SANDERS-BROWN CENTER ON AGING

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Subjective Memory Complaint in Aging: Neuropathological Associations

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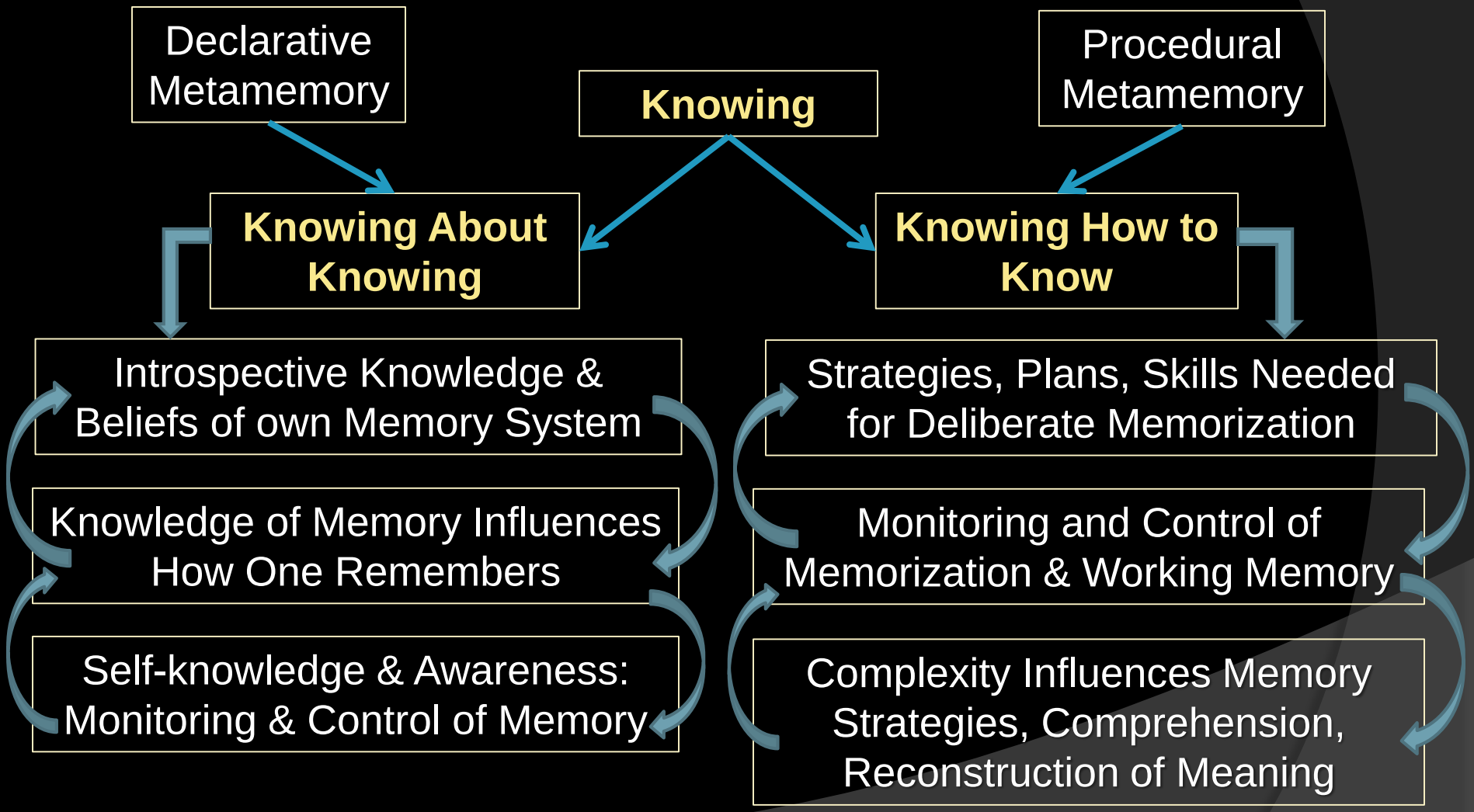
Wien Center for Alzheimer's Disease and Memory Disorders, Mount Sinai Medical Center 14th Mild Cognitive Impairment Symposium January, 2016

Prodromal / Preclinical AD

- **Memory complaints by patient or family**
- Progressive onset
- Normal or mildly impaired complex ADLs
- Amnestic syndrome of the ‘hippocampal type’
- Persistence of memory impairment at a subsequent assessment
- Absence of fully developed syndrome of dementia
- Exclusion of other disorders that may cause MCI (e.g., neuroimaging & biomarkers)

Metamemory



cf., Brown, 1975; Tarricone, 2011

Person Metamemory

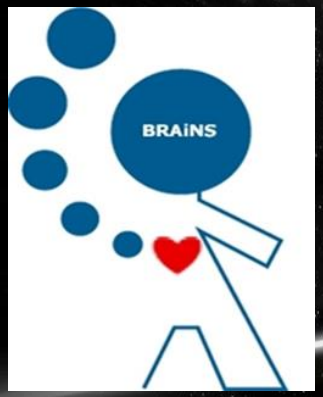
- Knowledge of memory relevant attributes or abilities
- Mnemonic self concept - accurate understanding or knowledge about memory abilities
  - Includes beliefs about one's own memory
- Knowledge of enduring mnemonic qualities, capabilities and limitations

cf., Flavell, 1977; Tarricone, 2011

SMC: Subjective Memory Complaint

- **Have you noticed a change in your memory since the last visit?**
- "YES" response implies a state called SMC
  - 55.7% answered "YES" on average 8.3 yrs. after study entry
- Determine risk factors associated with transitions into impaired states
- Assess neuropathology examinations for the 243 participants who came to autopsy

