Collaborative work on primary age-related tauopathy (PART)

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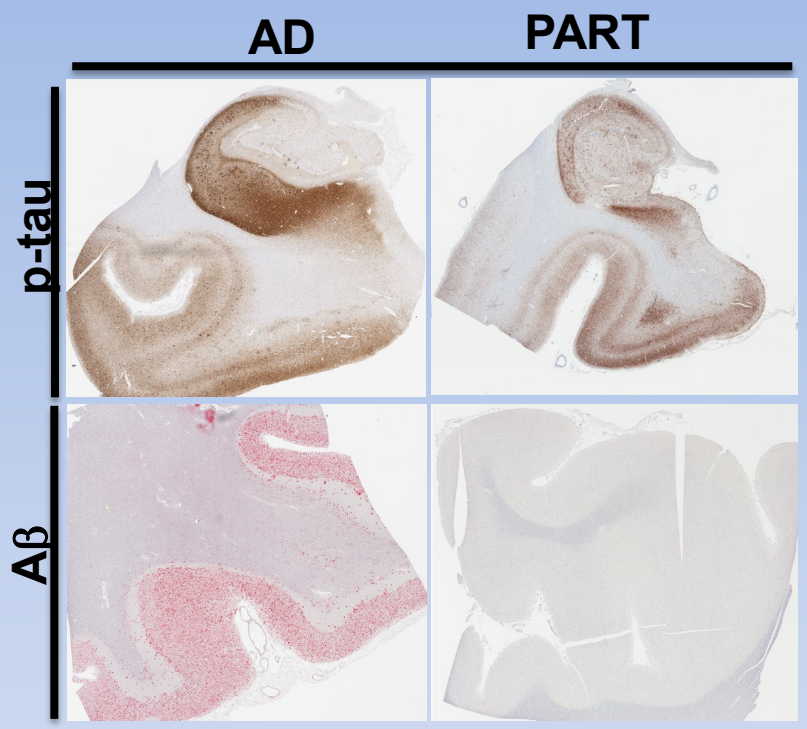

Pathology images courtesy of John Crary

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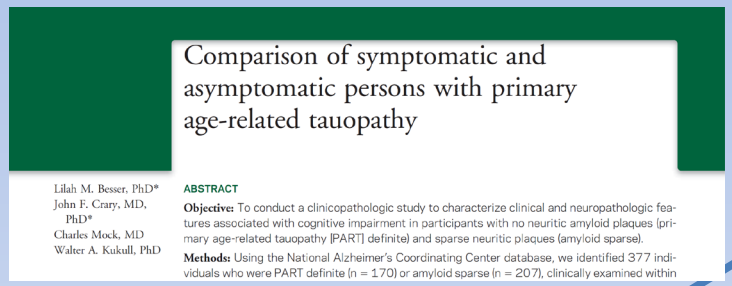
Collaborative studies on PART



Comparison of symptomatic and asymptomatic persons with primary age-related tauopathy

Lilah M. Besser, PhD*
John F. Crary, MD, PhD*
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Walter A. Kukull, PhD

ABSTRACT

Objective: To conduct a clinicopathologic study to characterize clinical and neuropathologic features associated with cognitive impairment in participants with no neuritic amyloid plaques (primary age-related tauopathy [PART] definite) and sparse neuritic plaques (amyloid sparse).

Methods: Using the National Alzheimer's Coordinating Center database, we identified 377 individuals who were PART definite (n = 170) or amyloid sparse (n = 207), clinically examined within

Basic model of sx vs asx: PART

Neuropsych tests: PART vs. AD NP

What is PART being diagnosed as?

Pathologic-radiologic correlation

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Primary Age-Related Tauopathy (PART)

AIMS: To characterize clinical and neuropathological features associated with cognitive impairment in participants with:

- no neuritic plaques
  - PART definite
- sparse neuritic plaques
  - early AD vs. PART possible: “amyloid sparse”

- Inclusion:
  - PART: Braak 0 – VI
  - Amyloid: characterized by neuritic plaques (CERAD score)

- Exclusions: (a) neuropathological evidence of FTLD, Lewy bodies, ALS, prion disease, or argyrophilic grains; (b) clinical evidence of DLB, Parkinson disease, Down syndrome, Huntington disease, prion disease, CBD, or PSP.

