Title: The Performance of Two Plasma pTau217 Immunoassays in Distinguishing Alzheimer's Disease Pathology at Different Stages

Hans Frykman [1-3], Anna Mammel[3], Ali Mousavi[1-3] Pankaj Kumar[1,2], Mary Encarnacion[2], Don Biehl[3], Kelsey Hallett[3], Ian Mackenzie [4], Veronica Hirsch-Reinshagen [4], Don Biehl [3], Pradip Gil[3], Shannon Pflueger[1], Ging-Yuek Robin Hsiung[1]

1. Department of Medicine, University of British Columbia, Vancouver, Vancouver, BC, Canada 2. BC Neuroimmunology lab, Vancouver, BC, Canada 3.Neurocode USA, Bellingham, WA, USA

4. Department of Pathology and Laboratory Medicine, University of British Columbia

Canadian Conference on Dementia
Hot Topics 2024 | Oct 18, 2024 | Virtual

Poster #16

Background

Plasma pTau217 is one of the most promising blood biomarkers for AD, due to its strong correlations with amyloid and tau pathologies. While plasma pTau217 is specific for AD pathology, it is crucial to evaluate its performance in diagnosing of AD in its different stages.

In the current study we assessed the performance of two commercial immunoassays in detecting alterations in plasma levels of pTau217 compared with the pathological stages of AD.

Methods

A cohort consisted of cases clinically diagnosed with AD referred to the UBC Hospital Clinic for dementia assessment (n=115)

EDTA plasma samples

Plasma pTau217 was measured using

Immune assays ALZpath Simoa pTau 217 v2 kits (Quanterix MA USA) on the Quanterix HD-X Analyzer platform

Lumipulse G pTau217 plasma kits on the Lumipulse G1200 platform

The extent of tau pathology according to Braak staging, the severity of senile neuritic plaque pathology following the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) recommendations, and the progression of amyloid-β plaque deposition according to the Thal amyloid phase were collected from autopsy reports.

Results

Braak stage

- Plasma pTau217 was significantly higher for individuals with Braak VI compared to individuals with Braak stage 0, I-II, III, IV, or V (Figure A, B).
- The ALZpath assay pTau217 measurement increase was apparent by Braak stage IV and was nearly significant by Braak stage V (p-value = 0.07), Braak V to 0 (p-value = 0.09) and Braak V to I & II. This increase was less pronounced with the Fujirebio p-tau217 assay (Figure B).

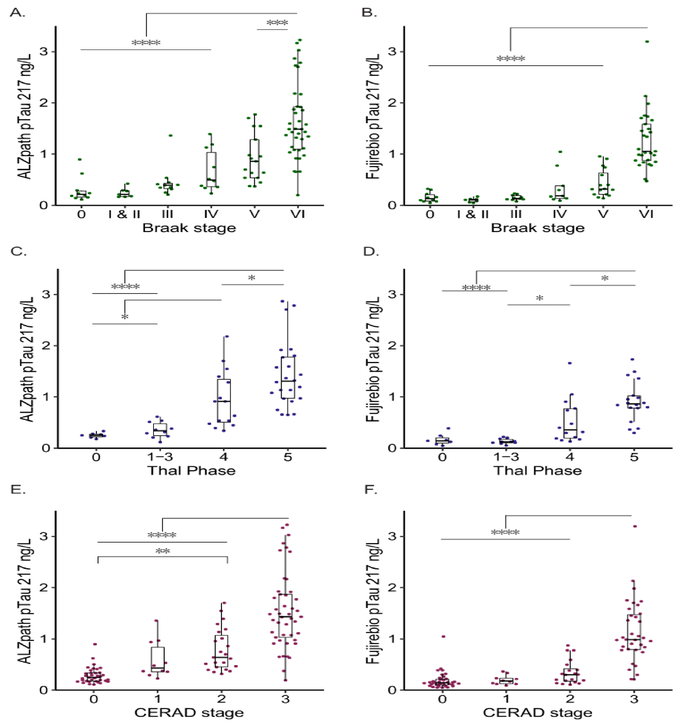
Thal phase

- pTau217 was significantly higher in individuals at Thal phase 4 (p-value < 0.05) and 5 (p-value < 0.0001) compared to phase 3 and below (Figure C,D).
- The largest fold increase was observed at phase 4 with a 2.6-fold increase with the ALZpath assay and 4.1-fold increase with the Fujirebio assay.
- There was a significant difference between phase 4 and 5 with both the ALZpath and Fujirebio p-tau217 assays (p-value < 0.0001; ALZpath – 1.5x fold change; Fujirebio - 1.7x fold change)
- A slight, but non-significant, increase was observed between phase 0 and phase 1-3 for the ALZpath assay(p-value > 0.05; 1.4x fold change)(Figure C)

CERAD stage

- ALZpath p-tau217 was increased in individuals with moderate plaque score at CERAD stage 2 (p-value < 0.01) and a substantial increase by CERAD stage 3 (p-value < 0.0001) (Figure E).
- This increase was only observed at CERAD stage 3 with the Fujirebio p-tau217 assay (p-value < 0.0001) and was not significant at earlier plaque stages (Figure F).
- The level of plasma p-tau217 for both ALZpath and Fujirebio increase according to AD disease staging, with increase observed at earlier disease staging with the ALZpath assay for both tau and amyloid pathology.

Results



Conclusion

With the ALZpath assay, the levels of p-tau217 show an increase as early as Braak stage III & IV, and a stepwise increase at each CERAD stage. The Fujirebio assay has a modest increase at Braak stage IV, and no significant increase until CERAD stage 3. These results together suggest that the ALZpath assay is able to detect amyloid and tau pathology at earlier disease staging compared to the Fujirebio assay.

ACKNOWLEDGEMENT

University of Gothenburg
Dr. Kaj Blennow
Hayder Shweliyya
BC Neuroimmunology
Dr. Pankaj Kumar
Dr. Andreas Jeromin
Mary Encarnacion
Dr. Ali Mousavi
neurocode
Roopa Reddy
Dr. Anna Mammel
Dr. Andreas Jeromin
Don Biehl
Pradip Gill
Massachusetts General Hospital
Harvard Medical School
Beth Israel Deaconess Medical Center
Wake Forest
Dr. Michelle Mielke
AVERO DIAGNOSTICS
Dr. Ryan Fortina
Kelly Lloyd
Becky Woodford
UBC Clinic for Alzheimer Disease and Related Disorders
Dr. Robin Hsiung
Dr. Ian Mackenzie
Dr. Hirsch-Reinshagen, Veronica
Shannon Kolind
University of Pittsburgh
Dr. Thomas K Karikari
FUJIREBIO
Nathalie Le Bastard
Manu Vandijck
ifcc
Lilly
Dr. Mark Mintun and the Canada team