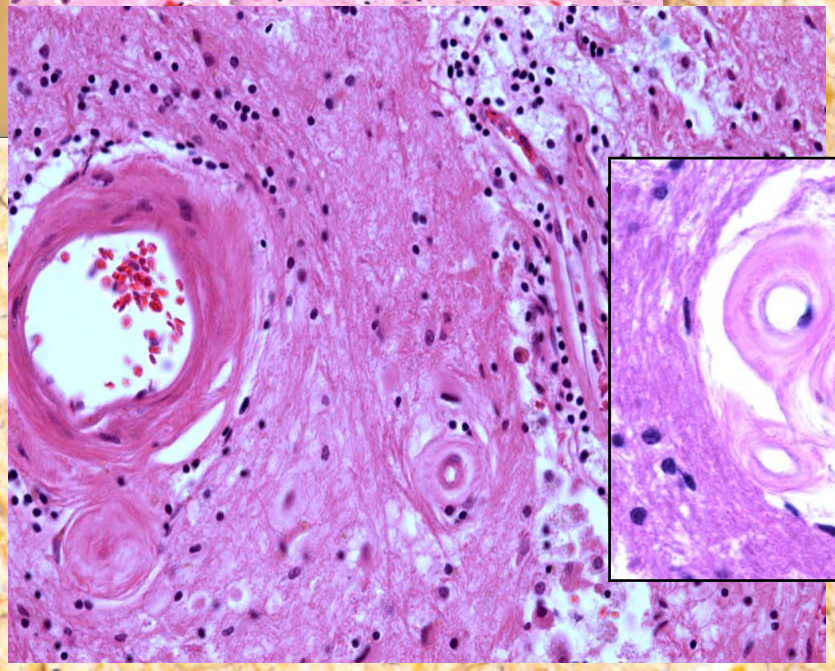
- **Microinfarcts**
- **CAA**
- **Atherosclerosis**
- **Arteriolosclerosis**

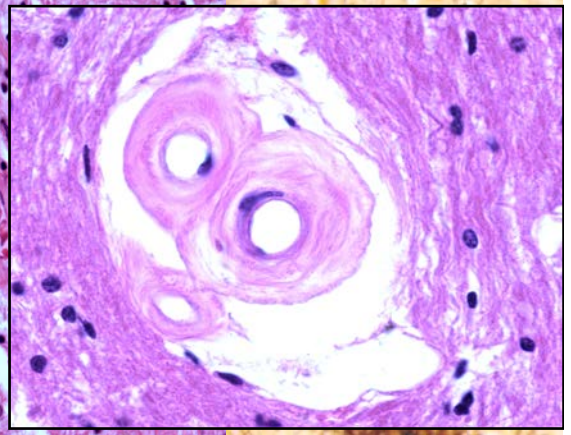


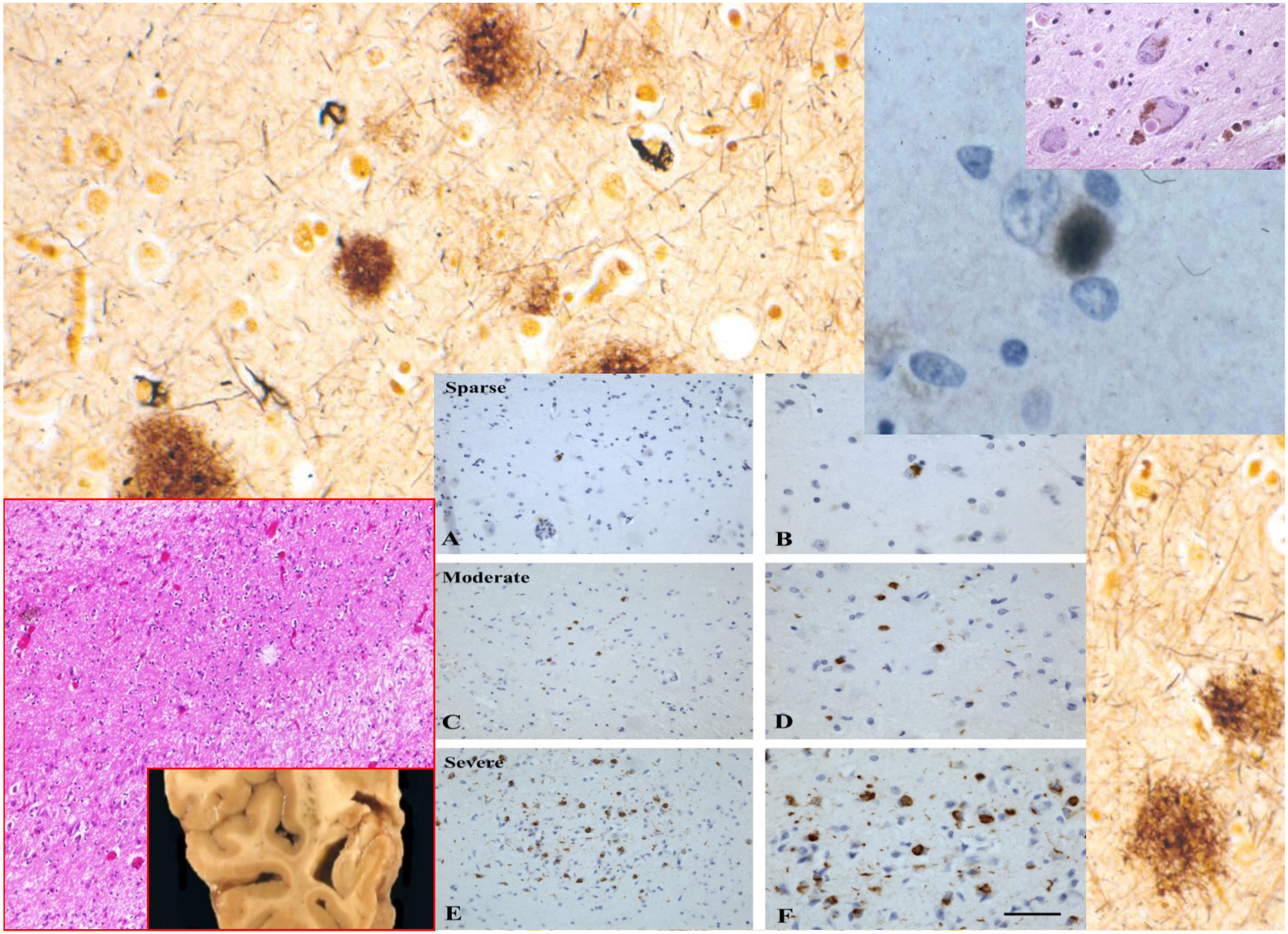











Sparse
A
B
Moderate
C
D
Severe
E
F

Mixed brain pathologies common in MCI and probable AD

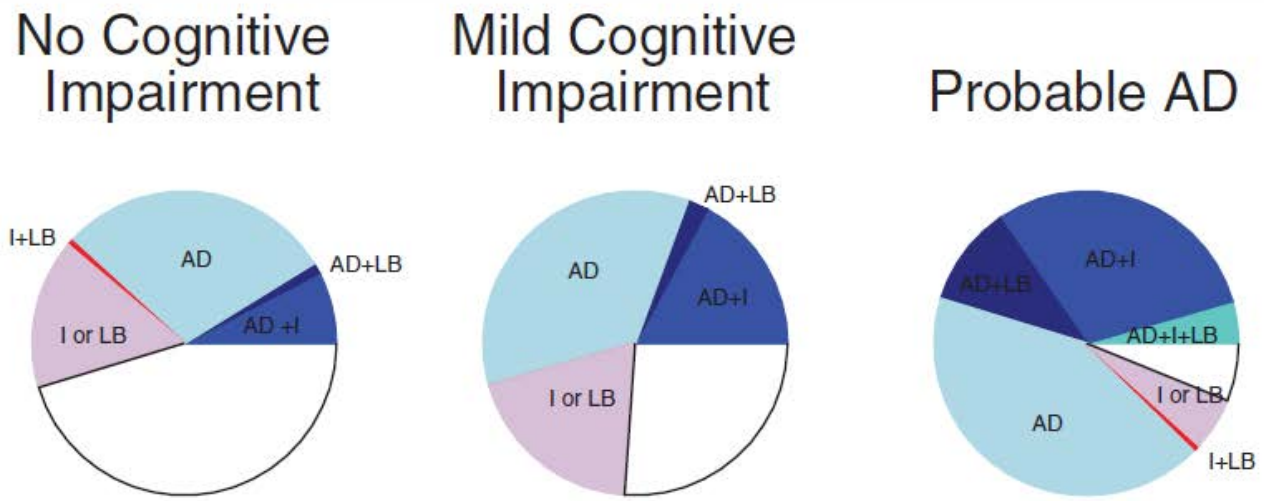
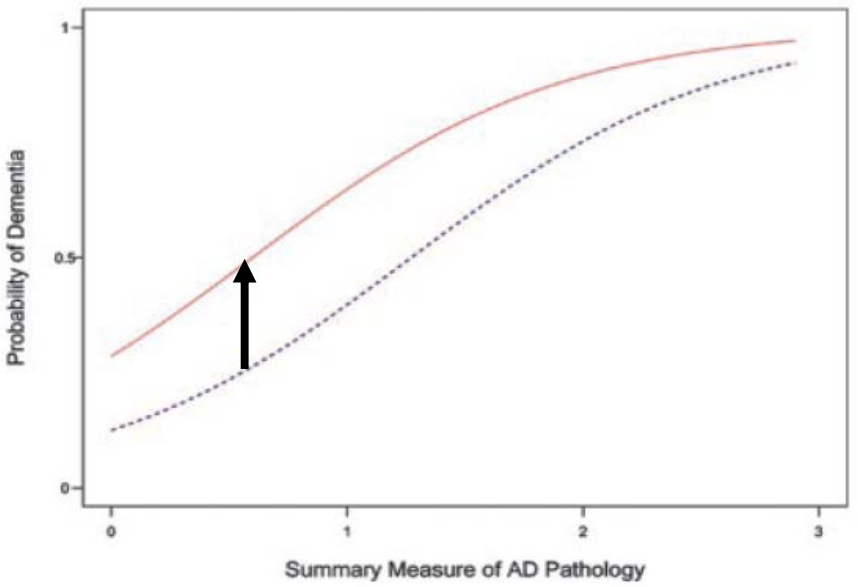
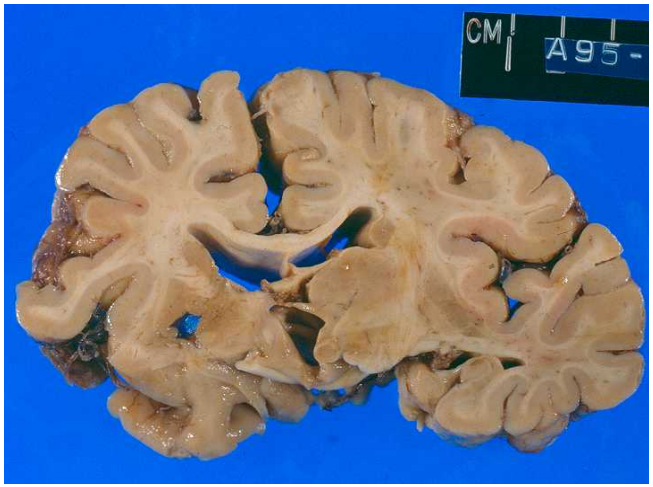