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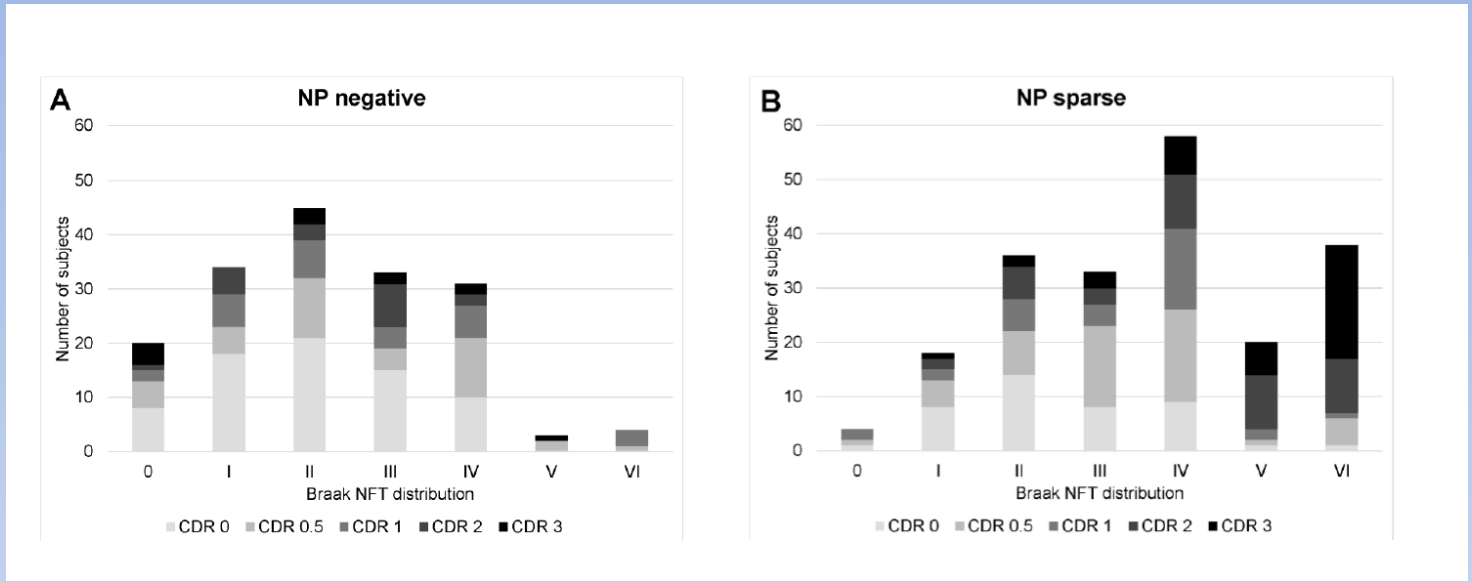
PART definite (n=170) **Amyloid sparse (n=207)**



PART definite:

- Less likely to have Braak stage V or VI
  - (4% for PART definite; 28% for amyloid sparse)*
- Less likely to be symptomatic (CDR > 0).
  - (58% for PART definite; 80% for amyloid sparse)*

*p<0.001

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Independent predictors of sx status (CDR global > 0)

- PART definite:
  - Depression (aOR: 4.20; CI: 2.15-8.19);
  - Braak stage (aOR: 1.42; CI: 1.04-1.95);
  - History of stroke (aOR: 8.09; CI: 2.63-24.82).

- Amyloid sparse group:
  - Education (aOR: 0.80; 95% CI: 0.65-0.99);
  - Braak stage (aOR: 1.91; 95% CI: 1.07-3.43);
  - Amyloid angiopathy (aOR: 2.75; 95% CI: 1.14-6.64).

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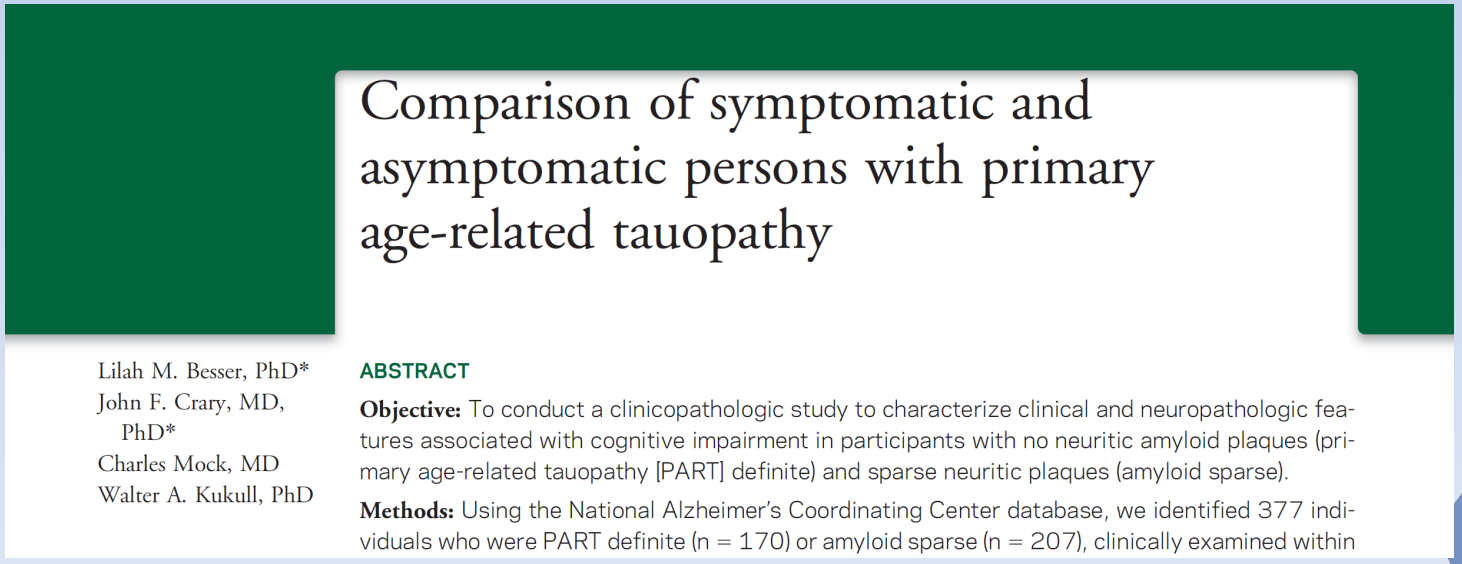
Conclusions (PART)

