criteria, 2004), recruited at 19 centers (Spain, Italy, Sweden and France) in longitudinal trial (AB255). All were clinically assessed (neuropsychological evaluation and neurological examination) at baseline and during the follow up at 12 and 24 months. Structural-MRI, FDG-PET, and APOE genotyping were performed in all subjects at baseline. An amyloid-PET study (11C-PIB) was additionally carried out in a subset of 59 subjects. An individual voxel-based analysis (Arbizu, et al. Eur J Nucl Med Mol Imaging, 2013) was used for FDG-PET evaluation. The parameters AD-index (similarity between each individual z-score map and the AD pattern); MCI-index (similarity between each individual z-score map and the posterior cingulate map); and AD conversion score (computation of age, gender, MIC-index, MMSE-score and APOE4 genotype), were explored according to the clinical diagnosis at baseline and at 24 months (stable-CN, stable-MCI, converted-MCI to AD) Besides, we analyzed the correlation between these parameters and PIB-PET Aβ-positivity (SUVR≥1.4). Descriptive values (Mean, SD, Median, IQR) are reported, and differences were explored using the Mann-Whitney-U test. **Results:** At baseline, FDG-PET risk parameters were found to be significantly higher in a-MCI subjects compared to CN: AD-index 43,36 (61,35) vs. 0,25 (1,85), p<0.001; MCI-Index 2,15 (13,3) vs. 0,0 (0,08), p<0.001; AD-Conv-Score 0.3202 (0.47) vs. 0.0876 (0.04), p<0.001. At 24 months, the differences were: AD-index 13,2 (31) stable-MCI vs 26 (89,95) converted-MCI (p<0.001), and vs. 0,3 (1,90) stable-CN (p<0.001); MCI-Index 0,9 (10,8) stable-MCI vs. 4,5 (30,85) converted-MCI (p<0.006), and vs. 0 (0,1) Stable-CN p<0.001, respectively); AD-Conv-Score 0,2683 (0,36) stable-MCI vs. 0,4087 (0,63) converted-MCI (p<0.006), and vs. 0,0893 (0,04) stable-CN (p<0.001). The subgroup of 11C-PIB positive subjects, showed significantly higher values respect to 11C-PIB negative: AD-Index_Aβ+ (45.08±58.39) vs. Aβ- (10.5±33.28, p0.002), MCI-index_Aβ+ (2.12±8.68) vs. Aβ- (8.99±12.58, p0.001), and AD-Conv-Score_Aβ+ (0.3840±0.259) vs. Aβ- (0.1331±0.162, p0.001). **Conclusions:** FDG-PET parameters obtained at the baseline in a-MCI subjects can be useful to identify in an appropriate way those subjects at higher risk of progression to AD dementia in 24 months. Subjects with higher risk of conversion according to FDG-PET parameters, exhibit a higher cortical Aβ burden. Therefore, further analysis in an individual bases to establish the usefulness of FDG-PET in the clinical setting are warranted.

## OP-709

### The value of combining molecular and structural imaging biomarkers with psychometric data in a system for predicting neurological decline validated by a 3 year outcomes study

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**Objectives:** A computer-based application for providing decision support in dementia, including predictions of cognitive decline based on imaging and other biomarkers, was developed by an EU framework-7 funded "PredictND" consortium. Here, this application was used with baseline PET and MRI imaging and psychometric scores to predict the cognitive trajectory of 222 amnestic mild cognitive impairment (aMCI) subjects. The prognostic indication was tested against known 3-year outcomes for these subjects. **Methods:** In this study, the system was trained with data from 244 cognitively normal subjects and 241 probable AD (pAD) subjects. The imaging data consisted of structural information derived from T1 3D MRIs and composite standard uptake value ratios (SUVRs) derived from [$^{18}$F]flutemetamol PET amyloid images, together with psychometric scores. The validation dataset comprised the same imaging/psychometric metrics[FG(H1] [BC(H2] [BC(H3] derived from of 222 subjects at baseline obtained from GE Healthcare's GE067-005 study. The subjects in this study were cognitively assessed by a clinical adjudication committee every 6 months to test for conversion to pAD. The baseline image data were stratified in a separate post-hoc analysis into four groups where their amyloid status (A-, A+) and their neuronal injury status (N-,N+) determined by threshold of hippocampal volumes. The system computed a Disease State Index (DSI) for each subject and these were compared against a Kaplan-Meier survival (non-conversion to AD) analysis which computed the survival fractions (SF) for the four (A,N) combinations. **Results:** Low computed DSI values predicted a high survival (non conversion to dementia) fraction (A-,N- group) and high values predicted a low survival fraction (A+,N+ group). The DSI's were also concordant with the (A+,N-) and (A-,N+) outcomes: (A- N-) 83 subjects with a median DSI of 0.16 (DSI-1 = 0.84) and a Kaplan-Meier Survival Fraction of 0.86 (A- N+) 42 subjects with median DSI of 0.43 (DSI-1 = 0.57) and a Kaplan-Meier Survival Fraction of 0.53 (A+ N-) 40 subjects with median DSI of 0.5 (DSI-1 = 0.5) and a Kaplan-Meier Survival Fraction of 0.46 (A+ N+) 40 subjects with median DSI of 0.91 (DSI-1 = 0.09) and a Kaplan-Meier Survival Fraction of 0.12 **Conclusions:** In this study, the use of the PredictND tool, which incorporates T1 MRI results, SUVRs from amyloid PET imaging, and psychometric data, provided DSI values that accurately predicted clinical status 3 years later. This study demonstrates that the predictive system provides accurate and useful prognostic information for patients at risk of AD dementia.