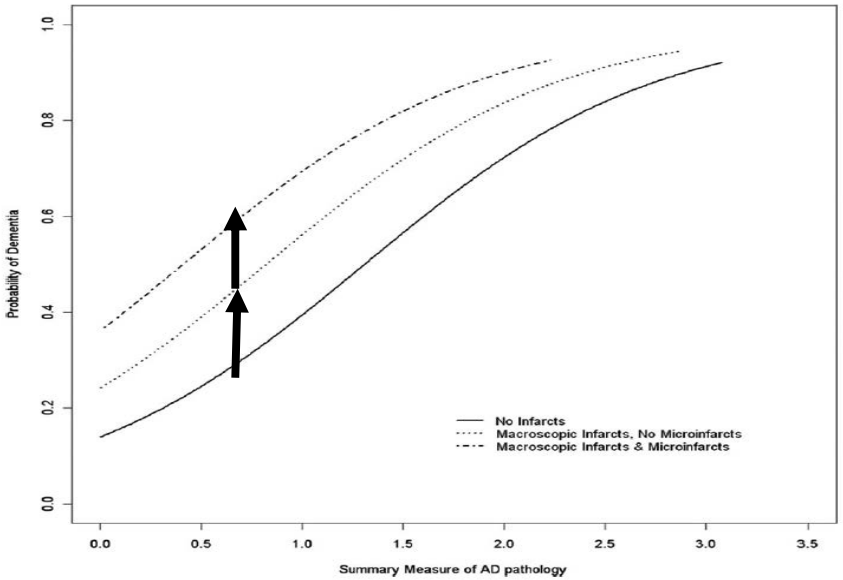
*Fig. Pathology by clinical status proximate to death. (*Blue shades*) Pathologic diagnosis of Alzheimer disease (AD). Clockwise: light blue = pathologic diagnosis of AD only; dark blue = pathologic diagnosis of AD and neocortical Lewy bodies (LB); medium blue = pathologic diagnosis of AD and cerebral infarcts (I); aqua = pathologic diagnosis of AD, I, and LB. (*Red shades*) I and/or LB (with no pathologic diagnosis of AD). Clockwise: pink = I or LB; red = I and LB. (*White*) No pathologic diagnosis of AD, no I, no LB.*

Schneider JA et al. *Ann Neurol* 2009;66:200–208.

Schneider JA et al. *Neurology* 2004;62:1148-1156.







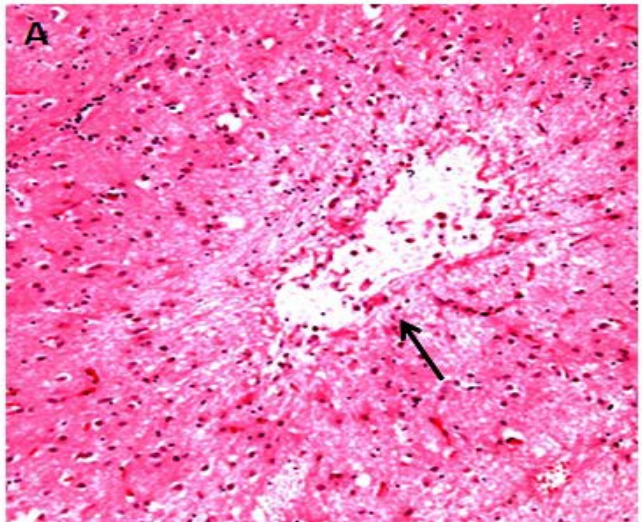


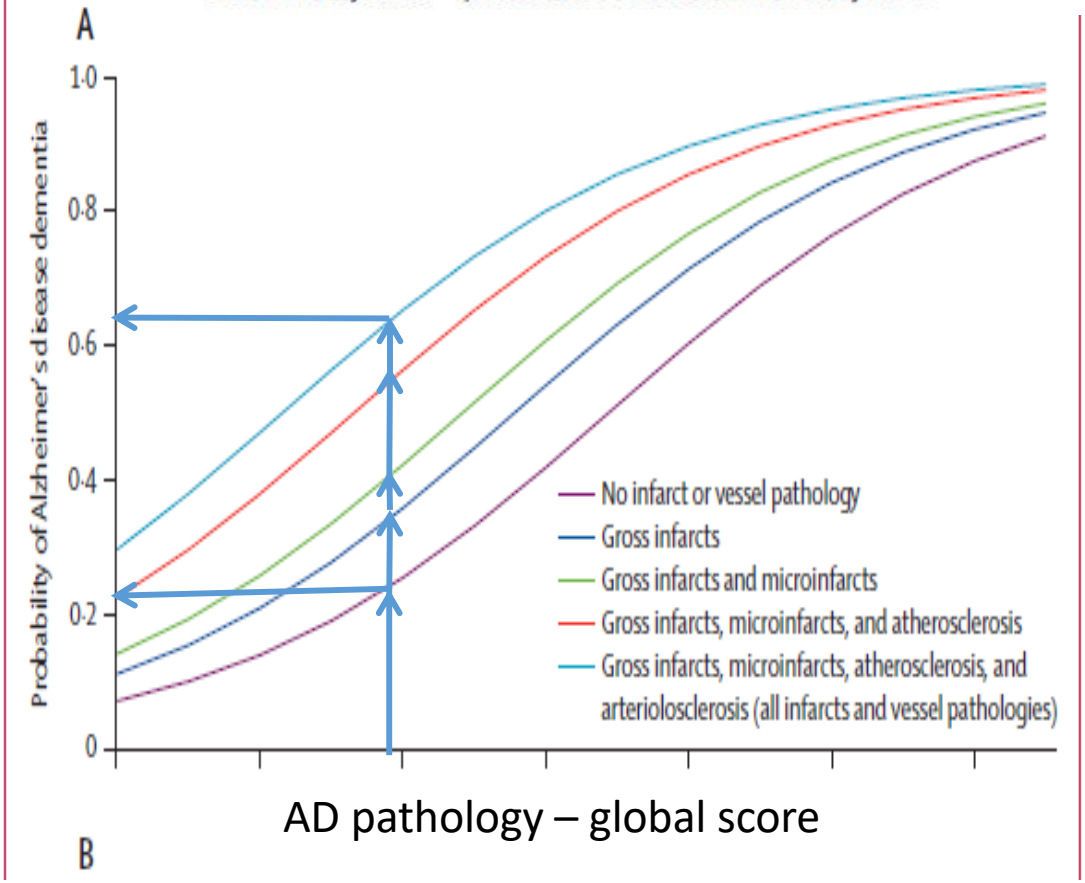
Figure 1. Probability of dementia by Alzheimer disease pathology showing additive effects of macroscopic infarcts and microinfarcts.

Arvanitakis Z, et.al. Stroke. 2011 Mar;42(3):722-7.

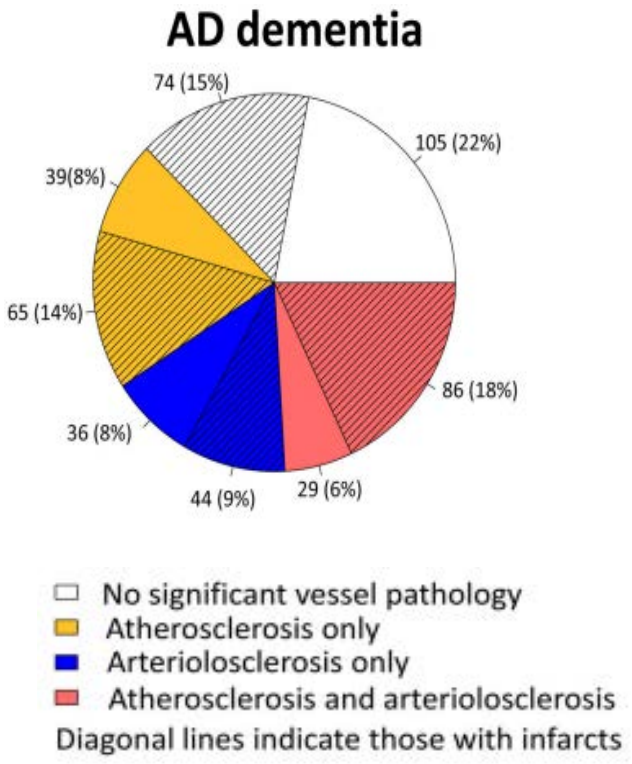
Published in final edited form as:
Lancet Neurol. 2016 August ; 15(9): 934–943. doi:10.1016/S1474-4422(16)30029-1.

