unpenalized stepwise regression when number of parameters approached or exceeded the number of training cases. Partial volume correction had a negative effect on the predictive performance of AV45-PET, but slightly improved the predictive value of FDG-PET data. **Conclusions:** Penalized regression yielded more parsimonious models than unpenalized stepwise regression for the integration of multiregional and multimodal imaging information. The advantage of penalized regression was particularly strong with a high number of collinear predictors.

IC-04-03 GREY MATTER NETWORK DISRUPTIONS ARE RELATED TO AMYLOID-BETA IN COGNITIVELY HEALTHY ELDERLY

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Background: Grey matter networks are disrupted in Alzheimer's disease. It is unclear when these disruptions start during the development of Alzheimer's disease. Amyloid deposition is among the earliest changes. A recent study demonstrated that abeta 42 affects grey matter networks. But since this network was derived at a group level these results could not be associated with risk of individual patients. Here we studied the effects of abeta 42 on single- subject grey matter networks in cognitively healthy elderly. **Methods:** Study participants were 193 cognitively healthy middle aged adults enrolled in the Gipuzkoa Alzheimer Project (GAP), a longitudinal study on pre-clinical AD recruiting subjects from the general population. Inclusion criteria were a MMSE $>$ 25 and a clinical dementia rating $=$ 0. CSF was obtained by lumbar puncture following international consensus recommendations. Levels of abeta 42 were determined with ELISA kits (InnotestTM β Amyloid1 42, Fujirebio Innogenetics). T1 weighted structural MRI scans were obtained at 3T. Native space grey matter segmentations (obtained with SPM8) were used to extract single subject grey matter networks. Normalized clustering coefficient γ and normalized path length λ were computed. Non parametric testing (based on 10.000 random permutations) was used to determine the significance of relationships between abeta42 deposition (dependent variable) and network property values (independent variable), including gender, whole brain volume and age as covariates. Multiple hypotheses testing was corrected for with false discovery rate (FDR). **Results:** All subjects had an age range between 39 and 79 years old (mean age $=$ 57 years), and 58% were female. Lower abeta42 CSF levels, indicative of a higher plaque load in the brain, were associated with lower connectivity density (β = 0.20; SE .07); p $<$ .05), lower clustering values (β = .18; SE =.08; p $<$ .05) and higher path length values (β = .21, SE =.08, p $<$ .01). Figure 1 shows the anatomical areas where lower clustering coefficient was related to decreased abeta42 CSF levels, and 6 areas in which higher path length values were associated with decreased abeta42 CSF levels. **Conclusions:** These results suggest that grey matter networks might have use as an early marker for AD pathology.

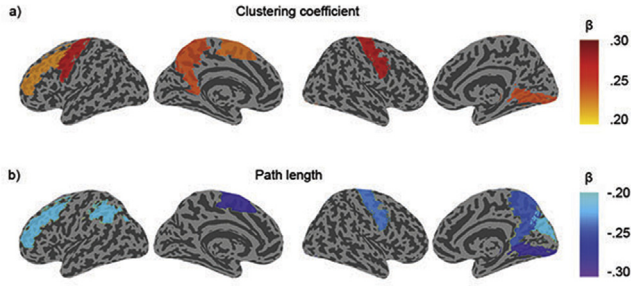

Figure 1. Surface plot of the standardised β values of the relationship between abeta42 with clustering and path length that were significant ($p_{FDR} < .05$). a) Lower clustering values were associated with low Aβ42 values in the bilateral precentral gyri, left precuneus, supplementary motor area, middle frontal gyrus and right lingual gyrus. b) Higher path length values in the left supplementary motor area, inferior parietal gyrus, middle temporal gyrus, right precuneus, lingual gyrus, precentral gyrus and cuneus were associated with low abeta42 CSF values.

IC-04-04 OPTIMIZING PIB-PET CHANGE-OVER-TIME MEASUREMENT BY ANALYSIS OF LONGITUDINAL RELIABILITY, PLAUSIBILITY, AND SEPARABILITY

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Background: Automatic measurement of Standardized Uptake Value Ratio (SUVR) from PiB-PET images is complicated by many methodological and implementational choices, such as reference region, gray matter (GM) target segmentation, and use of partial volume correction (PVC). These variations directly influence measurement reproducibility and confound cross-site comparability. Such choices have been hotly debated in the literature, but few studies have examined reliability, plausibility, or separability of change-over-time values, despite their potential importance for amyloid-modifying clinical trials. **Methods:** We studied 68 participants in the Mayo Clinic Study of Aging and Alzheimer's Disease Research Center studies with 3 serial PiB-PET scans each. Pseudo-steady-state (late uptake) PiB scans were registered to corresponding 3T T1-w MP-RAGE MRI, and an in-house standard template/atlas was warped to each MRI using ANTs software. Cortical GM was segmented using SPM12b and Longitudinal Freesurfer 5.3. PiB scans were (optionally) PVC'ed using a two-compartment (Meltzer) model. We calculated SUVR values for each PiB scan using 180 total variations, each with a different combination of reference, target, and PVC. **Results** were analyzed using a linear mixed-effects model. We compared methods on three independent criteria: longitudinal reliability (R^2 of serial