ADVANCING THE ACCURACY OF AUTOMATED FDG-PET MEASUREMENTS USING HIGH-DIMENSIONAL IMAGE NORMALIZATION

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Background

Fluorodeoxyglucose (FDG)-PET imaging is among the most important imaging modalities for in-vivo research on Alzheimer's disease. The gold standard for regional quantification of PET signal relies on manual delineation of anatomical regions-of-interest (ROIs) on coregistered high-resolution structural MRI scans of the same subject. Analysis of large-scale imaging datasets has been made possible through the development of automated image analysis techniques employing spatial normalization of the PET images to a standardized reference space with associated atlases of anatomical ROIs. Novel high-dimensional image warping algorithms for MRI allow matching individual images to a given reference template with much higher accuracy compared to earlier low-dimensional implementations. The potential benefits of these novel normalization procedures for the accuracy of automated FDG-PET measurements have not yet been investigated.

Methods

Hand-drawn hippocampus labels based on a harmonized delineation protocol were recently published for a subset of 100 subjects from the Alzheimer's Disease Neuroimaging Initiative. Coincident FDG-PET scans were available for 38 of these subjects and were rigidly coregistered to their corresponding MRIs. Quantification of hippocampal tracer-uptake was carried out using SPM8 software and the VBM8-toolbox and followed 4 different analysis approaches: (i) the “gold standard” of direct signal extraction within individual hippocampus labels in native space, as well as automated extraction within harmonized hippocampus labels in standard reference space using (ii) direct low-dimensional normalization of the PET scans to SPM's default H2O-PET template (“standard direct”), (iii) indirect normalization using parameters from standard low-dimensional normalization of the coregistered MRI (“standard indirect”), and (iii) indirect normalization using parameters from high-dimensional normalization of the coregistered MRI (“DARTEL”).

Results

Automatically estimated values for hippocampal FDG-uptake using “DARTEL” were highly correlated with the values extracted using the “gold standard” method (R2(left/right) = 0.94/0.93), with a mean percentage divergence below 3%. The correlations were significantly higher compared to those using “standard direct” (R2(left/right) = 0.85/0.87, p(difference) < 0.001/0.05) and “standard indirect” (R2(left/right) = 0.91/0.84, p(difference) < 0.01/0.0001) normalization strategies.

Conclusions

Even though PET images are generally limited by relatively low spatial resolution, novel high-dimensional image normalization techniques may still significantly improve the accuracy of automated regional signal measurements compared to more traditional normalization strategies.