**Methods:**

We perform factor analysis to derive a set of data-defined uptake topographies, or groups of brain regions that accumulate deposits in a positively or negatively correlated manner. The resulting factor scores, representing the extent to which specific topographies are manifest in a scan, serve as summary uptake measures unbiased by assumptions of regions of interest or reference regions.

The particular brand of factor analysis we used is called Nonparametric Sparse Factor Analysis [1] (NSFA), which optimizes for sparsity (and hence, interpretability) of latent topographical factors, while allowing the number of factors to grow as needed. We fit the model to 89 baseline AV1451 PET scans in the Alzheimer’s Disease Neuroimaging Initiative (ADNI) database, belonging to 31 Cognitively Normal (CN), 11 Subjective Memory Concern (SMC), 19 Early Cognitive Impairment (EMCI), 19 Late Cognitive Impairment (LMCI), and 9 Alzheimer’s Disease (AD) subjects.

To convert AV1451 scans into an input format amenable for factor analysis, we represent each scan as a vector consisting of the partial volume corrected means of 40 bilateral Freesurfer-defined brain regions. Each scan vector is normalized by its l1-norm, and then each region value is standardized to a z-score across all subjects. In other words, each input value represents the percentage contribution of a particular region to the total scan signal, normalized to standard deviations above the population mean.

The model was fit via Gibbs sampling. Results were averaged over the last 100 samples out of 10,000, and the model converged to K=12 factors.

[1] “Nonparametric Bayesian sparse factor models with application to gene expression modeling” by D. Knowles and Z. Ghahramani, 2011