Supplementary Data

Analytical procedures

Laboratory analyses

All laboratory analyses were performed by using standard methods in Turku University Hospital, and as previously described (1, 2).

Quantification of brain glucose uptake

Plasma input functions were visually checked, and in cases where the peak of the tracer in plasma was not adequately captured, an input recovery approach was used with an in-house implementation of the method described by Feng *et al* (3). PET data were processed using the automated Magia toolbox (4). During preprocessing, dynamic data were first motion-corrected; for static images the motion-correction step was skipped. Then for each individual we used a brain [^{18}F]FDG radioactivity template to estimate a transformation from the Montreal Neurological Institute space to the subject's individual space. We applied the transformation on Wake Forest University atlas-derived brain lobes (frontal, temporal, parietal, occipital, and limbic), and calculated regional fractional uptake rate (FUR) by dividing brain radioactivity in each lobe by the time-integral of the plasma radioactivity curve (5).

Statistical modelling

As the sample consisted of 'late' and 'early' scans, we used an independent data set consisting of subjects scanned in both conditions (N = 18) to estimate the difference between timing of scanning prior to running the statistical model. These analyses were also done using the BRMS package. Compared to the scans starting from injection, the 'late' scans had approximately 24% lower BGU, with a standard error of 1%. This information was incorporated into the prior distribution for the main

statistical analyses. For the standard deviation, we used 0.1 instead of 0.01 because in the larger data set the 'late' scans were somewhat different from the independent data set (*i.e.* delay since the injection, duration of the scan), and the original standard deviation did not capture these sources of uncertainty. For all other predictors, we used a zero-mean Gaussian distribution with standard deviation of 1 to provide weak regularization, which is useful when the predictors correlate, as they did here (**Supplementary Figure 1**, correlation matrix of the predictors). All other priors were the defaults of BMRS: for intercepts, we used the Student's t-distribution with scale 3 and 10 degrees of freedom. Half Student's *t*-distribution with 3 degrees of freedom was used for standard deviations of group-level effects; BRMS automatically selects the scale parameter to improve convergence and sampling efficiency. LKJ(1) was used as the prior for correlations of group-level random effects. The models were estimated using 15 chains, each of which had 1000 warmup samples and 2000 post-warmup samples, thus totaling 30000 post-warmup samples. The sampling parameters were modified to facilitate convergence (*adapt_delta* = 0.999; *max_treedepth* = 20). The sampling produced no divergent iterations and the Rhats were all 1.0, suggesting that the chains converged successfully. Before model estimation, continuous predictors were standardized to have zero mean and unit variance, thus making the regression coefficients comparable across predictors. BGU values were log-transformed because posterior predictive checking (6, 7) indicated that log-transformation significantly improves model fit. The log-transformation essentially switches the model from additive to multiplicative; it also helps in model fitting because the assumption of linear additivity works poorly when the dependent variable is restricted to positive value (8).

Supplementary Figure 1- Correlation matrix of the parameters tested as predictors of brain glucose uptake. The numbers in each square show the Pearson correlation coefficient (*r*).

References

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