Relation of Cerebral Vessel Disease to Alzheimer's Disease Dementia and Cognitive Function in Older Persons: A Cross-sectional Study

Zoe Arvanitakis, MD[1,2], Ana W. Capuano, PhD[1,2], Sue E. Leurgans, PhD[1,2], David A. Bennett, MD[1,2], and Julie A. Schneider, MD[1,2,3]



AD pathology – global score



Lewy Bodies - Pathology first decribed in Parkinson's disease

Lewy body Dementia

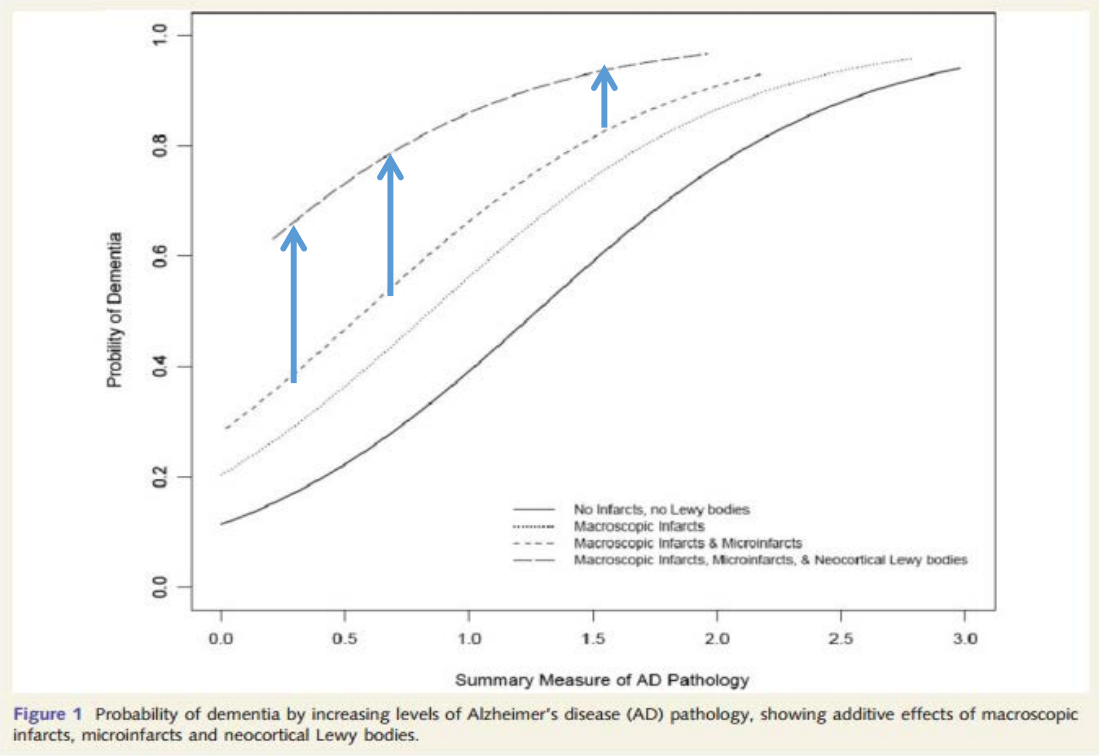
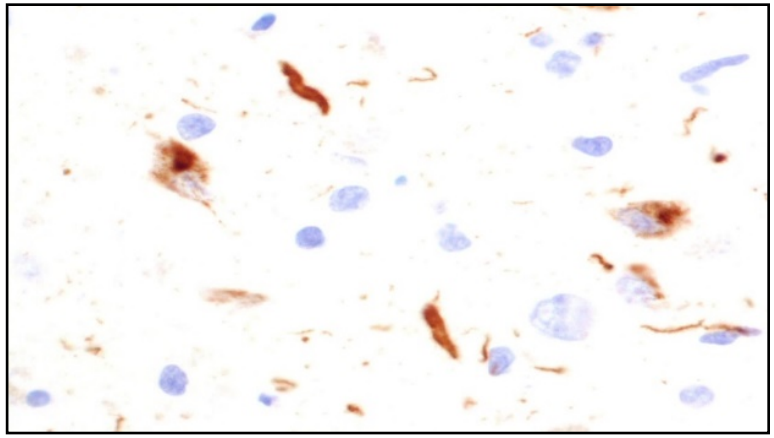


Figure 1 Probability of dementia by increasing levels of Alzheimer's disease (AD) pathology, showing additive effects of macroscopic infarcts, microinfarcts and neocortical Lewy bodies.

Schneider JA et al. Brain 2012;135:3005-3014

TDP-43 new “kid on the block” in aging and AD



ubiquinated protein in FTLD-U and ALS; 414 AA nuclear **DNA/RNA binding protein; regulates gene expression, splicing/stability of RNA transcripts**

- Related to amnestic dementia, mimics Alzheimer’s Dementia
- Commonly co-occurs with AD and lowers memory
- Strongly related to cognitive decline – especially memory
- Accumulation is associated with hippocampal degeneration and ultimately hippocampal sclerosis

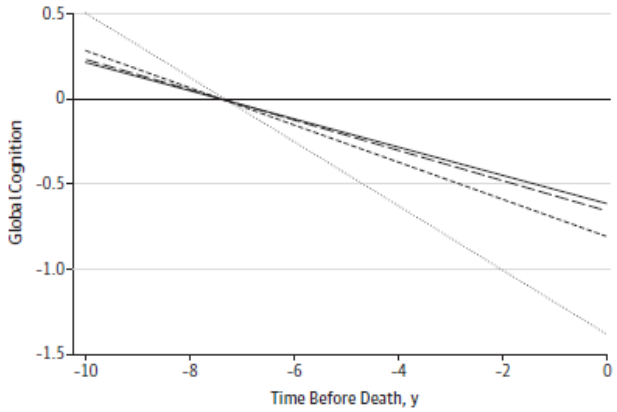
doi:10.1093/brain/awz099 BRAIN 2019: 0; 1–25 | 1

BRAIN
A JOURNAL OF NEUROLOGY

REVIEW

Limbic-predominant age-related TDP-43 encephalopathy (LATE): consensus working group report

Peter T. Nelson,[1] Dennis W. Dickson,[2] John Q. Trojanowski,[3] Clifford R. Jack Jr.,[4] Patricia A. Boyle,[5] Konstantinos Arfanakis,[5,6] Rosa Rademakers,[2] Irina Alafuzoff,[7] Johannes Attems,[8] Carol Brayne,[9] Ian T.S. Coyle-Gilchrist,[9] Helena C. Chui,[10] David W. Fardo,[1] Margaret E. Flanagan,[11] Glenda Halliday,[12] Suvi R.K. Hokkanen,[9] Sally Hunter,[9] Gregory A. Jicha,[1] Yuriko Katsumata,[1] Claudia H. Kawas,[13] C. Dirk Keene,[14] Gabor G. Kovacs,[15] Walter A. Kukull,[14] Allan I. Levey,[16] Nazanin Makkinejad,[6] Thomas J. Montine,[17] Shigeo Murayama,[18] Melissa E. Murray,[2] Sukriti Nag,[5] Robert A. Rissman,[19] William W. Seeley,[20] Reisa A. Sperling,[21] Charles L. White III,[22] Lei Yu[5] and Julie A. Schneider[5]



The top panel shows the individual rates of global cognitive decline, adjusted for age at death, plotted by level of TDP-43 pathology, and fitted with a locally reweighted linear smooth function. The bottom panel shows the 10-year paths of global cognitive decline in typical participants with no TDP-43 pathology (solid line) and with low (long dashes, 10th percentile), moderate (short dashes, 50th percentile), or high (dotted line, 90th percentile) levels of TDP-43 pathology, adjusted for age at death, amyloid, tangles, and hippocampal sclerosis.

Box 1 LATE and LATE-NC summary points

- LATE-NC features
  - A sampling and staging system for routine autopsy diagnosis is proposed to characterize the anatomical distribution of TDP-43 proteinopathy
    - Stage 1: amygdala only
    - Stage 2: + hippocampus
    - Stage 3: + middle frontal gyrus
  - Hippocampal sclerosis pathology may be observed (and should be reported), but is neither necessary nor sufficient for diagnosis of LATE-NC
- LATE-NC is present in >20% (up to 50%) of individuals past age 80 years according to large community-based autopsy series
- LATE is associated with substantial disease-specific cognitive impairment, usually an amnestic dementia syndrome ('dementia of the Alzheimer's type')
- The overall public health impact of LATE is on the same order of magnitude as Alzheimer's disease neuropathological changes; the diseases are often comorbid, but which pathology is more severe varies greatly between individuals
- Genetic risk factors for LATE have some overlap with FTLD-TDP and with Alzheimer's disease
- There is no molecule-specific biomarker for LATE. This is an important area of need for use in clinical trials (including as a potential exclusion criterion for Alzheimer's disease clinical trials) and longitudinal studies of the clinical and pathological progression of LATE

