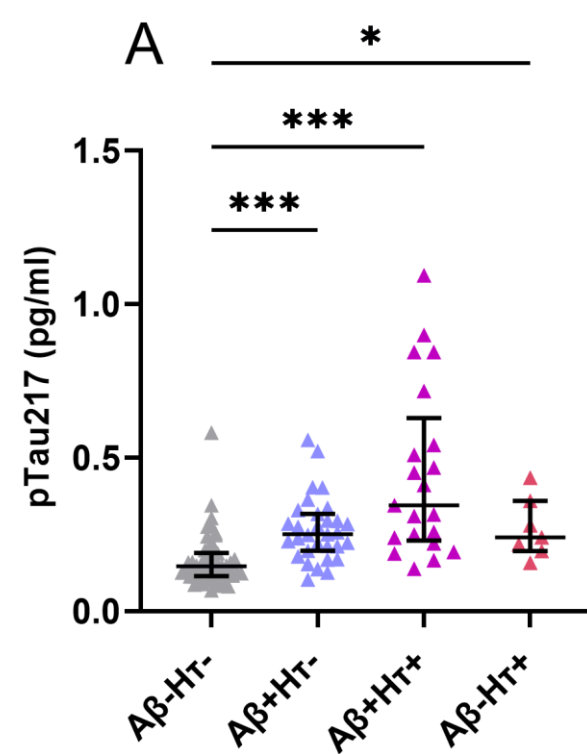
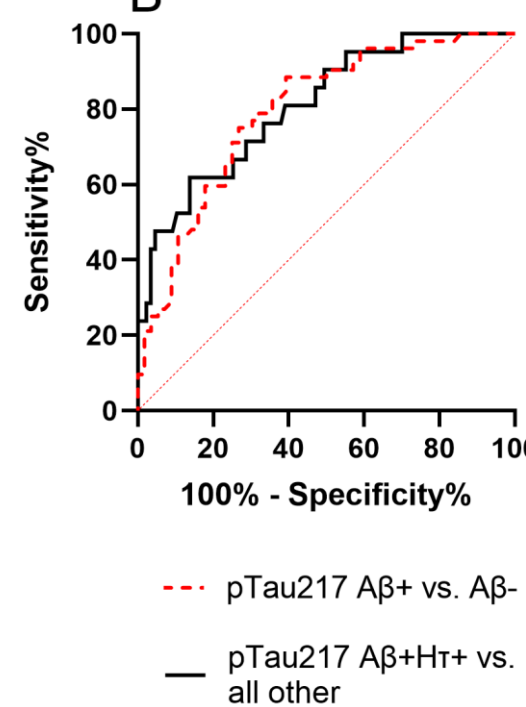
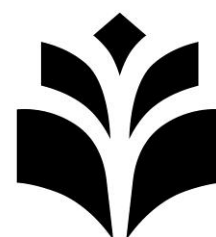


Plasma Phosphorylated Tau 217 in Idiopathic Normal-pressure Hydrocephalus: Predicting Brain Biopsy Pathology and Alzheimer’s Disease.

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AD frequently co-occurs with iNPH. We assessed whether plasma pTau217 predicts Aβ and Hτ in the brain biopsies of patients with iNPH. We demonstrate that plasma pTau217 reliably reflects Aβ and Hτ brain pathology in iNPH. Furthermore, pTau217 can predict the development of clinical AD during follow-up in iNPH patients.