Awareness of Memory Changes: Subjective Memory Complaint



NIA: P30AG028383

Statistical Modeling of Aging and Risk of Transitions

SMART

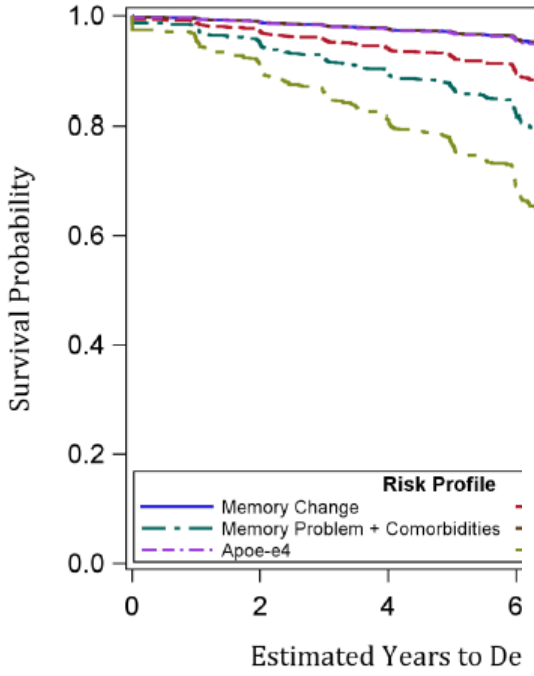
NIA: R01AG038651

PREADVISE
ALZHEIMER'S DISEASE PREVENTION STUDY
Prevention of Alzheimer's Disease by Vitamin E and Selenium
UK Sanders-Brown Center on Aging
UK UNIVERSITY OF KENTUCKY Chandler Medical Center

NIA: R01AG019241

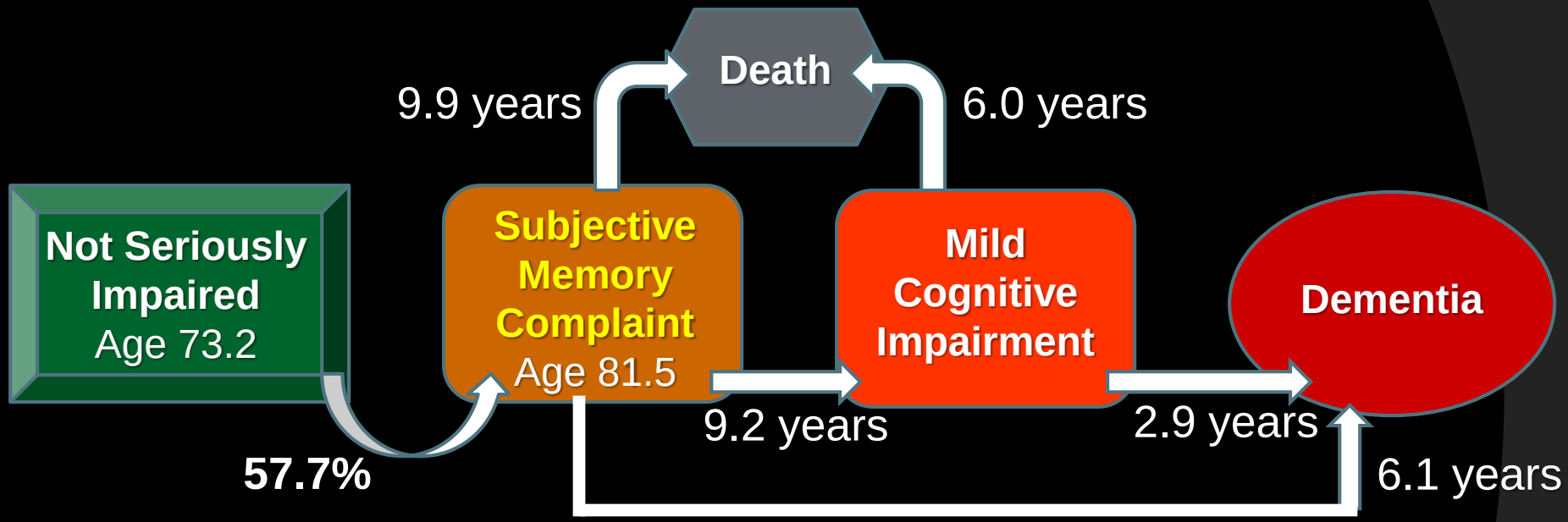
Kryscio et al., *Neurology*, 2014; *J Prev Alzheimers Disease*, in press; Abner et al., *J Prev Alzheimers Disease, 2015*

SMC & Incident Dementia (PREADViSE)



