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BIOMARKERS

POSTER PRESENTATION

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BIOMARKERS (NON-NEUROIMAGING)

CSF markers of inflammation help identify tau pathology but not amyloid in a heterogenous clinical population

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Abstract

Background: Neuroinflammation and activation of the immune system is an integral part of Alzheimer's Dementia (AD) pathology. Inflammatory mediators exacerbate the production of amyloid-β, the propagation of tau pathology and neuronal loss. This study evaluates whether CSF markers of inflammation can help evaluate changes in amyloid and tau pathology in a heterogenous clinical population.

Methods: CSF samples from 105 patients referred to the Wessex Neurology Clinic due to cognitive complaints were analysed. Measurements of AD biomarkers were used to classify the samples based on previously published thresholds (Ab42<680pg/ml for an amyloid positive test, pTau>56pg/ml for a Tau positive test and Total Tau>355pg/ml for a test positive for neurodegeneration). Based on these biomarker results, the likelihood of AD was evaluated using the Paris Lille Montpellier (PLM) scale. 102 markers of inflammation were measured on CSF using the Mesoscale and OLINK platforms. Receiver Operator Characteristic (ROC) curves were used to evaluate if inflammation markers can accurately identify patients with amyloid and tau pathology.

Results: 56 patients were amyloid positive, 43 were tau positive and 44 were positive for neurodegeneration. 52 different inflammation markers were detected in over 90% of samples. From these, 26 markers correlate significantly with pTau and Total Tau measurements, while no markers correlate with Ab42 measurements. Adenosine Deaminase (ADA), an enzyme of purine metabolism and marker of cellular immunity, most strongly correlates with pTau and Total Tau (Spearman's Rho 0.62 and 0.60 respectively, p<0.001). Analysis of Variance indicates significantly higher levels of ADA in patients with higher PLM scores and thus higher likelihood of AD (p<0.001). Finally, ROC analysis indicates that ADA can identify Tau positive patients (pTau>56pg/ml) with an Area Under the Curve (AUC) of 0.76 and Neurodegeneration positive patients (Total Tau>355pg/ml) with an AUC of 0.82.

Conclusion: In this clinical patient cohort, inflammation levels increase with tau pathology but do not change with amyloid. ADA, a marker of cellular immunity, provides a sensitive and specific marker of Tau and Neurodegeneration in AD. Further work is required to assess the prognostic capabilities of ADA in larger patient cohorts and when used in conjunction with established AD biomarkers.

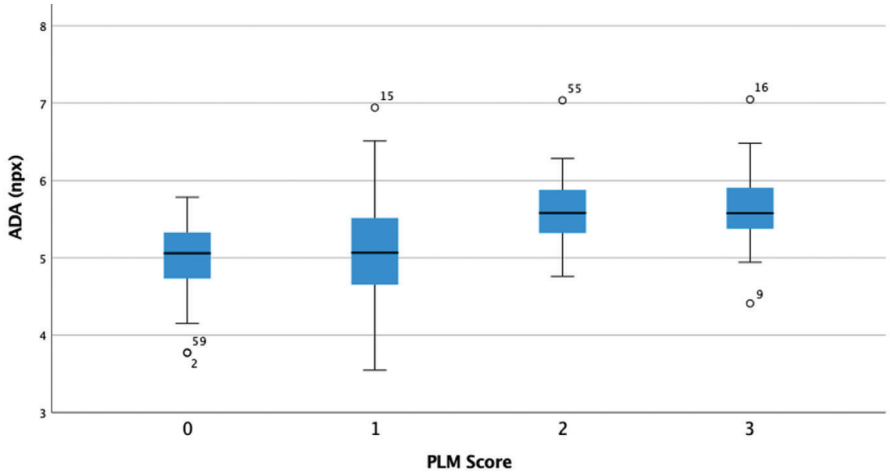

Figure 1. Boxplot outlining changes in ADA in units of normalised protein expression (npx) with PLM score. A step change in ADA values occurs when moving from PLM score of 1 corresponding to AD likelihood of <25% to PLM score of 2 corresponding to AD likelihood > 75%.

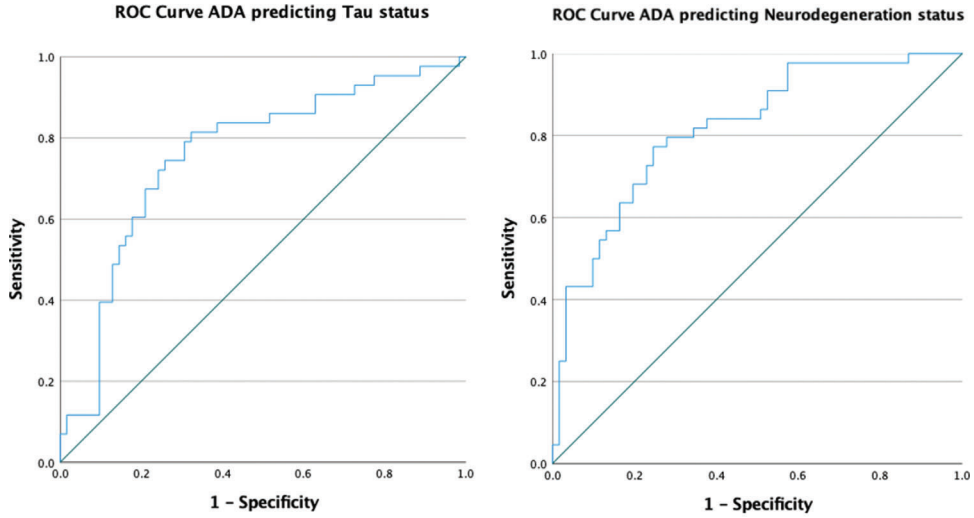

Figure 2. Receiver Operator Characteristic curve for prediction of Tau status (Left, AUROC=0.76) and Neurodegeneration status (Right, AUROC=0.82).