INTRODUCTION	METHODS	RESULTS	REFERENCES																														
- Alzheimer's disease (AD) frequently co-occurs with idiopathic normal-pressure hydrocephalus (iNPH).^{1, 2, 3} - We aimed to assess whether plasma phosphorylated tau 217 (pTau217) predicts β amyloid (Aβ) and hyperphosphorylated tau (Hτ) in the brain biopsies of patients with iNPH. - We also assessed whether pTau217 predicts the development of clinical AD during follow-up.	- Frontal cortical biopsies were obtained from patients with iNPH in shunt surgery procedure and immunostained for Aβ and Hτ. - Receiver operating characteristic (ROC) analyses and area under the curve (AUC) values were used to evaluate the diagnostic performance of plasma pTau217. - Cutoffs for pTau217 were determined using Youden's index for biopsy-defined Aβ positivity (Aβ+) and combined Aβ and Hτ positivity (Aβ+Hτ+). - Determined cutoffs were used in binomial logistic regression models to estimate the relative risk of developing clinical AD during follow-up, adjusting for age, sex and APOE ε4 carriership.	A  B  - The cohort consisted of 108 patients shunted for iNPH. - The brain biopsy group with Aβ-Hτ- findings displayed the lowest pTau217 levels (median 0.15pg/ml) whereas the Aβ+Hτ+ group exhibited the highest levels (median 0.35pg/ml) (Figure A). - ROC analyses yielded AUC values of 0.80 and 0.81 for pTau217 in distinguishing brain biopsy findings of Aβ+ and Aβ+Hτ+, respectively (Figure B). - Binomial regression analysis demonstrated increased relative risk of AD in follow-up (mean 2.7 years) with odds ratios (OR) of 12.9 and 6.1 for the lower (0.163 pg/ml) and higher cutoffs (0.306 pg/ml), respectively	<table><tr><th></th><th colspan="4">pTau217 cutoff (pg/ml)</th></tr><tr><th>Predictor</th><th>Lower cutoff (0.163) OR (95 % CI)</th><th>p-value</th><th>Upper cutoff (0.306) OR (95 % CI)</th><th>p-value</th></tr><tr><td>Elevated pTau217</td><td>12.9 (2.6–64.2)</td><td>0.002</td><td>6.1 (2.1–17.7)</td><td><0.001</td></tr><tr><td>Age</td><td>1.0 (0.9–1.1)</td><td>0.853</td><td>1.0 (1.0–1.1)</td><td>0.400</td></tr><tr><td>APOE ε4 carriership</td><td>0.7 (0.2–1.8)</td><td>0.425</td><td>0.7 (0.3–2.0)</td><td>0.540</td></tr><tr><td>Male sex</td><td>0.5 (0.2–1.3)</td><td>0.174</td><td>0.6 (0.2–1.5)</td><td>0.256</td></tr></table> 1 Luikku AJ, Hall A, Nerg O, et al. Predicting Development of Alzheimer's Disease in Patients with Shunted Idiopathic Normal Pressure Hydrocephalus. <i>Journal of Alzheimer's Disease</i>. 2019;71(4):1233-1243. doi:10.3233/JAD-190334 2 Junkkari A, Luikku AJ, Danner N, et al. The Kuopio idiopathic normal pressure hydrocephalus protocol : initial outcome of 175 patients. <i>Fluids Barriers CNS</i>. 2019;16(1):1-12. doi:10.1186/s12987-019-0142-9 3 Rissanen JA, Kärkkäinen S, Katisko K, et al. The performance of plasma pTau181 and pTau217 in distinguishing Alzheimer's disease from various neurodegenerative disorders, psychiatric disorders, and cognitively unimpaired controls. <i>Journal of Alzheimer's Disease</i>. 2026;111(1):385-396. doi:10.1177/13872877261431800		pTau217 cutoff (pg/ml)				Predictor	Lower cutoff (0.163) OR (95 % CI)	p-value	Upper cutoff (0.306) OR (95 % CI)	p-value	Elevated pTau217	12.9 (2.6–64.2)	0.002	6.1 (2.1–17.7)	<0.001	Age	1.0 (0.9–1.1)	0.853	1.0 (1.0–1.1)	0.400	APOE ε4 carriership	0.7 (0.2–1.8)	0.425	0.7 (0.3–2.0)	0.540	Male sex	0.5 (0.2–1.3)	0.174	0.6 (0.2–1.5)	0.256
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CONCLUSIONS			CONTACT																														
- Plasma pTau217 reliably reflects Aβ and Hτ brain pathology in patients with iNPH. - pTau217 can also predict cognitive decline and the development of clinical AD during follow-up in iNPH patients.			Email: jirissan@uef.fi  UNIVERSITY OF EASTERN FINLAND  Kuopio University Hospital  ALZHEIMER'S ASSOCIATION  AAIC>26																														