Comparison	Main Effects Model Adjusted HR (95% CI)	Interaction Model Adjusted HR (95% CI)
Memory Change vs. No Complaint	**1.87 (1.47–2.38)**	
Memory Problem vs. No Complaint	**6.01 (3.68–9.74)**	
Memory Change vs. No Complaint (Black = Y)		**2.46 (1.15–5.27)**
Memory Problem vs. No Complaint (Black = Y)		**35.7 (12.99–100.0)**
Memory Change vs. No Complaint (Black = N)		**1.81 (1.41–2.33)**
Memory Problem vs. No Complaint (Black = N)		**4.50 (2.55–7.94)**
Baseline age, 1 year	**1.11 (1.09–1.13)**	**1.11 (1.09–1.13)**
Black vs. not black race	**1.86 (1.28–2.70)**	
Education, 1 year	0.97 (0.93–1.01)	0.97 (0.93–1.01)
APOE-ε4 carrier vs. not	**1.91 (1.52–2.41)**	**1.88 (1.49–2.38)**
Diabetes vs. none	1.07 (0.75–1.51)	1.08 (0.76–1.53)
Hypertension vs. none	0.91 (0.72–1.16)	0.91 (0.72–1.15)
Sleep apnea vs. none	1.34 (0.91–1.99)	1.34 (0.90–1.99)
Head injury vs. none	**1.39 (1.03–1.88)**	**1.36 (1.01–1.85)**

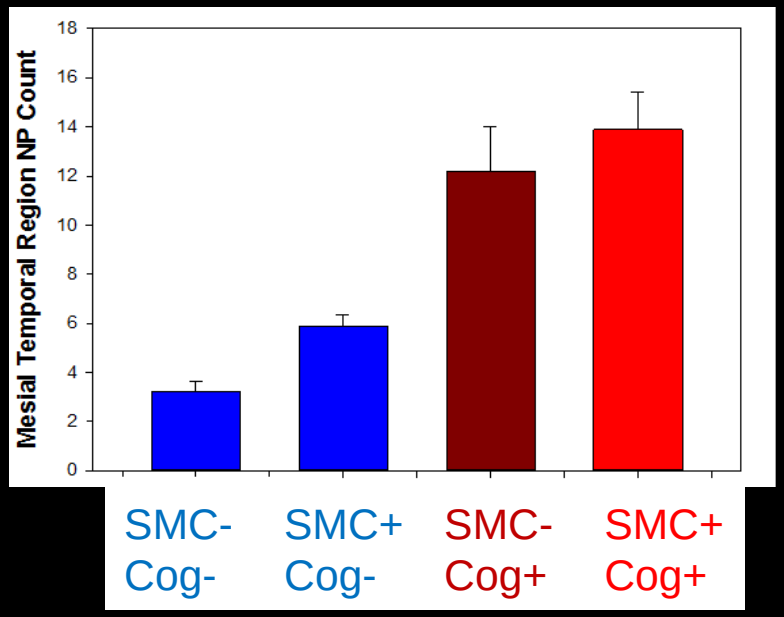
SMC, Risk Factors & Progression

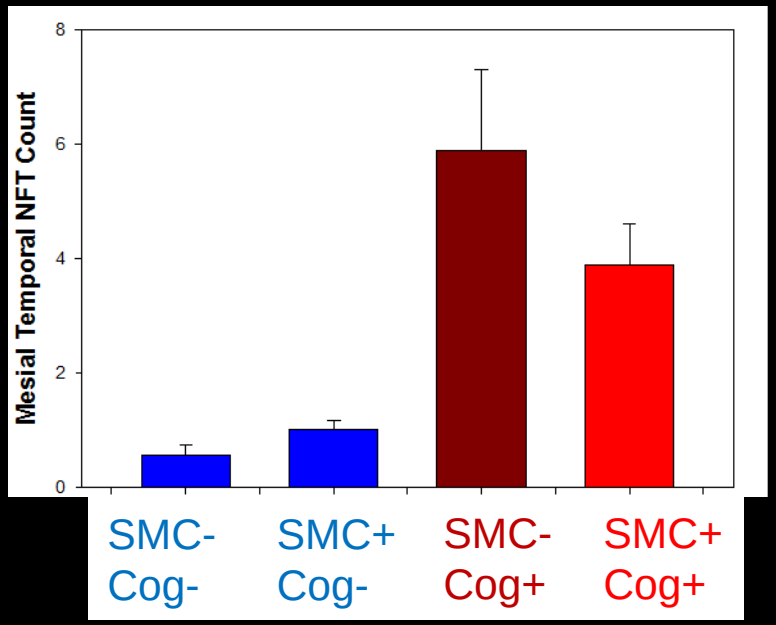


- Positive dementia family history & overweight decrease time to SMC by 2 years
- Smoking history reduces time from SMC to MCI by 3 years
- ApoE4+ doubles risk of an event once in SMC
- Baseline HTN & female gender promote SMC to dementia

