

MRI-derived, ROI-based Whole-brain Comparison of FDG- and PIB-PET in Prodromal and Mild Alzheimer's Disease

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INTRODUCTION: [C11] PIB-PET (amyloid imaging agent) and [F18] FDG-PET have the potential to serve as non-invasive biomarkers for the diagnosis and treatment monitoring of Alzheimer's Disease (AD). Previous PET studies have relied principally on manually drawn ROIs or automatically-derived, template-based methods. Manual drawing of ROIs is time consuming and subject to inter- and intra-rater variability. Template-based methods are faster, but can be inaccurate depending on the choice of template. Toward improving this reliability, we have applied a nearly-automated procedure for quantifying PET activity within subject-specific, MRI-derived anatomical ROIs using data from the Alzheimer's Disease Neuroimaging Initiative (ADNI).

METHODS: We studied 69 subjects cross-sectionally from the ADNI database (16 controls (NC), mean age 78.4y; 39 MCI, 75.7y; 14 AD, 74.6y). Groups did not differ in age or gender distribution. ANOVAs, as expected, did show significant group differences for MMSE ($F = 31.7, p < .001$) and CDR ($F = 189, p < .001$). For each subject, FDG- or PIB-PET frames were averaged and registered to the corresponding distortion-corrected and intensity-normalized MRI volume. ROIs were derived from MRI images using an enhanced version of the FreeSurfer software. Aside from minimal manual editing of topological errors and visual quality assurance of results, these procedures are fully automated. A total of 44 ROIs were examined, after averaging left and right hemispheres. PET activity was averaged within each ROI and normalized to the activity within the pons. ANCOVA analyses were then performed to examine group differences while co-varying age and gender.

RESULTS: We observed significant omnibus group effects in multiple ROIs: In FDG-PET scans, ROIs with the greatest group effect included lateral temporal, middle temporal and inferior parietal cortices ($p < .005$ and $F > 6$); posterior cingulate cortex ($p < .01, F > 5$); entorhinal cortex and hippocampus ($p < .05, F > 3$). Group effects for FDG-PET were not significant in any frontal ROIs. In contrast, ROIs showing the greatest PIB-PET group differences included medial orbital frontal, lateral orbital frontal and rostral middle frontal cortices ($p < .005, F > 6$). Smaller group differences were observed in inferior temporal and middle temporal ROIs ($p < .05, F > 4$) while group differences in PIB-PET activity were not significant in the hippocampus, entorhinal cortex, posterior cingulate and inferior parietal cortex.

CONCLUSIONS: Significant group differences were found across groups in temporoparietal ROIs in FDG-PET scans in agreement with previous studies showing reduced metabolism in temporoparietal regions. PIB-PET scans showed group differences which were qualitatively different, exhibiting only modest or insignificant group effects in temporoparietal ROIs, but strong effects in frontal ROIs. The disassociation between amyloid plaque burden and glucose metabolism is in agreement with other studies and raises the question of the role of plaque formation in neurodegeneration. The present results also demonstrate the feasibility of using automated MRI-derived, ROI-based analyses for evaluation of structure-specific metabolism and PIB uptake in large-scale clinical trials.

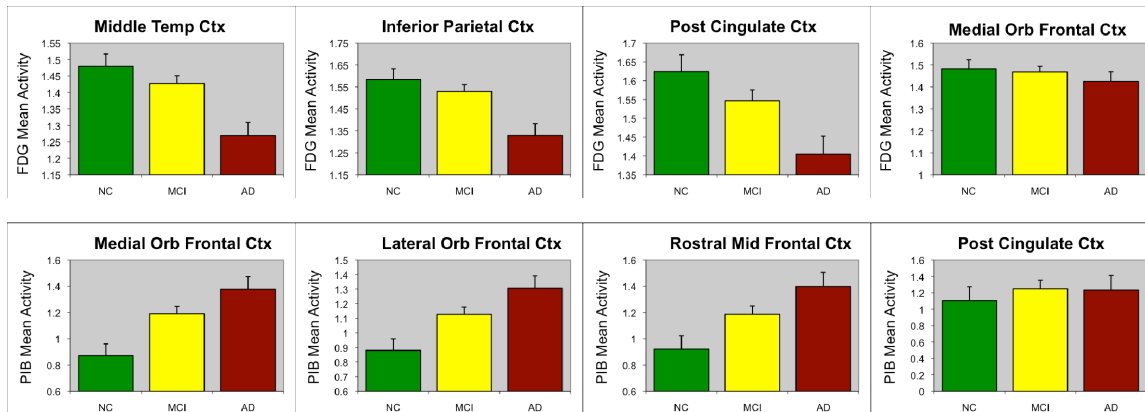


Figure 1: Mean activity for select ROIs for FDG-PET (top) and PIB (bottom): Activity normalized to pons. Y-axes scaled to data. Error bars=SE.

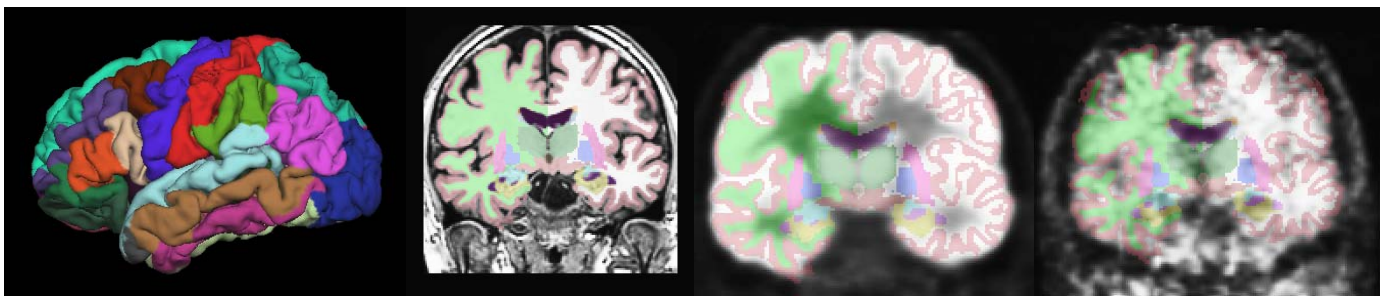


Figure 2: (left) Automated, subject-specific cortical MRI parcellation of a healthy control subject (PET activity was sampled onto the cortical surface; not shown). ROIs on the lateral surface include inferior (violet), middle (brown), and superior (light blue) temporal cortices, caudal (brown) and rostral (purple) midfrontal cortices and inferior parietal cortex (pink).

MRI subcortical segmentation (middle left) and the segmentation applied to the co-registered PET volume, FDG (middle right) and PIB (right). Regions of interest include amygdala (sky blue), hippocampus (gold), caudate (blue), putamen (pink), thalamus (green) and lateral ventricle (purple). The right and left hemisphere white matter (green and white, respectively) and grey matter (maroon) are also shown.