Wilson et al. JAMA Neurol. 2013;70(11):1418-1424

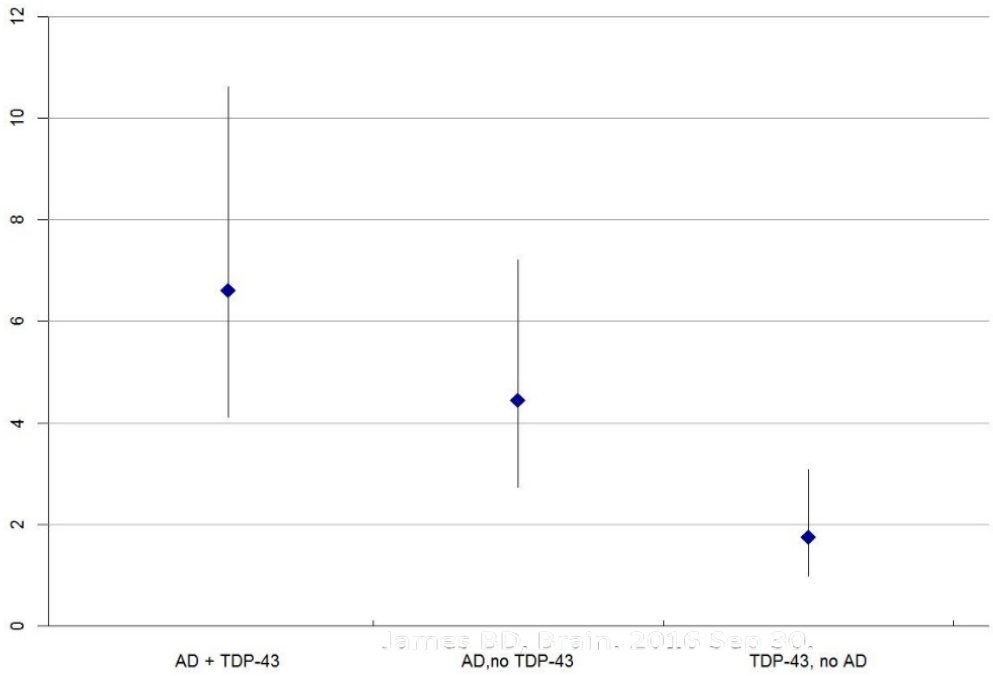
Figure 2. Odds ratios for clinical Alzheimer's-type dementia

~ 900 cases

N= 946 ROS/MAP
n=398 AD dementia
n= 548 no AD dementia

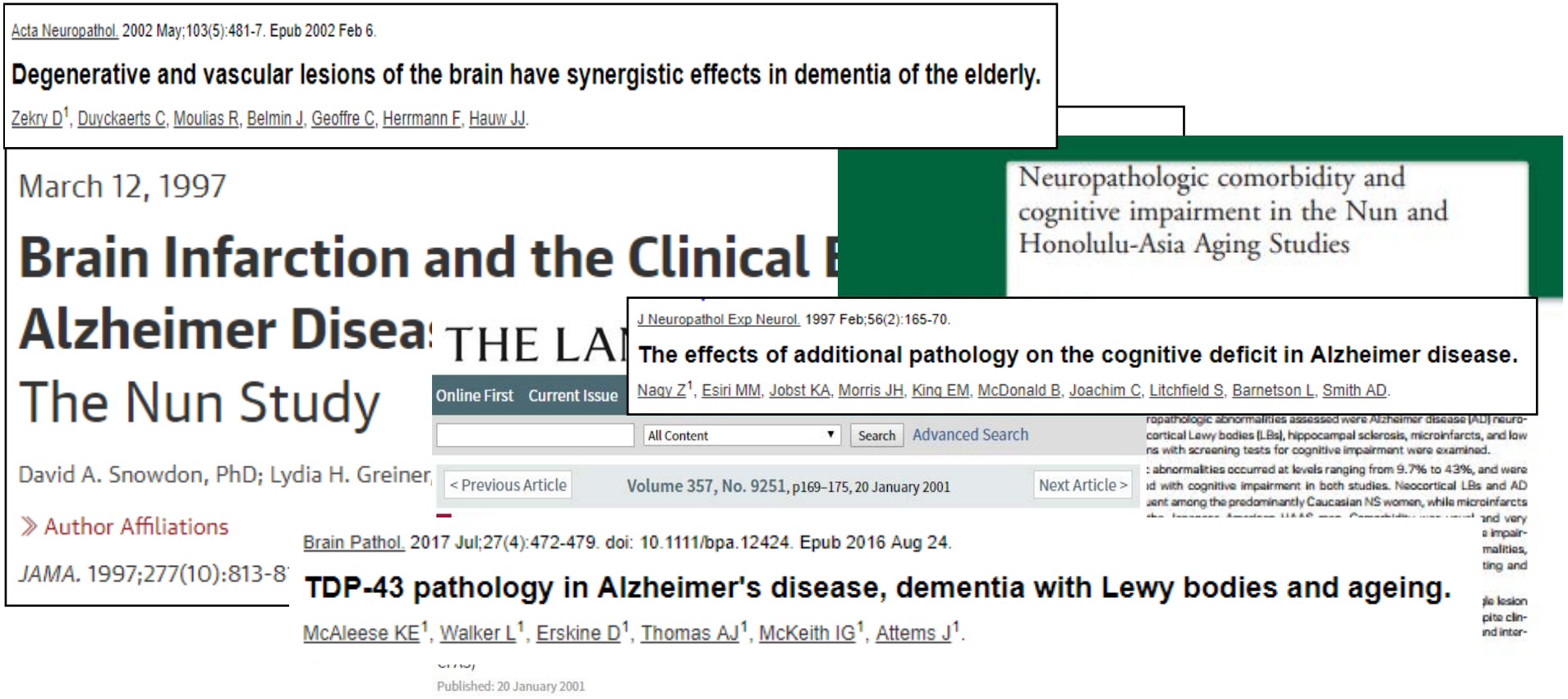
496 (52%) with TDP

% of mixed pathologies in clinical AD increased 60% to over 80% when considering TDP -43.



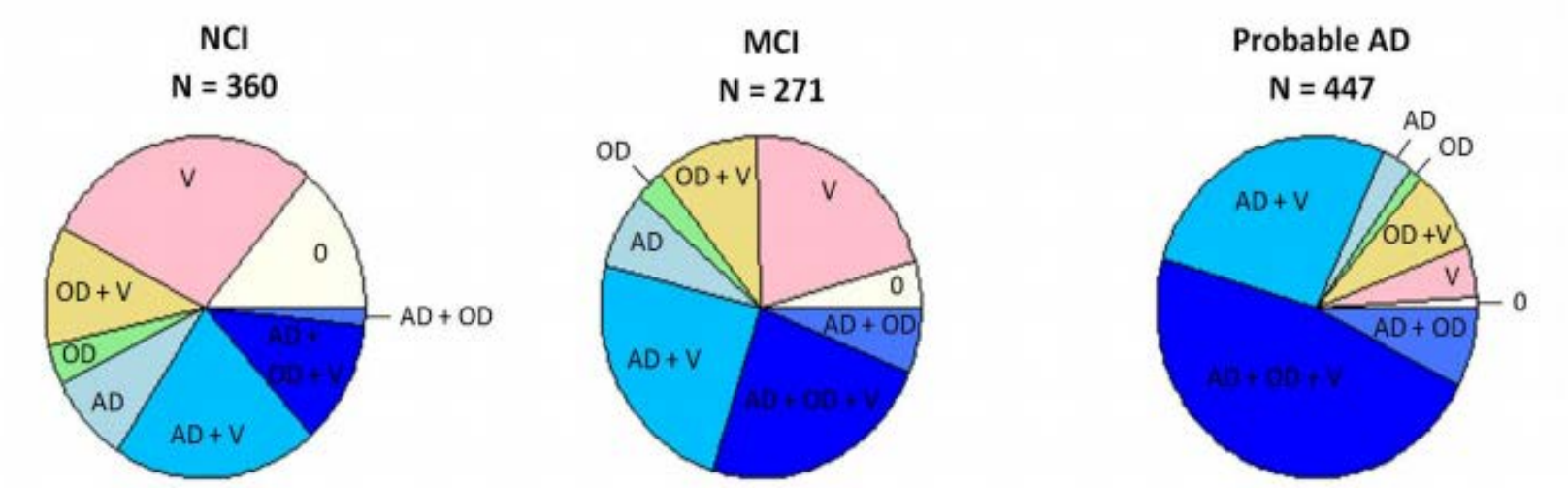
James BD, Brain. 2016 Sep 30.

Mixed pathologies published in multiple cohorts/populations/groups



UPDATE ON MIXED PATHOLOGIES INCLUDING NEW FINDINGS

	NCI	MCI	Probable AD
AD path diagnosis	**42.5%** 153/360	**61.2%** 166/271	**85%** 380/447
Pure AD path dx	**8.3%**	**7.4%**	**3.1%**
Mixed AD path + other Degenerative + vascular	**11.67%**	**23.62%**	**47.0%**



Kapasi A et al. Acta Neuropathologica 2017

Published in final edited form as:
Ann Neurol. 2018 January ; 83(1): 74–83. doi:10.1002/ana.25123.

Person-specific contribution of neuropathologies to cognitive loss in old age

Patricia A. Boyle[1,2], **Lei Yu**[1,3], **Robert S. Wilson**[1,2,3], **Sue E. Leurgans**[1,3], **Julie A. Schneider**[1,3,4], and **David A. Bennett**[1,3]

[1]Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, IL, USA

- AD most common pathology (65%)
- But AD occurred alone < 9%
- AD, TDP-43, and CAA most commonly co-morbid but depending on specific combination present in between 22 and 41 persons
- More than 230 combinations of pathology –
- most combinations in less than 20 persons

Top 10 most specific combinations of pathology

1. AD only;n=64; 5.9%

2. none of the 9; n=62; 5.8%

3. AD and CAA, n=41; 3.8%

4. AD +CAA+TDP, n=26; 2.4%

5. Gross infarcts, n=24; 2.2%

6. Atherosclerosis, n=22, 2.0%

7. AD +TDP, n= 18, 1.7%

8. TDP43, n= 17; 1.6%

9. AD + atherosclerosis, n=17; 1.6%,

10. Microinfarcts, n=16; 1.5%

236 combinations of pathology!

How much dementia could be averted by eliminating specific groups of pathology?

(Using logistic regression models that include age and pathologies with dementia as outcome)

Ann Neurol. 2019 Jan;85(1):114-124. doi: 10.1002/ana.25380. Epub 2018 Dec 19.

Attributable risk of Alzheimer's dementia attributed to age-related neuropathologies.

Boyle PA[1,2], Yu L[1,3], Leurgans SE[1,3], Wilson RS[1,2,3], Brookmeyer R[4], Schneider JA[1,3,5], Bennett DA[1,3].