Neuropathology, SMC & Conversions to MCI / Dementia

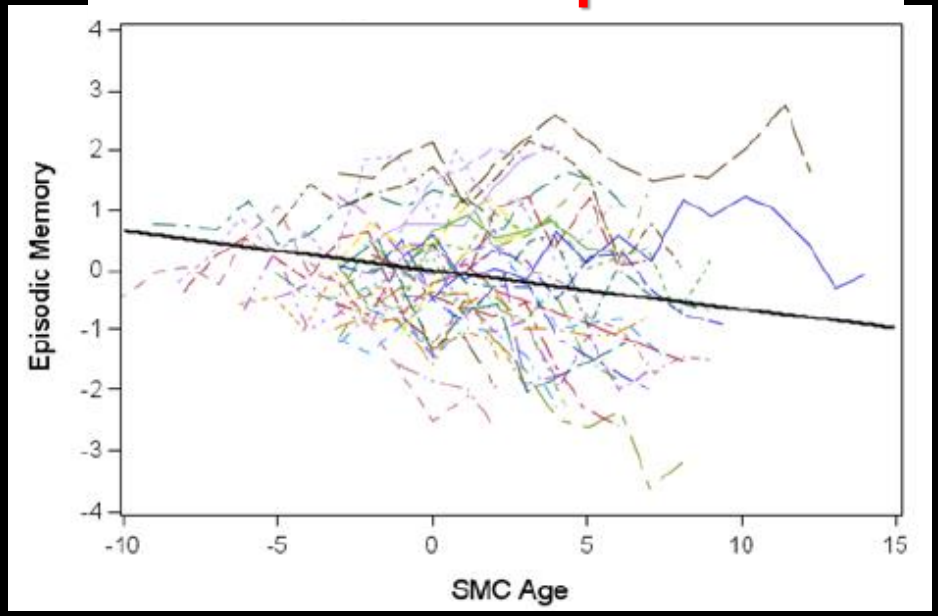
SMC?	MCI or dementia?	Number of Autopsies	Neuritic Plaques	NFT
No	No	56	Low	Low
Yes	No	120	Moderate*	Moderate*
Yes	Yes	50	High**	High**





Memory Trajectories in SMC

SMC+ With Impairment



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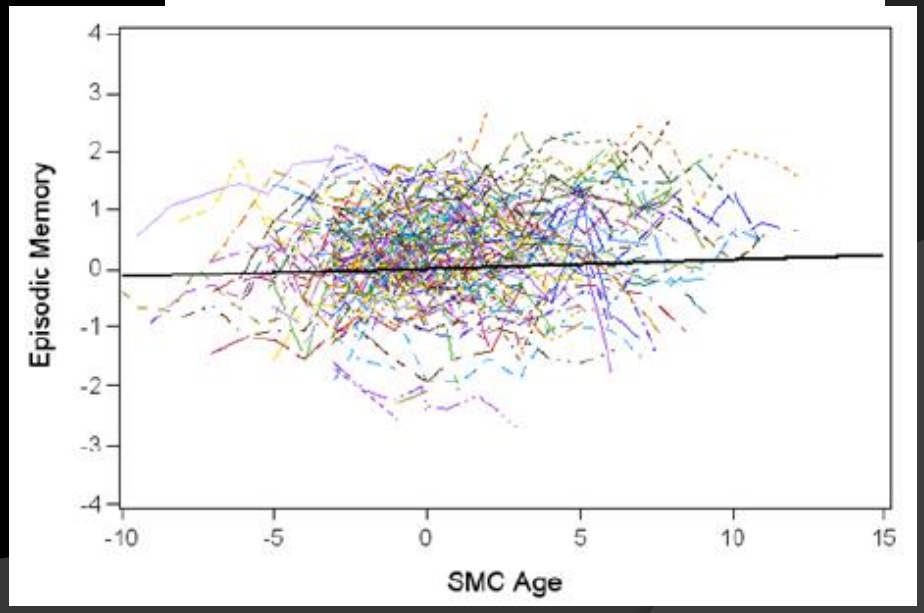
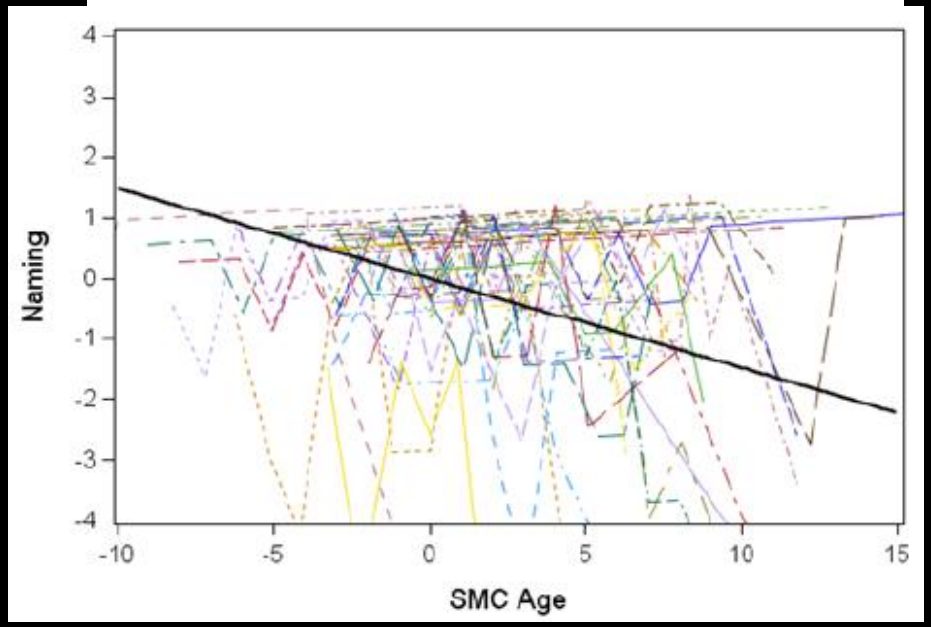
SMC+ No Impairment



