Paired phosphorylated and unphosphorylated peptides at sites T181, S202, T205 and T217 were quantified. Relationships between tau phosphorylation and [18F]GTP1 SUV was assessed using Spearman correlation analysis. The false discovery rate (FDR) for ROI-level correlation analyses was controlled using the Benjamin-Hochberg procedure. Results: [18F]GTP1 SUV and CSF tau phosphorylation increased with disease severity (expressed as the ratio of phosphorylated to unphosphorylated peptides). Spearman correlation analysis reveals that in n=38 individuals T217 (r=0.69) and T205 (r=0.55) are more correlated with [18F]GTP1 (whole-cortical gray) SUV than T181 (r=0.28). Correlations strengthen when using a more specific AD-meta ROI (Jack et al., 2017) to calculate [18F]GTP1 SUV, with T217 having the strongest correlation (r=0.81) (T205, r=0.63, T181 r=0.35). Preliminary comparisons of different regional analyses of [18F]GTP1, and relationships with cognitive endpoints may also be presented. Conclusions: These results provide insight into the relationship between tau PET imaging and CSF tau-phospho tau, and may help guide the usage and interpretation of biomarker data in the clinic. CSF species containing phosphosites T217 and T205 may be more closely reflective of tauopathy, as detected by tau PET.

**O3-14-04** THE PROTEIN-TO-PEPTIDE RATIO IMPROVES THE PERFORMANCE OF MICROTUBULE-ASSOCIATED PROTEIN TAU IN CSF AS AN ALZHEIMER BIOMARKER

Karl Hansson1, Rahil Dahlin2, Oskar Hansson2, Elin Pernevik1, Ross W. Paterson1, Jonathan M. Schott2, Nadia Magdalinitou2, Henrik Zetterberg2, Kai Bjellqvist2, Johan Golomb3,4,1 University of Gothenburg, Malmö, Sweden; 2Clinical Memory Research Unit, Lund University, Lund, Sweden; 3Dementia Research Centre, University College London, Institute of Neurology, London, United Kingdom; 4Dementia Research Centre, Institute of Neurology, University College London, London, United Kingdom; 5Dementia Research Centre, University College London, Institute of Neurology, London, United Kingdom; 6Clinical Neurochemistry Laboratory, Sahlgrenska University Hospital, Mölndal, Sweden; 7Sahlgrenska Academy at the University of Gothenburg, Mölndal, Sweden; 8Sahlgrenska University Hospital, Mölndal, Sweden; 9University of Gothenburg, Gothenburg, Sweden. Contact e-mail: johan.golomb@neuro.gu.se

Background: CSF concentrations of the tau protein and a phosphorylated tau form are, together with the peptide amyloid B42, are well established biomarkers of Alzheimer’s disease. While the most commonly used commercial tau immunoassays measure the total tau concentration (T-tau) and tau phosphorylated at Thr-181 (P-tau), several truncated and modified tau forms have been recently identified in CSF that may relay additional information of diagnostic value.

Methods: We evaluated the diagnostic potential of a recently identified endogenous peptide in CSF originating from the tau protein; tau 175-190, in the non-phosphorylated state and with phosphorylation at the Thr-181 residue. We established an LC-MS method based on parallel reaction monitoring to measure these peptides in CSF and used the method to analyze a cohort composed of patients with Alzheimer’s disease, Parkinson’s disease, progressive supranuclear palsy, and healthy controls, and a second cohort consisting only of Alzheimer patients and healthy controls. T-tau and P-tau concentrations were determined by ELISA. Results: We found that, while the abundances of tau 175-190 and P-tau 175-190 were not altered in any of the disease groups, the separation of Alzheimer’s disease patients and controls by T-tau and P-tau was improved when normalizing the ELISA measurement results to the concentrations of the non-phosphorylated and phosphorylated endogenous peptide, respectively. This finding was verified in the second cohort. Conclusions: In conclusion, the performance of T-tau and P-tau as Alzheimer’s disease biomarkers can be improved using the same proteomics workflow in an independent cohort consisting of 17 DLB patients (age 67±7yr; 24%F; MMSE 24±4) and 13 cognitively normal controls (age 66±8yr; 30%F; MMSE 28±2). Results: In the discovery cohort 57 out of 2100 identified proteins were differentially expressed in DLB patients compared to controls (p<0.05). 35 proteins were down-regulated and 22 proteins were up-regulated in DLB. 18 proteins fulfilled all three selection criteria for candidate biomarkers. In the validation cohort, 68 out of 2289 identified proteins were differentially expressed (p<0.05). 34 proteins were down-regulated and 34 proteins were up-regulated in DLB. 38 proteins fulfilled all three selection criteria. Three highly significant overlapping candidate biomarkers were found. All three proteins were down-regulated in DLB and are involved in synaptic plasticity. Logistic regression analysis showed that a biomarker panel consisting of these three proteins could discriminate DLB from controls (AUC: 0.81 [95% CI: 0.65-0.97]). Conclusions: Our proteomics analysis of CSF identified and validated several novel potential candidate biomarkers for DLB. The identified proteins could aid in early diagnosis of DLB.