## OP-710

### Neuronal Injury Biomarkers for Assessment of Cognitive Reserve in Alzheimer's Disease

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**Introduction:** The model of cognitive reserve has been extensively investigated in patients with Alzheimer's Disease (AD). Many factors could be identified as being influencing or predictive for a higher cognitive reserve. Neuronal injury correlates with cognitive decline in AD with [$^{18}$F]-fluordesoxyglucose positron-emission-tomography (FDG-PET), structural MRI and total tau in cerebrospinal fluid ($CSF_{t\text{-}tau}$) as the most important biomarkers of neuronal injury according to the A/T/N-classification. The aim of this study was to compare neuronal injury biomarkers with the cognitive performance and further cognitive development to evaluate their potential to predict the individual cognitive reserve. **Subjects & Methods:** In 110 mild cognitive impaired and demented subjects (age 71 ± 8 years) with a final diagnosis of AD dementia were assessed at baseline by mini-mental-state-examination (MMSE), FDG-PET, MRI and $CSF_{t\text{-}tau}$. Using partial correlation, we tested first for each neuronal injury marker the correlation with MMSE, controlled for age, gender and leukoencephalopathy. Next using multiple regression analysis, we calculated the expected MMSE score based on neuronal injury markers and covariates ($MMSE_{NI}$). The residuals of the partial correlation for each biomarker and the difference between $MMSE_{NI}$ and $MMSE_{CLI}$ were correlated with the cognitive outcome of patients at clinical follow-up (27 ± 13 months). **Results:** FDG-PET correlated highly with $MMSE_{CLI}$ ($R = -0.49$, $p < 0.01$), whereas hippocampal atrophy in MRI ($R = -0.15$, $p = 0.14$) and $CSF_{t\text{-}tau}$ ($R = -0.12$, $p = 0.22$) showed only weak correlations. High neuronal injury relative to cognitive performance was associated with more pronounced cognitive deterioration at follow-up for the residuals of FDG-PET ($R = -0.40$, $p = 0.005$) and the combined model ($R = -0.43$, $p = 0.04$). **Conclusions:** The residuals in the correlation of neuronal injury in FDG-PET and cognitive performance represent the individual cognitive reserve in patients with AD and may allow a prediction of an individual's clinical course. Thus, the individual cognitive reserve should be considered as a covariate in therapeutic trials.

## OP-711

### Characterization of disease-specific covariance patterns of neurodegeneration in FTLD-variants

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**Aim:** Frontotemporal lobar degeneration (FTLD) is the most common form of dementia after Alzheimer's disease and covers a whole spectrum of clinically separable diagnoses, including the behavioral variant (bvFTD) as well as the non-fluent (nfvPPA), semantic (svPPA) and logopenic (lvPPA) variants of primary progressive aphasia. Our primary goal here was to characterize disease specific metabolic patterns usable in an automated, data-driven diagnostic approach to help in the early classification to a specific clinical diagnosis. **Materials and Methods:** FDG PET was performed in a total of 102 patients with FTLD at 10 different German centers (bvFTD: n=55, nfvPPA: n = 19, lvPPA: n = 15 and svPPA: n= 13). Clinical diagnosis was confirmed by clinical follow-up of at least one year after the PET scan. The data was supplemented by a set of 24 healthy controls of similar age and gender from the ADNI-database. All files were spatially normalized and voxel-wise T-tests were performed to compare FTLD variants against healthy controls. Secondly, a group-wise scaled subprofile modelling/principal component analysis (SSM/PCA; according to Eidelberg et al. Trends Neurosci 2009) was performed to identify covariance patterns with respect to a sample of healthy controls. **Results:** Areas of strongest hypometabolism in the voxel-wise T-test were bilateral frontal cortex for bvFTD, left temporo-parietal cortex and precuneus for lvPPA, temporopolar cortex (left >> right) for svPPA and left centro-mesial and perisylvian frontolateral cortex for nfvPPA. Similar regions were also identified as main components explaining a relevant amount of variance in the group-wise SSM/PCA approach. **Conclusion:** Typical patterns of neurodegeneration were characterized in a cohort of 109 patients with clinically confirmed FTLD. Group-wise combinations of the components identified in the SSM/PCA method seem to be suitable to characterize disease specific patterns for bvFTD, lvPPA, nfvPPA and svPPA in an automated, data-driven approach. Once validated, these patterns can be used to score the respective expression strength in individual patients with respect to healthy controls and thereby assist in differential diagnosis of suspected FTLD.

## OP-712

### Determination of FTD Candidates in an MCI-SNAP Cohort by PET Amyloid and MRI Structural Analysis

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**Introduction:** GE Healthcare conducted a 3-year outcome study in which 232 patients with amnestic Mild Cognitive Impairment (aMCI) underwent baseline amyloid PET imaging with [$^{18}$F]flutemetamol to determine time to conversion to dementia in relation to baseline amyloid status. Conversion was determined by an independent clinical adjudication committee (CAC) which reviewed the results of 6-monthly neuropsychiatric testing for up to 36 months. While amyloid positivity was a significant and independent predictor of conversion, a fraction (23%) of the amyloid-negative subjects (suspected non-Alzheimer's pathology - SNAP) also converted in the 3-year study window. In a post hoc analysis, we determined the number of these amyloid negative subjects who were candidates for Frontotemporal Dementia (FTD) based on their right-hemisphere temporal pole to occipital lobe cortical thickness. **Methods:** In this analysis, the subjects' [$^{18}$F]flutemetamol PET Standard Uptake