Naming Trajectories in SMC

SMC+ With Impairment



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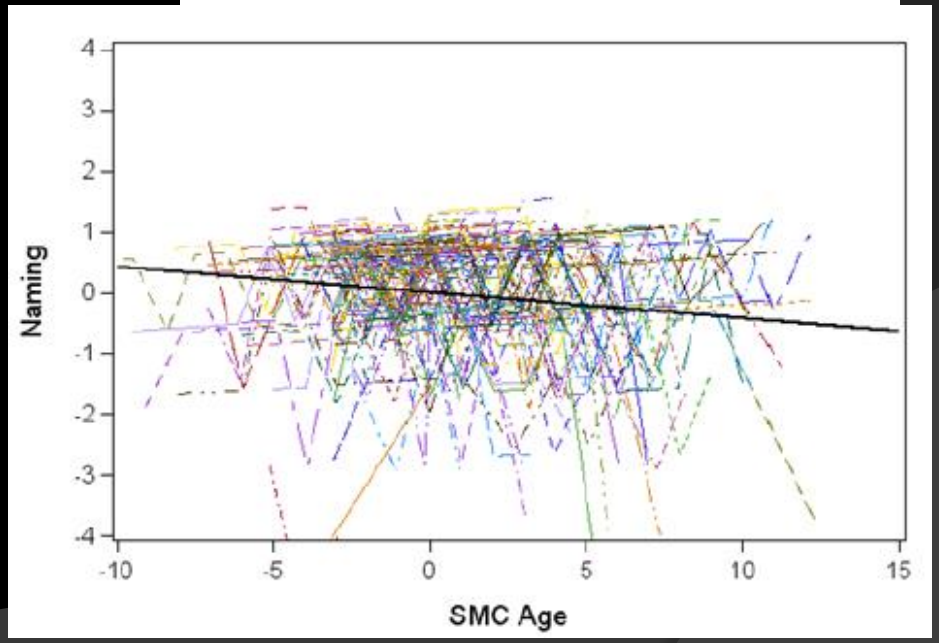
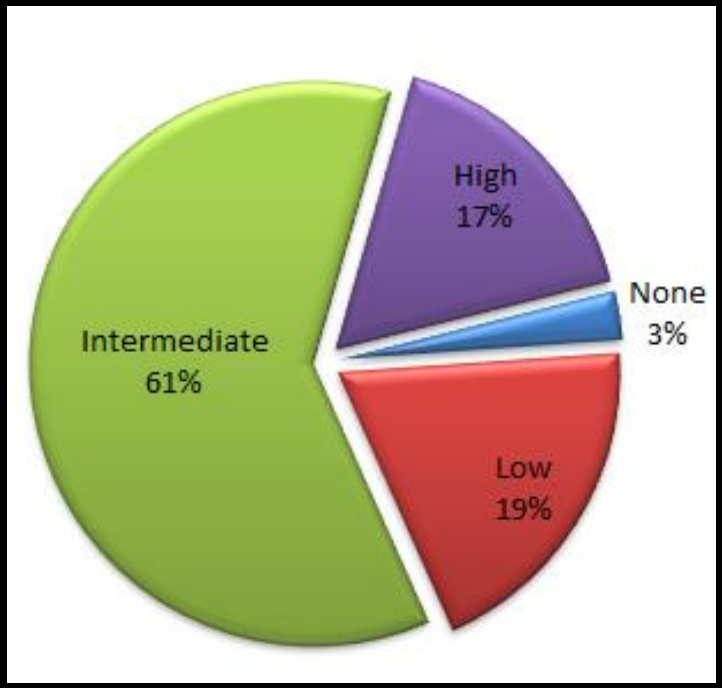
SMC+ No Impairment

