QUANTIFICATION OF SNAP-25 AND VAMP-2 IN PLASMA AND CSF FROM PATIENTS WITH EARLY ALZHEIMER'S DISEASE USING TWO NOVEL DIGITAL IMMUNOASSAYS (0344)

Topic
Theme A: ?-Amyloid Diseases

Authors
Goossens J., Rocker C.D., Das S., Alcolea D., Herries E., Ladenson J., Lleó A., Belbin O., Vanmechelen E.

Aims
Development of sensitive immunoassays to detect SNAP-25 and VAMP-2 in plasma and investigate if these synaptic biomarkers hold diagnostic potential for Alzheimer's disease (AD) in blood.

Methods
Prototype Simoa assays for SNAP-25 and VAMP-2 were established as more sensitive versions of previously validated in-house CSF assays using high affinity detector antibodies and diluent suited for both plasma and CSF. The SNARE proteins were quantified in 333 paired samples from the SPIN cohort (96 AD dementia [dAD], 193 prodromal AD [pAD] and 44 cognitively unimpaired controls) using the same assay conditions for each fluid type, except for the dilution factor.

Results
All samples were detected within the measuring range of VAMP-2 (500 – 0,5 pg/mL) and SNAP-25 (25 – 0,02 pg/mL). Plasma inter-run variability was 9,1% (SNAP-25) and 13,5% (VAMP-2). The mean intra-assay variability on the clinical measurements was below 10% for both SNAP-25 (CSF: 2,8%, plasma: 5,8%) and VAMP-2 (CSF: 2,6%, plasma: 4,2%). SNAP-25 increased significantly in plasma and CSF of pAD and dAD patients compared to controls (all p-values<0.0001). VAMP-2 was significantly elevated in CSF at the pAD stage (p=0,018) versus controls, but no changes were observed in plasma. An overall strong correlation between VAMP-2 and SNAP-25 levels was present in CSF (Spearman rho=0,825, p<0.0001), but this correlation was lost in plasma. Plasma SNAP-25 (AUC=0,755, p<0,0001) performed equally well as CSF SNAP-25 (AUC=0,737, p<0,0001) to discriminate AD patients from controls.

Conclusions
Two novel sensitive digital immunoassays can measure SNAP-25 and VAMP-2 robustly in plasma. SNAP-25 is a promising novel synaptic blood biomarker for AD that requires validation in independent cohorts. Exploration of the relationship with in vivo PET imaging of synaptic density could inform on the physiological basis of plasma SNAP-25 changes in AD.