First Measurement of Brain-Derived Tau in Plasma Using a Novel Luminescence Immunoassay.

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Background

Early detection of Alzheimer's disease (AD) risk requires sensitive and specific biomarkers measurable in blood. We evaluated a new Luminescence Immunoassay (LUM) for the quantification of brain-derived tau (BD-Tau) in plasma or serum. The method includes an upstream enrichment step, termed Neuro-IP, employing a monoclonal antibody specific for BD-Tau.

Methods

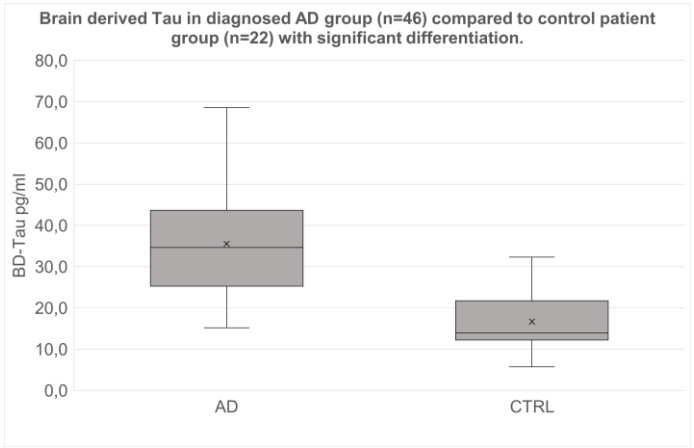
Three panels of plasma samples obtained from the University of Goettingen, MVZ Labor Limbach, and a commercial source, all classified as characterized by CSF levels of Aβ40/42, p181Tau, and hTau, measured with the Lumipulse system, were used. The subjects were classified according to the clinical cutoff point into the diagnostic groups Aß-positive (AD, n=46) and Aß-negative (CTRL, n=22). BD-Tau was extracted from a 200 µl sample using BD-specific Neuro-IP according to the protocol. The eluates were quantified using BD-Tau-specific Luminescence Immunoassay.

Conclusion

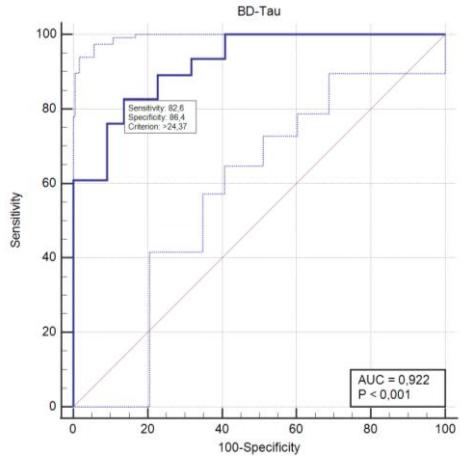
For the first time, our laboratory investigated the measurement of BD-Tau on routine plasma samples using a standard luminescence microplate immunoassay after Neuro-IP enrichment. This immunoprecipitation step minimizes matrix effects and enables sensitive BD-Tau detection. The BD-Tau LUM assay provides information that complements existing plasma tau biomarkers and may improve the interpretation of patient status in the context of Alzheimer's disease risk assessment.

Results

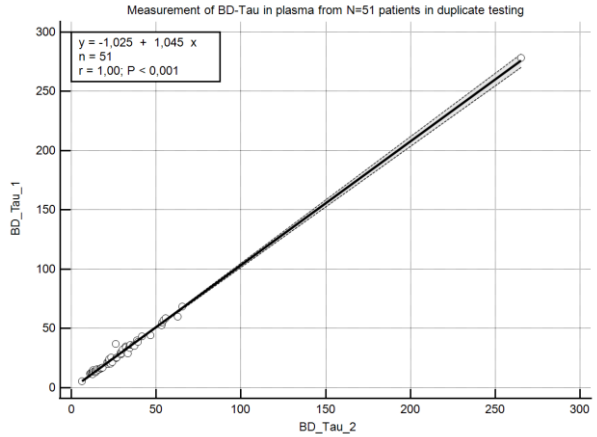
(A)



(B)



(C)



(A) BD-specific Neuro-IP with subsequent measurement of BD-Tau concentration using the BD-Tau LUM assay showed significant differentiation between the AD group and control group (p<0.001). (B) The ROC analysis for differentiation of the two diagnostic groups showed an AUC of 0.922 for the BD-Tau LUM assay (p<0.001). (C) Duplicate testing of BD-Tau in plasma from n=51 patients shows perfect positive correlation for the two runs (r=1.00; p<0.001). Furthermore, plasma pTau217 levels showed a strong correlation with BD-Tau concentrations determined by the LUM assay (not shown). Notably, BD-Tau demonstrated the strongest association with CSF Aβ pathology among all measured parameters.