Author information

1 Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, IL.

Pathologic AD - fraction averted 52%*

Lewy bodies, HS, and TDP……..36.8%

Infarcts, CAA, athero-, arteriolosclerosis……46.8%

* Cohort specific estimates/ not accounting for other pathologies

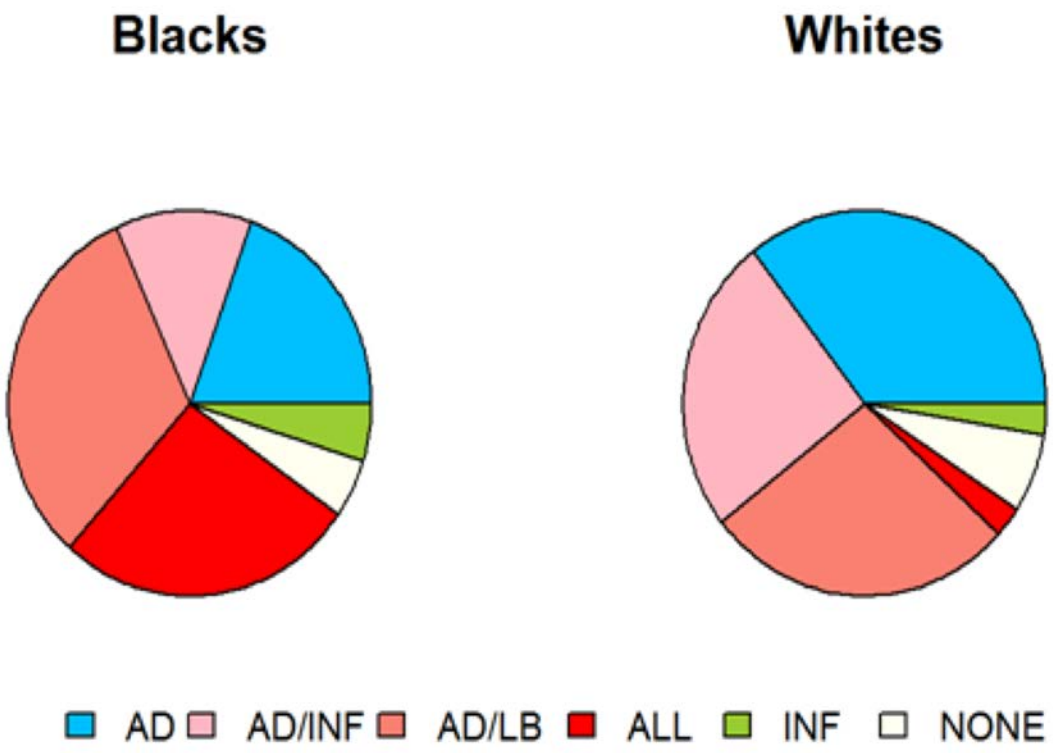
** Note numbers do not add up to 100 since there is inter-relationships between pathologies.

Pathology and dementia in the oldest old

(age 90+ vs. <90)

James BD et al., JAMA. 2012 May 2;307(17):1798-800.

Characteristic	Total (n=804)	Age 65-89 (n=503)	Age 90 + (n = 301)	P value
Age at death, yrs(SD)	87.7 (6.7)	83.8 (4.8)	94.3 (3.3)	<0.001
Dementia[a], no. (%)	304 (37.8%)	143 (28.4%)	161 (53.5%)	<0.001
AD[c]	493 (61.3%)	279 (55.5%)	214 (71.1%)	< 0.001
Infarcts[d]	272 (33.8%)	147 (29.2%)	125 (41.5%)	< 0.001
Single path	374 (46.5%)	238 (47.3%)	136 (45.2%)	0.56
Mixed path	225 (28.0%)	113 (22.5%)	112 (37.2%)	<0.001
AD + LB	41 (5.1%)	25 (5.0%)	16 (5.3%)	0.83
AD + Infarcts	162 (20.2%	79 (15.7%)	83 (27.6%)	<0.001



Barnes LL et al. Neurology 2015

What are we learning from the precious gift of brain donation from older persons?

- Alzheimer's disease pathology is often mixed with other pathologies (mixed pathology)
- Risk factors may work through increasing/decreasing pathology.
- Persons without cognitive impairment may have a lot of "subclinical" pathology
- There is pathologically unexplained cognitive change and risk factors

Multiple Potential Pathways to Dementia

Lifestyle Factors
- physical activity
- diet
- drug/alcohol abuse

Environmental Factors
- education
- head trauma
- toxins/other

Psychosocial Factors
- depression/anxiety

Aging

Genetic Factors

Sex F>M

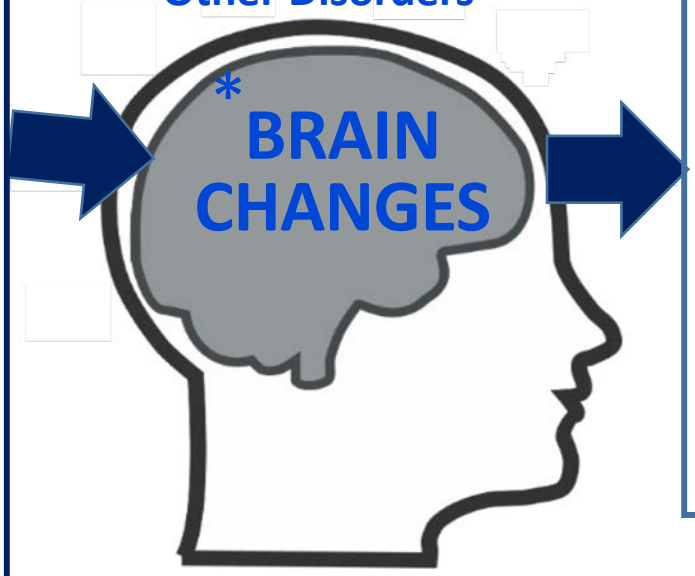
Other Medical Risks
- hypertension
- obesity
- stroke
- heart disease
- diabetes
- metabolic
- inflammation
- certain infectious diseases
- certain medications

Health Disparities Factors

***Misfolded proteins**
- amyloid
- tau
- alpha synuclein
- TDP-43

***Vascular Disorders**
- infarct (stroke)
- white matter disease
- blood vessel disease

***Other Disorders**



Cognitive Impairment Including Dementia

- Alzheimer's Dementia
- Lewy Body Dementias
- Vascular Dementias
- Frontotemporal Dementias
- Limbic Predominant TDP
- Mixed Dementias
- Other Cognitive Impairment
- Other Dementias

Concept by:
Julie A. Schneider, MD, MS, Rush University &
Roderick A. Corriveau, PhD, NINDS

NIH National Institute of Neurological Disorders and Stroke

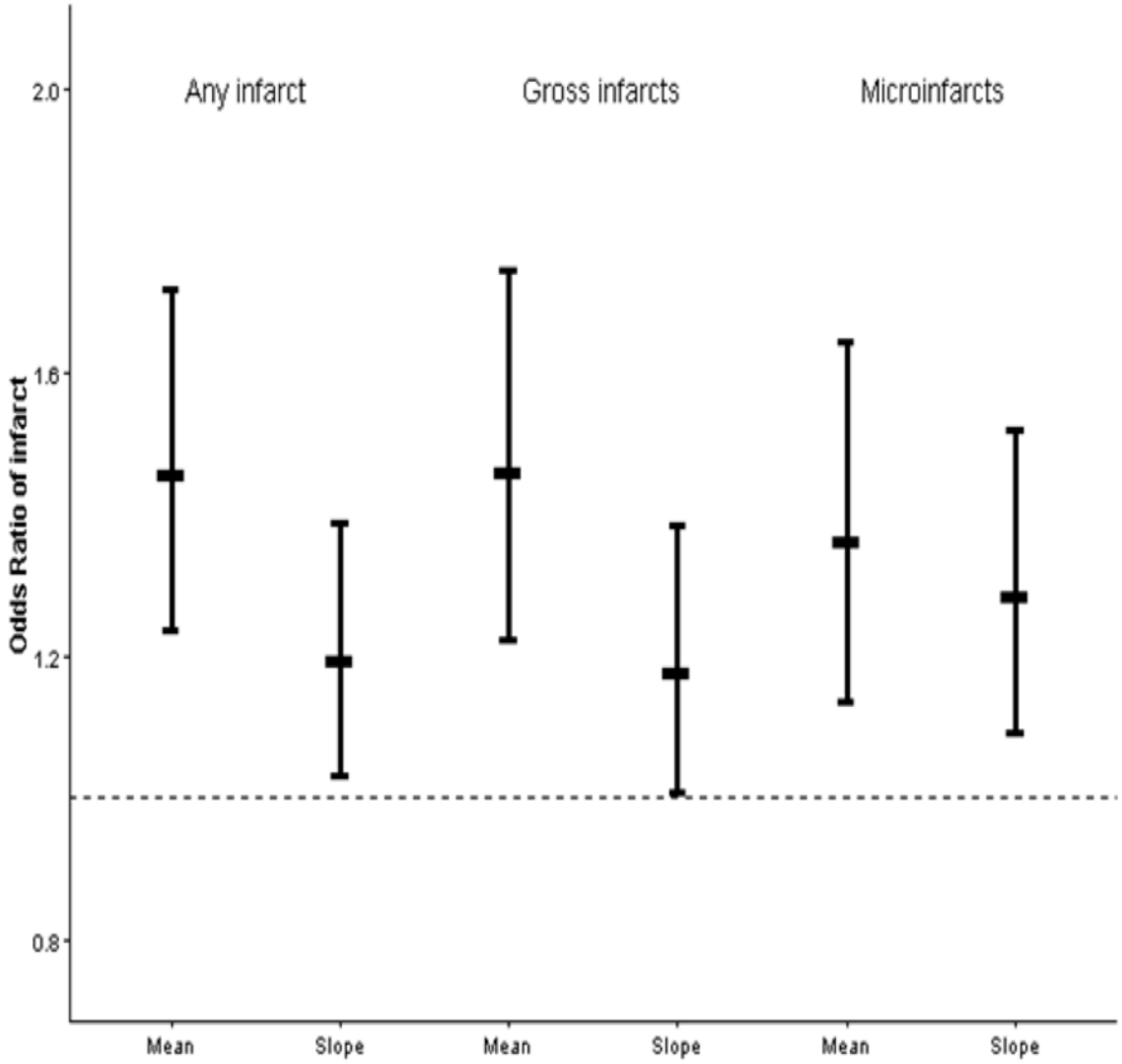
ARTICLE

Late-life blood pressure association with cerebrovascular and Alzheimer disease pathology

