

Plasma Biomarkers Of Alzheimer’s Disease
in Late Onset Unexplained Epilepsy

P3-0349

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Background

Late-onset unexplained epilepsy (LoUE), defined as unexplained seizures arising after age 55, is associated with a 2 to 3-fold increased risk of developing dementia. While the mechanisms driving dementia in LoUE remain unknown, it is thought that Alzheimer disease (AD) pathology drives risk for both epilepsy and cognitive decline in this population. **Hypothesis:** The rate of amyloid positivity is higher in LoUE compared to the general population (without epilepsy).

Methods

The **ELUCID Study** (Epilepsy of Late-onset Unknown etiology as a risk factor for Cognitive Impairment and Dementia) is a **multi-center, prospective longitudinal observational study of LoUE**, focused on understanding mechanisms and predicting outcomes of dementia in LoUE. ELUCID participants experienced their first seizure after age 55 and within 3 years of enrollment; have no obvious cause for seizure; and have no dementia at baseline. Participants undergo detailed clinical history, neuropsychological testing, brain MRI, overnight scalp EEG, and blood draw at baseline followed by longitudinal monitoring to track cognitive outcomes. Diagnosis of mild cognitive impairment at baseline was made during diagnostic consensus conferences attended by the study behavioral neurologist and neuropsychologist, based on NIA-AA criteria.

Blood samples were uniformly collected and processed using standardized kits from the BioSEND repository. Baseline plasma samples from ELUCID participants were analyzed using C2N Diagnostics PrecivityAD2™ blood test to measure amyloid beta (Aβ42/40) and p-tau217/np-tau217 (%p-tau217) concentration ratios and calculate Amyloid Probability Score 2 (APS2). Participants were considered amyloid positive if they had plasma %p-tau217 ≥ 4.2% or APS2 ≥ 48.

Funding

The ELUCID study is funded by NIH / NIA R01 NS130119

Results

ELUCID Participant demographics

93 ELUCID participants with PrecivityAD2 results

- Age (mean ± SD): 67.8±6.9 years
- Sex: 38.7% F / 61.3% M
- Education (mean ± SD): 16.5±2.7 years
- MMSE score (mean ± SD): : MMSE 28.9±1.3

% Amyloid positive in ELUCID:

- Based on %p-tau217 cut-off: **10.8%**
- Based on APS2 cut-off: **4.3%**

Comparison of % amyloid positive in ELUCID vs. reference population without epilepsy

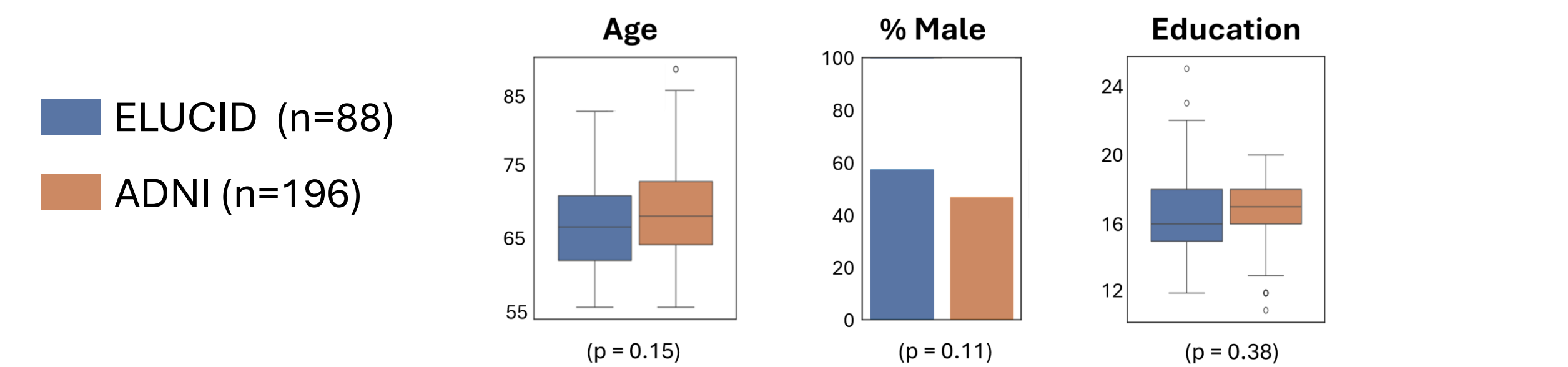
Reference population

- Based on Jansen et al. "Prevalence of cerebral amyloid pathology in persons without dementia: a meta-analysis." JAMA 313.19 (2015): 1924-1938.
- Reference Aβ+ criteria: based on amyloid PET and/or CSF amyloid

Age	Cognitively Unimpaired				Cognitively Impaired			
	ELUCID Total	ELUCID AB+	ELUCID AB+ %	Ref AB+ % (95% CI)	ELUCID Total	ELUCID AB+	ELUCID AB+ %	Ref AB+ % (95% CI)
55-59	9	1	11.11	12.9 - 15.8 (10.3 - 19.1)	1	0	0.00	31.8 - 37.1 (27.5 - 41.6)
60-69	46	2	4.35	15.8 - 23.1 (12.9 - 27.2)	3	0	0.00	37.1 - 48.7 (32.9 - 53.0)
70-79	27	4	14.81	23.1 - 32.6 (19.5 - 38.0)	5	1	20.00	48.7 - 60.4 (44.5 - 65.0)
80+	6	2	33.33	32.6 - 43.8 (27.6 - 50.7)	0	0	-	69.4 - 71.1 (55.7 - 75.9)

