NOVEL SIMOA ASSAY FORMATS CAPABLE OF MEASURING VAMP2 AND SNAP25 IN PLASMA AND CSF: ANALYTICAL VALIDATION ASPECTS (0382)

Topic
Theme A: ?-Amyloid Diseases

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Aims
New developments in ultra-sensitive measurements of brain-specific proteins are likely to change the Alzheimer diagnostic criteria, but analytical aspects of assay performance are often poorly reported. In this work we describe an approach to develop two promising CSF biomarkers, pre-synaptic VAMP2 and SNAP25, into an assay format capable to measure analytes in plasma and CSF.

Methods
Novel Simoa immunoassays were optimized for two matrices and quantified presynaptic VAMP2 and SNAP25 in a paired CSF-plasma clinical cohort in which CSF synaptic markers were available for half of the samples.

Results
For both synaptic markers, a change of detector antibody allows for an improved analytical sensitivity of at least 4-fold. Other optimizations of the two assays included buffer formulation, dilution factors and the use of peptide calibrators. For VAMP2, we were able to quantify VAMP2 levels in all samples with an optimal dilution factor of 16. Compared to a previously described clinical CSF study, the clinical performance of this new VAMP2 format was confirmed: Bland-Altman method comparison showed less than 10% deviation on the absolute VAMP2 concentrations between the two formats. With a dilution factor of three we were also able to quantify VAMP2 in all plasma (n>350) but one. Plasma precision profiles ranges from 0,1-16,7% with an median of 3,5%, while for CSF this was 4% (0,02-17,7%). SNAP25 data are being generated and will be reported side-by-side with VAMP2.

Conclusions
Using a rational approach, we have demonstrated analytically validated formats for two synaptic proteins in CSF and plasma. Further Clinical performance evaluation with respect to recent promising plasma biomarkers will determine potential added value for Alzheimer or dementia diagnosis of these synaptic markers in plasma.