Zoe Arvanitakis, MD, Ana W. Capuano, PhD, Melissa Lama
David A. Bennett, MD, and Julie A. Schneider, MD

Neurology® 2018;91:e517-e525. doi:10.1212/WNL.000000

Elevated systolic blood pressure related to infarcts and tangles



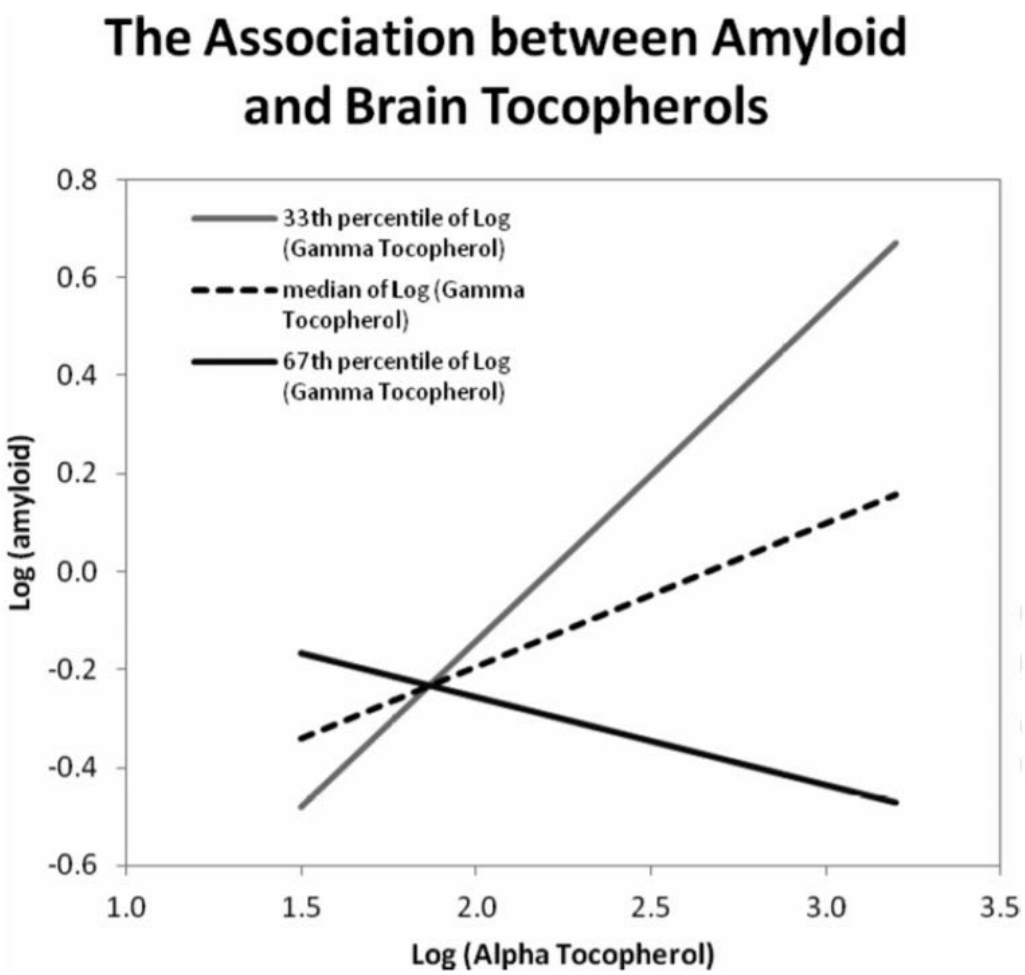
Published in final edited form as:
Alzheimers Dement. 2015 January ; 11(1): 32–39. doi:10.1016/j.jalz.2013.12.015.

Brain Tocopherols Related to Alzheimer Disease Neuropathology in Humans

Martha Clare Morris, Sc.D.[1], **Julie A Schneider, MD, MPH**[2,3], **Hong Li, MS**[1], **Christy C Tangney, PhD**[4], **Sukrit Nag, MD**[2,3], **David A Bennett, MD**[2], **William G. Honer, MD**[5], and **Lisa Barnes, PhD**[2]

Martha Clare Morris: Martha_C_Morris@rush.edu; Julie A Schneider: Julie_
76@gmail.com; Christy C Tangney: Christy_Tangney@rush.edu; Sukrit Na
David_A_Bennett@rush.edu; William G. Honer: honer@mail.ubc.ca; Lisa B

Vitamin E in the brain related to more vs. less amyloid depending on the type of tocopherol!



Stroke. Author manuscript, available in PMC 2016 Apr 1.
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Stroke. 2015 Apr; 46(4): 1071–1076.
doi: 10.1161/STROKEAHA.114.008010
PMCID: PMC4401202
NIHMSID: NIHMS663731
PMID: 25791714

Purpose in Life and Cerebral Infarcts in Community Dwelling Older Persons

Lei Yu, PhD,[1,2] Patricia A. Boyl
MD,[1,2,6] and David A. Bennett,

Author information Copy

Stroke. Author manuscript; available in PMC 2017 Feb 1.
Published in final edited form as:
Stroke. 2016 Feb; 47(2): 516–518.
Published online 2016 Jan 14. doi: 10.1161/STROKEAHA.115.011608
PMCID: PMC4780848
NIHMSID: NIHMS740250
PMID: 26768207

Sleep Fragmentation, Cerebral Arteriolosclerosis, and Brain Infarct Pathology in Community-Dwelling Older People

Andrew S.P. Lim, MD,[1,*] Lei Yu, PhD,[2] Julie A. Schneider, MD,[2,3] David A. Bennett, MD,[2] and Aron S. Buchman, MD[2]

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JAMA. 2016 February 02; 315(5): 489–497. doi:10.1001/jama.2015.19451.

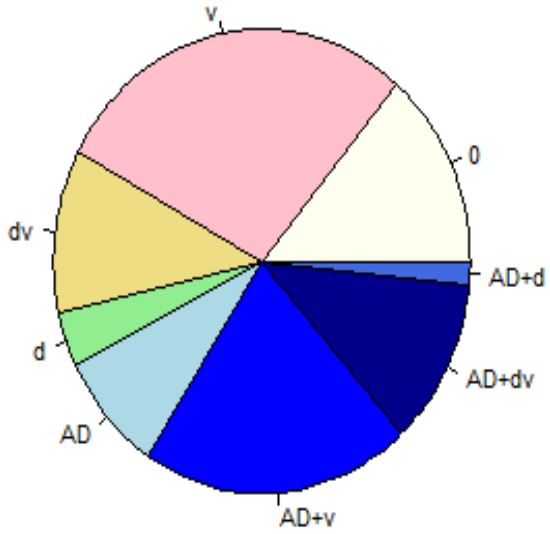
Association of Seafood Consumption, Brain Mercury Level, and *APOE ε4* Status With Brain Neuropathology in Older Adults

Martha Clare Morris, ScD,
Section on Nutrition and Nutritional Epidemiology, Department of Internal Medicine, Rush University Medical Center, Chicago, Illinois

What are we learning from the precious gift of brain donation from older persons?

- Alzheimer's pathology often mixed with other pathologies (mixed pathology)
- Risk factors and genetics may work through increasing pathology, resilience or unknown mechanisms.
- Persons without cognitive impairment may have a lot of subclinical pathology (resilience)
- There is a lot we still don't know about the brain changes of cognitive decline in aging.

Pathology in those without MCI or dementia



Pathology without cognitive impairment…

Lesser amounts of pathology

? Better repair mechanisms

? Less or “better” inflammation

? Compensation via other pathways

Published in final edited form as:
Neurology. 2006 November 14; 67(9): 1581–1585. doi:10.1212/01.wnl.0000242734.16663.09.

Memory complaints are related to Alzheimer disease pathology in older persons

L.L. Barnes, PhD, **J.A. Schneider, MD**, **P.A. Boyle, PhD**, **J.L. Bienias, ScD**, and **D.A. Bennett, MD**
Rush Alzheimer's Disease Center (L.L.B., J.A.S., P.A.B., D.A.B.) and Rush Institute for Healthy Aging (J.L.B.) and Departments of Neurological Sciences (L.L.B., J.A.S., D.A.B.), Internal Medicine (J.L.B.), and Behavioral Sciences (L.L.B., P.A.B.), Rush University Medical Center, Chicago, IL.

Published in final edited form as:
Ann Neurol. 2018 April ; 83(4): 718–729. doi:10.1002/ana.25189.

Memory Complaints, Dementia, and Neuropathology in Older Blacks and Whites

Zoe Arvanitakis, MD, MS[a,b], Sue E. Leurgans, PhD[a,b], Debra A. Fleischman, PhD[a,b,c], Julie A. Schneider, MD, MS[a,b,d], Kumar B. Rajan, PhD[e], Jeremy J. Pruzin, MD[a,b], Raj C. Shah, MD[a,f], Denis A. Evans, MD[e], Lisa L. Barnes, PhD[a,b,c], and **David A. Bennett, MD[a,b]**

Ann N Y Acad Sci. 2009 Jul;1170:730-5. doi: 10.1111/j.1749-6632.2009.04013.x.

Olfactory impairment in presymptomatic Alzheimer's disease.