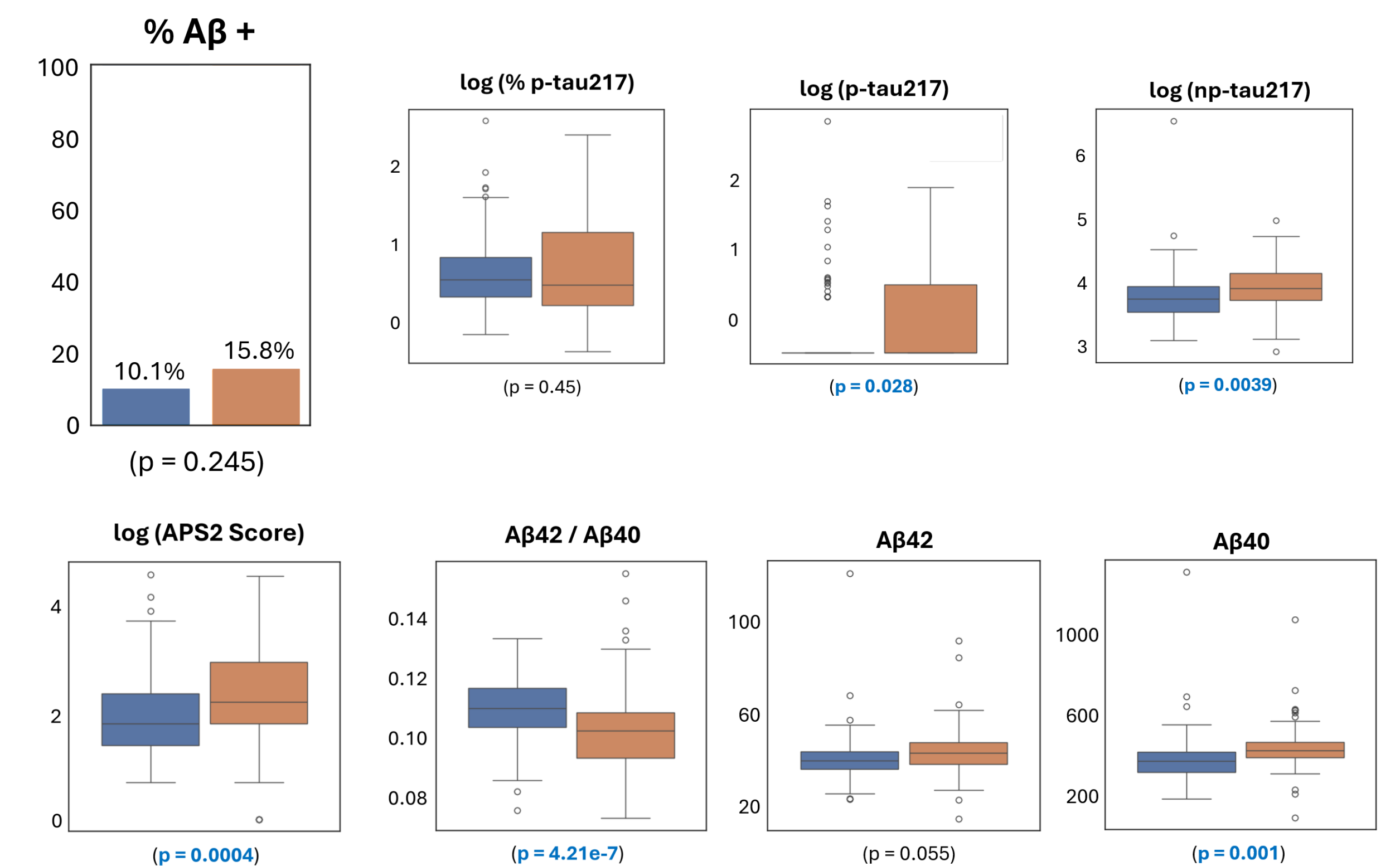
Comparison of PrecivityAD2 in ELUCID vs. ADNI (no epilepsy) cohorts

Cognitively unimpaired ADNI participants (without epilepsy) and with PrecivityAD2 results were matched (~ 1:2) with cognitively unimpaired ELUCID participants by age and sex



The percentage of Aβ+ participants did not differ significantly between ELUCID vs. ADNI. However, there were significant differences in concentrations of plasma tau and Aβ ...

- ELUCID had lower p-tau217, np-tau217, and Aβ40, and trend towards lower Aβ42 compared to ADNI



Conclusions

- The prevalence of amyloid pathology in LoUE appears comparable to (if not lower than) in those without epilepsy.
- Amyloid pathology does not appear to be a major contributor to baseline cognitive impairment in LoUE (only ~ 12% with MCI were Aβ+)
- Differences in plasma concentrations of p-tau217, np-tau217, and Aβ40 between ELUCID and ADNI cohorts warrants further investigation