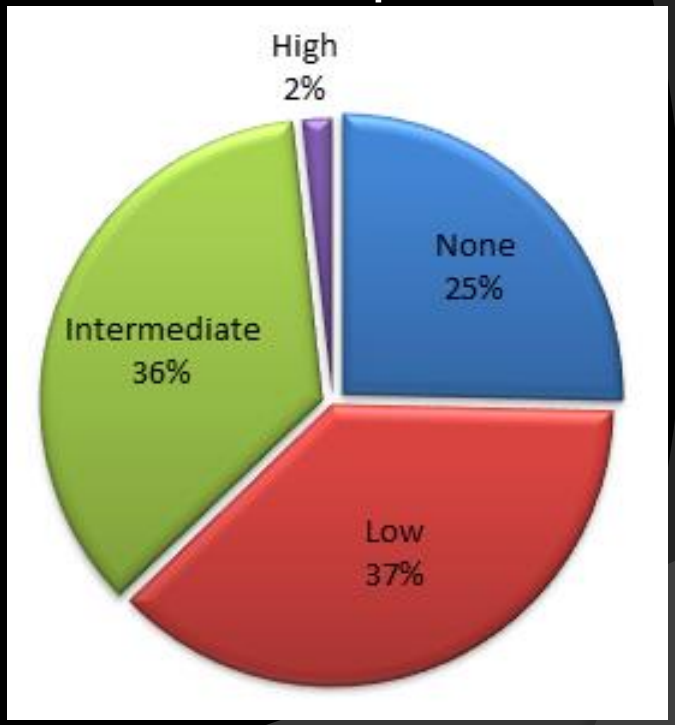


AD Pathologies in SMC

SMC with Impairment



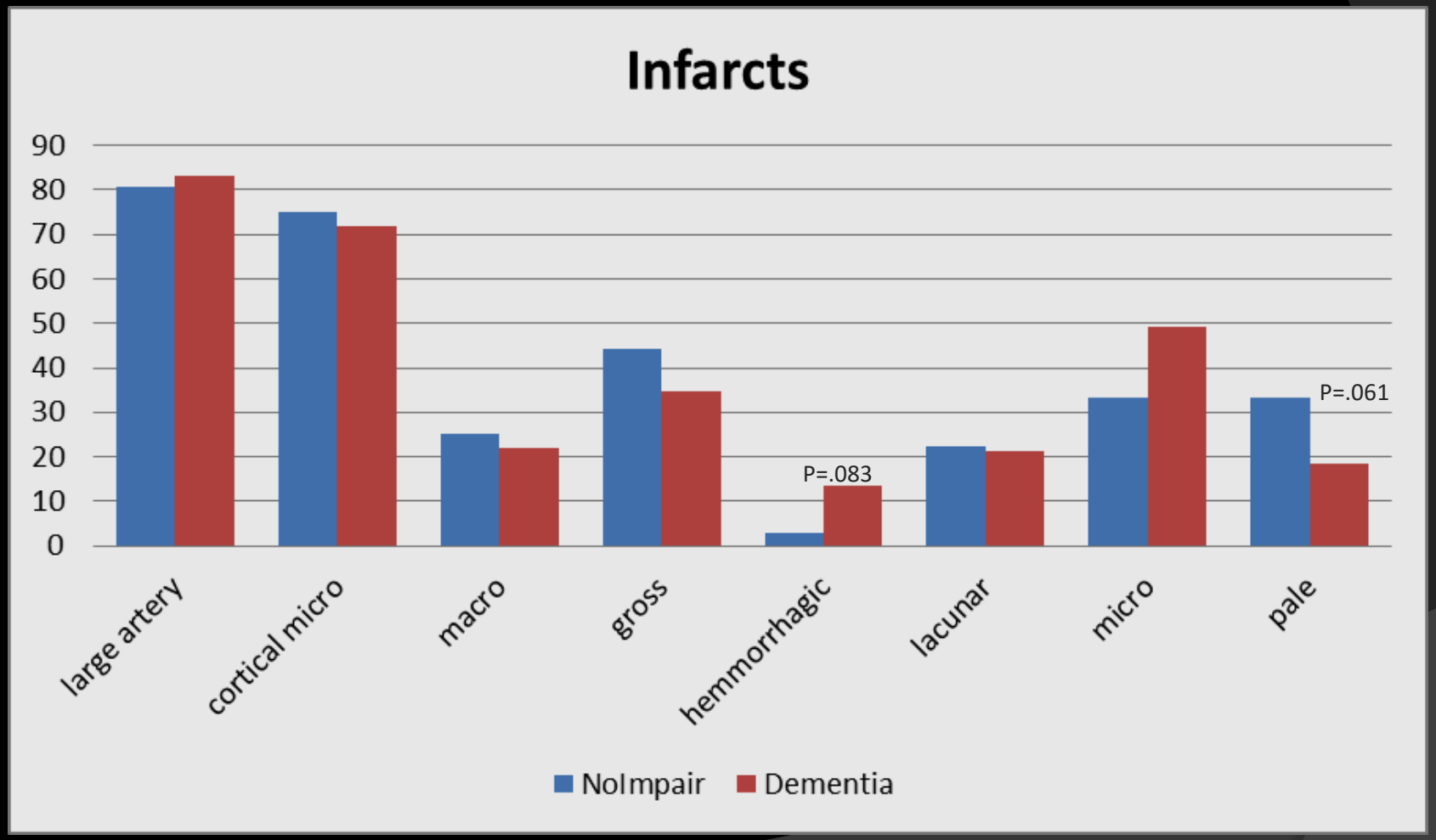
SMC NO Impairment



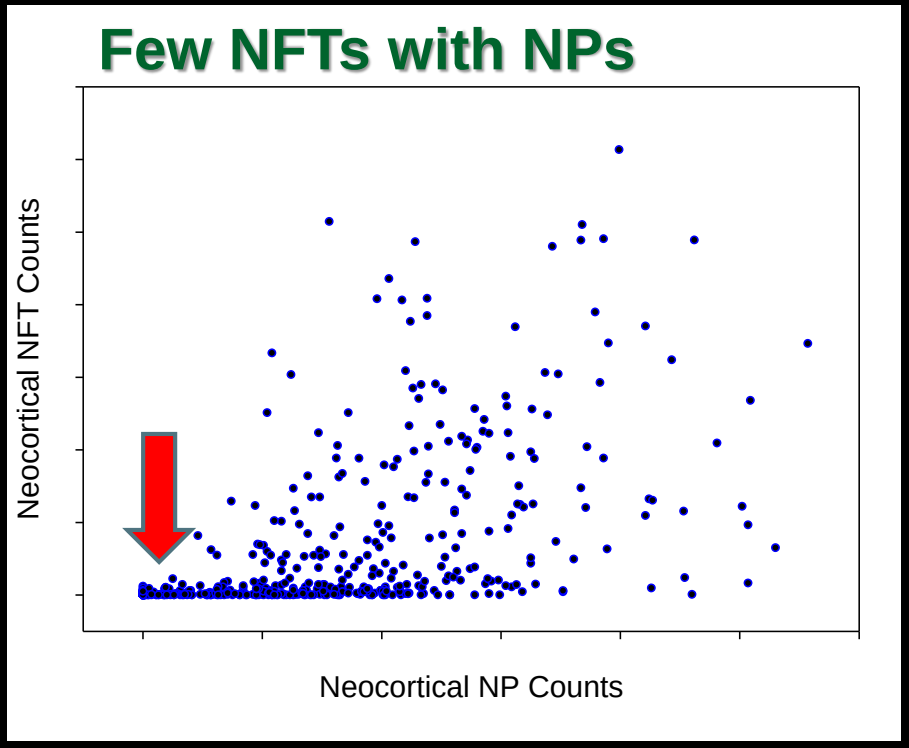
Implications of SMC

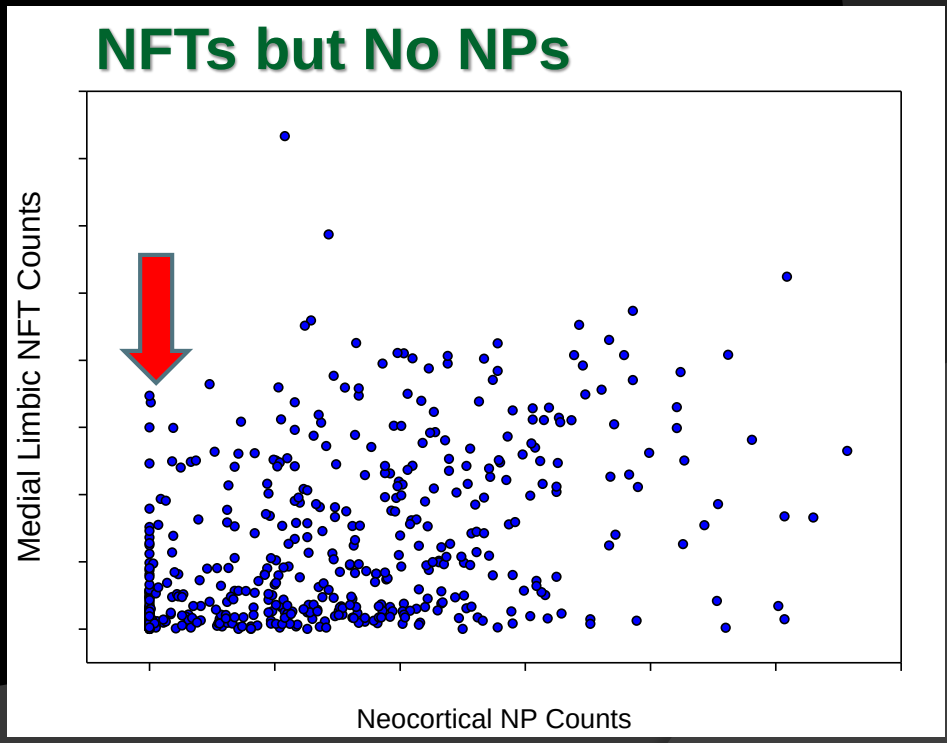
- Over half of volunteers have Subjective Memory Complaints during follow-up
- SMC accounts for most MCI/dementia transitions (OR = 2.8)
- SMC is no guarantee MCI/dementia will occur
- Identified risks affect the time and probability for transitions to occur
- Autopsy results indicate a subset of individuals (but not all) have AD type pathology
- Can inform the design of future prevention trials

SMC & Other Pathologies 1



PART: Neuropathological Evidence





J Neuropathol Exp Neurol

Vol. 68, No. 7
July 2009
pp. 774–784

ORIGINAL ARTICLE

Brains With Medial Temporal Lobe Neurofibrillary Tangles But No Neuritic Amyloid Plaques Are a Diagnostic Dilemma But May Have Pathogenetic Aspects Distinct From Alzheimer Disease

Peter T. Nelson, MD, PhD, Erin L. Abner, MS, Frederick A. Schmitt, PhD, Richard J. Kryscio, PhD, Gregory A. Jicha, MD, PhD, Karen Santacruz, MD, Charles D. Smith, MD, Ela Patel, HT, and William R. Markesbery, MD