Wilson RS[1], Arnold SE, Schneider JA, Boyle PA, Buchman AS, Bennett DA.

J Elder Abuse Negl. Author manuscript; available in PMC 2015 Jan 1.
Published in final edited form as:
J Elder Abuse Negl. 2014; 26(2): 107–122.
doi: 10.1080/08946566.2013.821809

PMCID: PMC3916958
NIHMSID: NIHMS509695
PMID: 24499279

Correlates of Susceptibility to Scams in Older Adults Without Dementia

Bryan D. James, PhD, Assistant professor,[1,2] Patricia A. Boyle, PhD, Associate professor,[1,3] and David A. Bennett, MD, Professor and Director[1,4]

Ann Intern Med. 2019 May 21;170(10):702-709. doi: 10.7326/M18-2711. Epub 2019 Apr 16.

Scam Awareness Related to Incident Alzheimer Dementia and Mild Cognitive Impairment: A Prospective Cohort Study.

Boyle PA[1], Yu L[1], Schneider JA[1], Wilson RS[1], Bennett DA[1].

Author information

1 Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, Illinois (P.A.B., L.Y., J.A.S., R.S.W., D.A.B.).

HEALTH

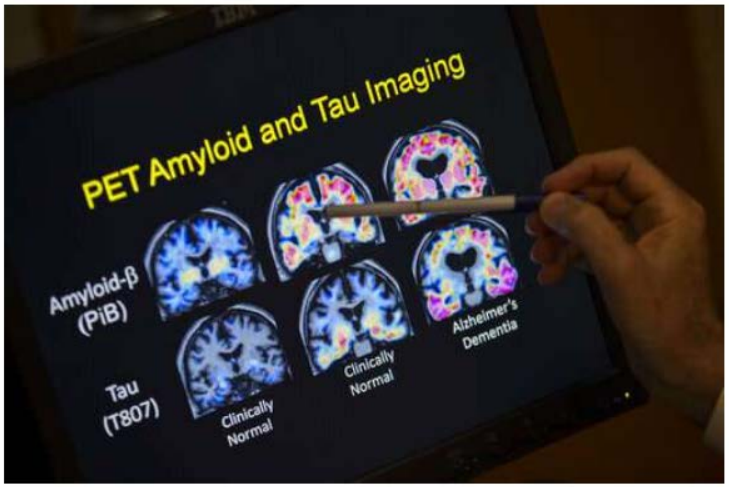
ALZHEIMER'S EARLY WARNING: FALLING FOR SCAMS COULD BE SIGN OF DEMENTIA

BY KASHMIRA GANDER ON 4/15/19 AT 5:00 PM EDT

APRIL 16, 2019

Senior's weakness for scams may be warning sign of dementia

by Lauran Neergaard



In this May 19, 2015, file photo, a doctor points to PET scan results that are part of a study o...

Does an older friend or relative have a hard time hanging up on telemarketers? Or get excited about a "You've won a prize" voicemail? New research suggests seniors who aren't on guard against scams also might be at risk for eventually developing Alzheimer's disease.

What are we learning from the precious gift of brain donation from older persons?

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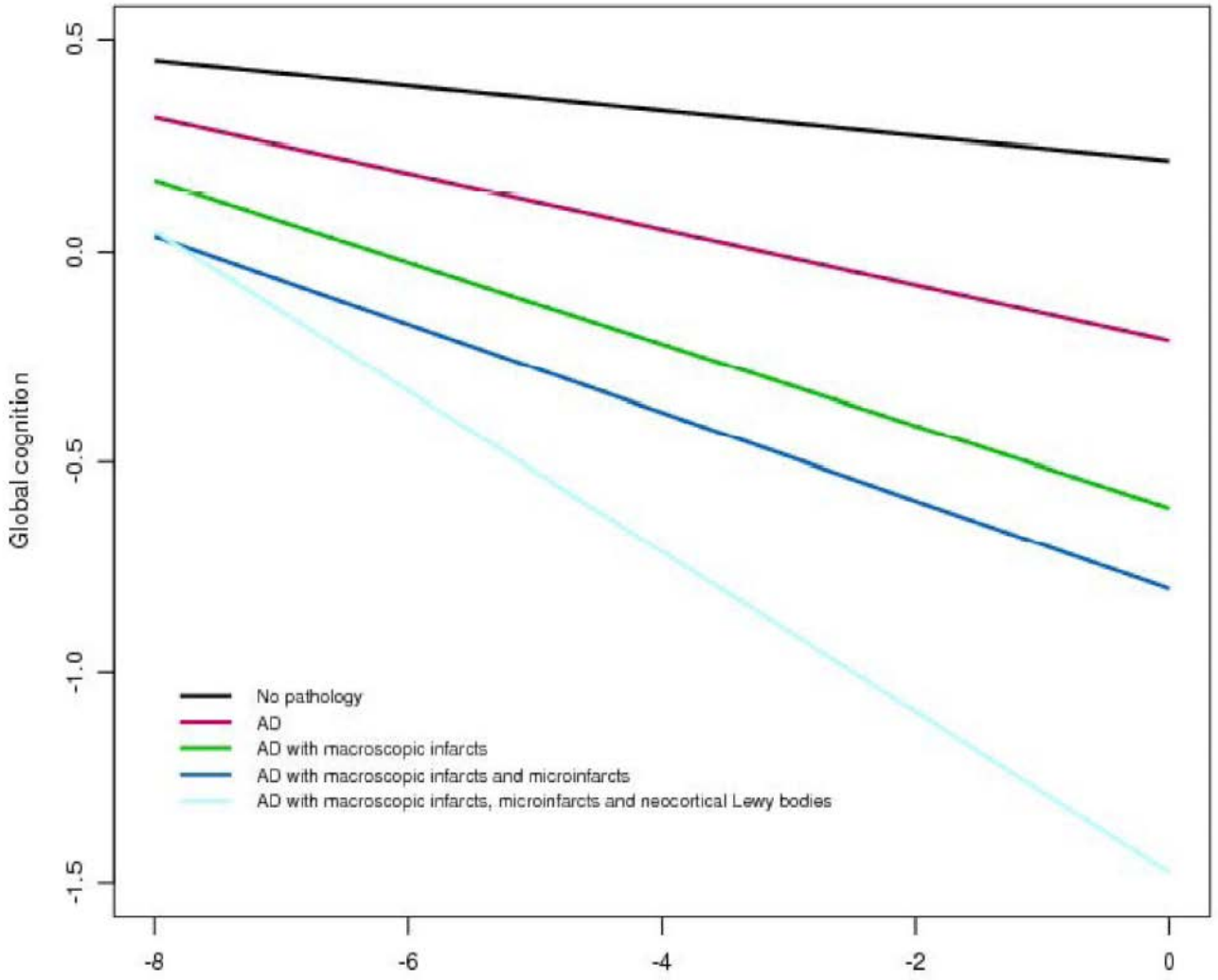
- Persons without cognitive impairment may have a lot of subclinical pathology (resilience)
- There is a lot we still don't know about the brain changes of cognitive decline in aging.


Global cognition
0.5
0.0
-0.5
-1.0
-1.5
-8
-6
-4
-2
0
No pathology
AD
AD with macroscopic infarcts
AD with macroscopic infarcts and microinfarcts
AD with macroscopic infarcts, microinfarcts and neocortical Lewy bodies

Published in final edited form as:
Ann Neurol. 2013 September ; 74(3): . doi:10.1002/ana.23964.

Much of late life cognitive decline is not due to common neurodegenerative pathologies

Patricia A. Boyle, PhD[1,2], **Robert S. Wilson, PhD**[1,2,3], **Lei Yu, PhD**[1,3], **Alasdair M Barr, PhD**[4], **William G. Honer, M.D.**[5], **Julie A. Schneider, MD**[1,3,6], and **David A. Bennett, MD**[1,3]
[1]Rush Alzheimer's Disease Center, Rush University Medical Center

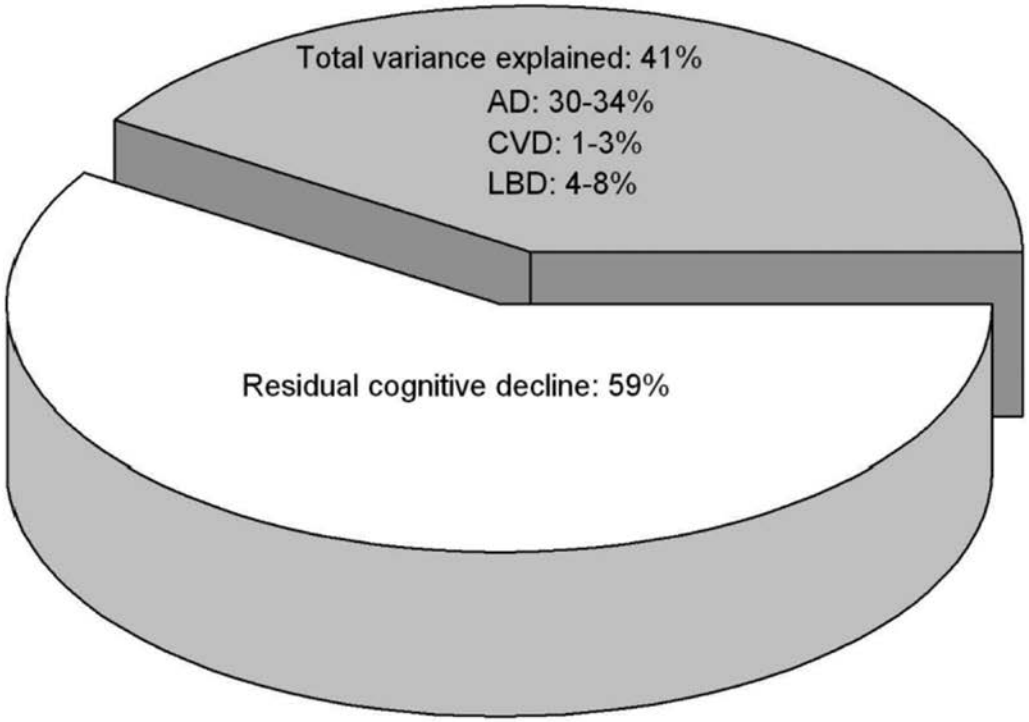


Figure 3.
Variation in cognitive decline explained by the pathologic indices (grey) and the residual, unexplained variation in cognitive decline (white) derived from fully adjusted models.