These findings support the hypothesis that people with PART have an amyloid-independent dementing AD-like temporal lobe tauopathy.



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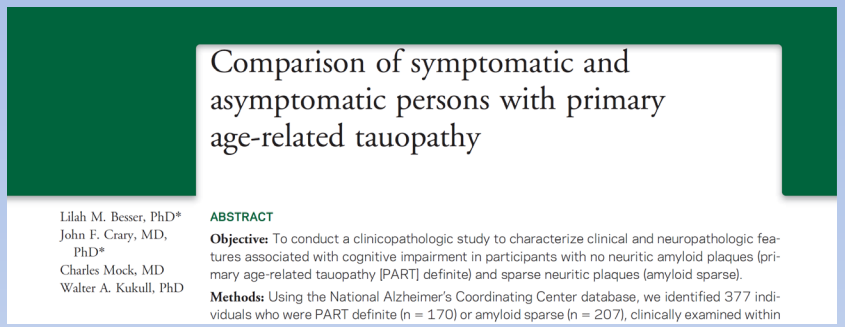

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Neuropsychological changes in PART

- **Broad goal:** To determine how do the neuropsychological characteristics of people with PART differ from those of people with AD neuropathology.

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Neuropsychological changes in PART

- **Specific aims:** Compare the z-scores for the following domains (attention, episodic memory, executive function, language) at the last UDS visit, for people with PART definite neuropathology vs. AD neuropathology.

Derivation of Z-score: Hayden et al. Alzheimer Dis Assoc Disord 2011;25:128–137.

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Summary of findings

Compared to AD, individuals with definite PART:

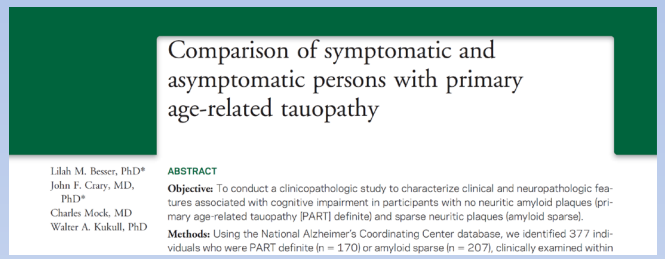
Less severe cognitive impairment

Differential patterns of neuropsychological change

- Relative sparing of semantic memory/language in those with any impairment (CDR ≥ 0.5)
- One of first studies comparing cognitive domain scores in PART vs AD

- Future work: Longitudinal change in cognitive domains

Collaborative studies on PART



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Subtle changes on neuropsych tests

Static: *under review*

Trajectory: *under development*

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Summary of study on diagnosis

- Clinicians appear to be recognizing the clinical distinction between PART and ADNP.
- Nonetheless, clinical AD was diagnosed greater than 50% of the time in PART participants with MCI or dementia.
- Ante-mortem criteria for diagnosis of PART need to be established.

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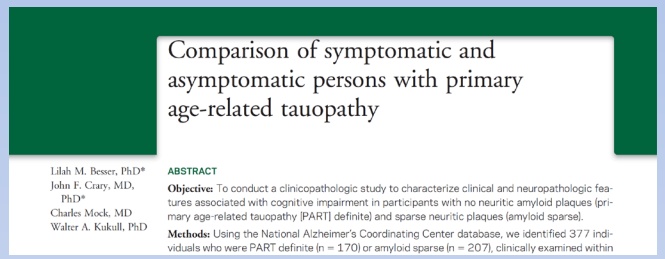
Collaborative studies on PART



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Static: Under review

Trajectory: *under development*

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AAIC, poster.

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Conclusion

- NACC data (UDS, NP) have helped to explore PART further.
- Add support the hypothesis that people with PART have an amyloid-independent dementing AD-like temporal lobe tauopathy.
- Less severe than AD.
- Different cognitive pattern than AD.
- Different prognosis. Ante-mortem criteria for diagnosis of PART need to be established.

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