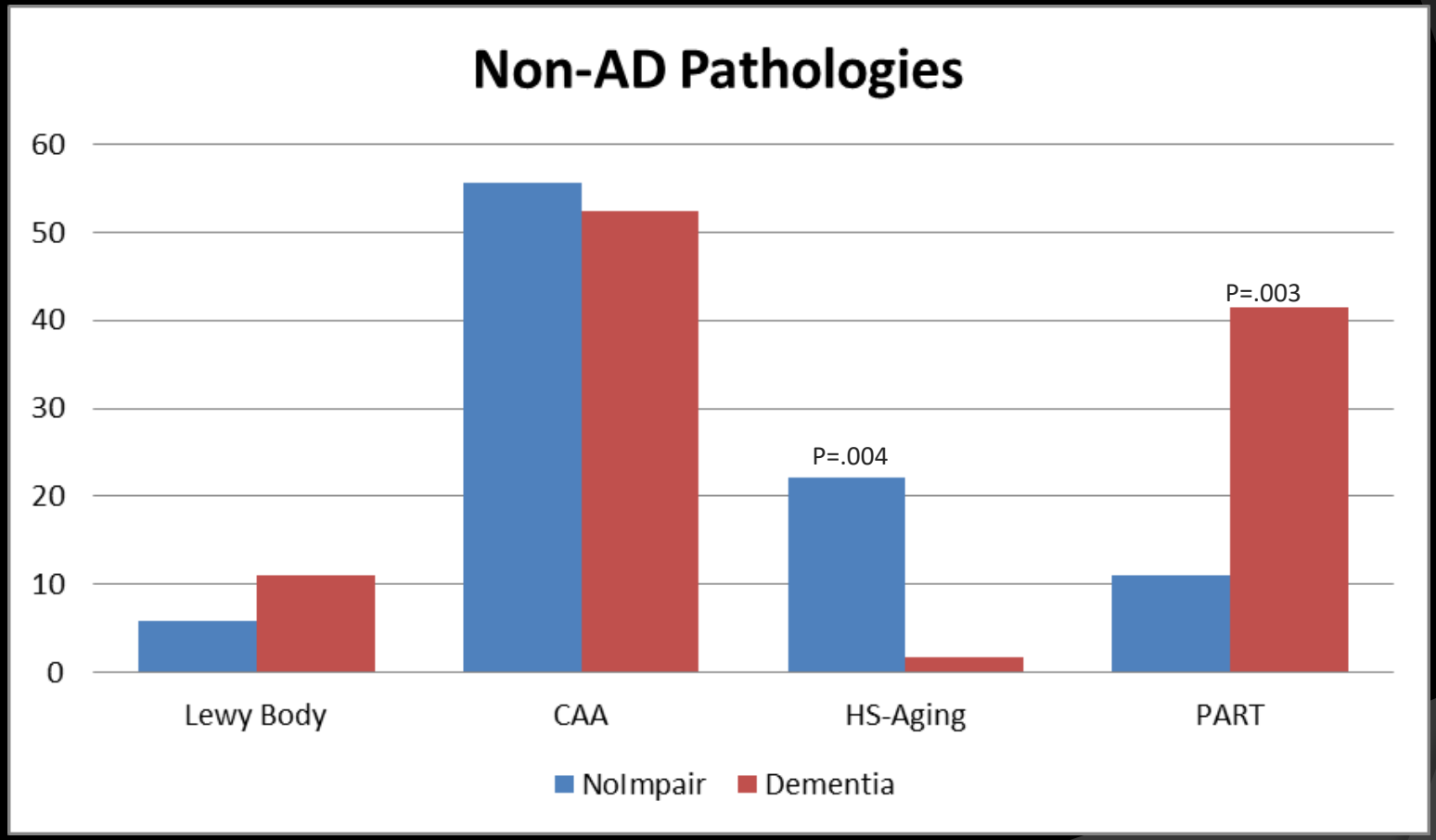
Acta Neuropathol
DOI 10.1007/s00401-014-1349-0

CONSENSUS PAPER

Primary age-related tauopathy (PART): a common pathology associated with human aging

John F. Crary · John Q. Trojanowski · Julie A. Schneider · Jose F. Abisambra · Erin L. Abner · Irina Alafuzoff · Steven E. Arnold · Johannes Attems · Thomas G. Beach · Eileen H. Bigio · Nigel J. Cairns · Dennis W. Dickson · Marla Gearing · Lea T. Grinberg · Patrick R. Hof · Bradley T. Hyman · Kurt Jellinger · Gregory A. Jicha · Gabor G. Kovacs · David S. Knopman · Julia Kofler · Walter A. Kukull · Ian R. Mackenzie · Eliezer Masliah · Ann McKee · Thomas J. Montine · Melissa E. Murray · Janna H. Neltner · Ismael Santa-Maria · William W. Seeley · Alberto Serrano-Pozo · Michael L. Shelanski · Thor Stein · Masaki Takao · Dietmar R. Thal · Jonathan B. Toledo · Juan C. Troncoso · Jean Paul Vonsattel · Charles L. White 3rd · Thomas Wisniewski · Randall L. Woltjer · Masahito Yamada · Peter T. Nelson

SMC & Other Pathologies 2



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