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Neuropsychology. 2016 February ; 30(2): 135–142. doi:10.1037/neu0000223.

Late-Life Depression is Not Associated with Dementia Related Pathology

Robert S. Wilson, PhD, **Patricia A. Boyle, PhD**, **Ana W. Capuano, PhD**, **Raj C. Shah, MD**, **George M. Hoganson, MD**, **Sukriti Nag, MD, PhD**, and **David A. Bennett, MD**
Rush University Medical Center

J Affect Disord. 2019 May 1;250:313-318. doi: 10.1016/j.jad.2019.03.051. Epub 2019 Mar 8.

Brain IGFBP-5 modifies the relation of depressive symptoms to decline in cognition in older persons.

Capuano AW[1], Wilson RS[2], Honer WG[3], Petyuk VA[4], Leurgans SE[5], Yu L[5], Gatchel JR[6], Arnold S[7], Bennett DA[5], Arvanitakis Z[5].

Author information

1 Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, IL, USA; Department of Neurological Sciences, Rush University Medical Center, Chicago, IL, USA. Electronic address: ana_capuano@rush.edu.

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Am J Geriatr Psychiatry. 2011 April ; 19(4): 327–334. doi:10.1097/JGP.0b013e31820119da.

Vulnerability to Stress, Anxiety, and Development of Dementia in Old Age

Robert S. Wilson, PhD, **Christopher T. Begeny, BA**, **Patricia A. Boyle, PhD**, **Julie A. Schneider, MD**, and **David A. Bennett, MD**
Rush Alzheimer's Disease Center and Departments of Neurological Sciences (RSW, JAS, DAB), Behavioral Sciences (RSW, PAB), and Pathology (JAS), Rush University Medical Center, Chicago, IL, USA

Published in final edited form as:
Neurobiol Aging. 2013 April ; 34(4): 1045–1050. doi:10.1016/j.neurobiolaging.2012.08.008.

Personality and resilience to Alzheimer's disease neuropathology: A prospective autopsy study

Antonio Terracciano, PhD[1,4,*], **Diego Iacono, MD PhD**[2,5,*], **Richard J O'Brien, MD PhD**[3], **Juan C Troncoso, MD**[2,3], **Yang An, MS**[1], **Angelina R Sutin, PhD**[1,4], **Luigi Ferrucci, MD PhD**[1], **Alan B Zonderman, PhD**[1], and **Susan M Resnick, PhD**[1]

[1]National Institute on Aging, National Institutes of Health

[2]Division of Neuropathology, Johns Hopkins University

[3]Department of Neurology, Johns Hopkins University

[4]College of Medicine, Florida State University, Tallahassee, FL, USA

[5]The Brain Bank at Karolinska Institutet, Department of Neurobiology, Care Sciences and Society (NVS), Stockolm, Sweden.

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Association of Seafood Consumption, Brain Mercury Level, and *APOE ε4* Status With Brain Neuropathology in Older Adults

Martha Clare Morris, ScD,

Section on Nutrition and Nutritional Epidemiology, Department of Internal Medicine, Rush University Medical Center, Chicago, Illinois

Brain iron is associated with accelerated cognitive decline in people with Alzheimer pathology

Scott Ayton[1], **Yamin Wang**[2], **Ibrahima Diouf**[1,3], **Julie A Schneider**[4], **John Brockman**[5], **Martha Clare Morris**[2,*,#], **Ashley I. Bush**[1,*,#]

[1]Melbourne Dementia Research Centre, Florey Institute of Neuroscience and Mental Health, and The University of Melbourne, Parkville, Australia

[2]Rush Institute for Healthy Aging, Rush University Medical Center, Chicago, USA

[3]CSIRO Health and Biosecurity, Australian E-Health Research Centre, Brisbane, Australia

[4]Rush Alzheimer Disease Center, Rush University Medical Center, Chicago, USA

[5]Missouri University Research Reactor, Columbia (Brockman), USA

ARTICLE

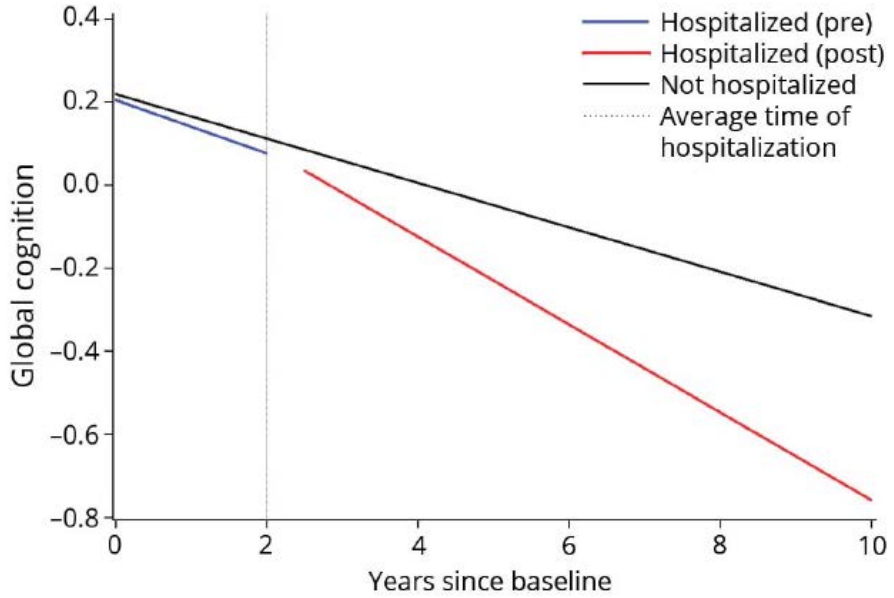
Cognitive decline after elective and nonelective hospitalizations in older adults

Bryan D. James, PhD, Robert S. Wilson, PhD, Ana W. Capuano, PhD, Patricia A. Boyle, PhD, Raj C. Shah, MD, Melissa Lamar, PhD, E. Wesley Ely, MD, David A. Bennett, MD, and Julie A. Schneider, MD

Correspondence
Dr. James
Bryan_James@rush.edu

Neurology® 2019;92:1-10. doi:10.1212/WNL.0000000000006918

Figure 2 Rate of decline in global cognition in those who had hospitalization (before and after) or no hospitalization



Conclusions

- Alzheimer's dementia is a complex brain disease with many potential therapeutic targets.
- There are a multitude of risk and protective factors. A better understanding of these is important. For now vascular risk factors important to control.
- Persons without cognitive impairment may have a lot of "subclinical" pathology. Important to recognize but also opportunity for prevention/treatment.
- Pathologically unexplained cognitive change and related risk factors also an opportunity for new prevention and treatment strategies.

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Rush Alzheimer's Disease Center

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Debra Fleischman, PhD
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Crystal Glover, PhD
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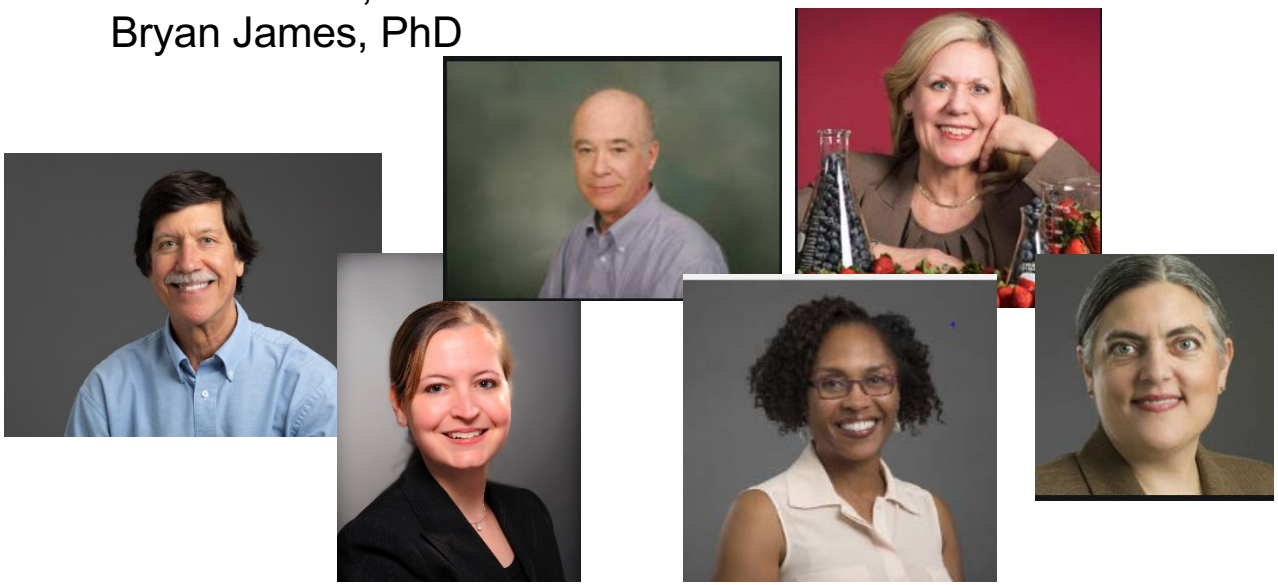
Namhee Kim, PhD
Melissa Lamar PhD
Sue Leurgans, PhD
Sukriti Nag, MD, PhD
Shahram Oveisgharan, MD
Raj Shah, MD
Shinya Tasaki, PhD
Jingyun Yang, PhD
Lei Yu, PhD
Robert Wilson, PhD



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