Preliminary Cross-Sectional MRI-derived ROI-based Analysis of PET Data from the Alzheimer's Disease Neuroimaging Initiative

D. S. Karow[1], C. Fennema-Notestine[2], D. J. Hagler Jr. [3], E. Wu[4], J. B. Brewer[5], A. S. Fleisher[5], E. T. Han[6], C. K. Hoh[4], and A. M. Dale[7]

[1]Radiology, University of California, San Diego, La Jolla, CA, United States, [2]Psychiatry, University of California, San Diego, CA, United States, [3]Cognitive Science, University of California, San Diego, CA, United States, [4]Radiology, University of California, San Diego, CA, United States, [5]Neurosciences, University of California, San Diego, CA, United States, [6]Global Applied Science Laboratory, GE Healthcare, Menlo Park, CA, United States, [7]Neurosciences and Radiology, University of California, San Diego, CA, United States

INTRODUCTION: PET is an imaging modality with potential applicability to the diagnosis and treatment monitoring of Alzheimer's Disease (AD). Previous PET studies have relied principally on manually drawn ROIs to evaluate regional metabolism. More recently, automatically-derived, MRI-based ROI procedures have been employed, but have been less reliable. For example, few have reported reductions in metabolism in the hippocampus in either mild cognitive impairment (MCI) or AD. Toward improving this reliability, we have applied an automated procedure developed within the Morphometry BIRN for quantifying PET activity within MRI-derived anatomically-defined regions-of-interest (ROIs) derived from the initial set of Alzheimer's Disease Neuroimaging Initiative (ADNI) subjects.

METHODS: We studied 112 subjects from the ADNI database (41 controls (NC), mean age 75.7y; 47 MCI, 74.2y; 24 AD, 76.1y). For each subject, FDG-PET frames were averaged and registered to the corresponding distortion-corrected and intensity-normalized MRI volume. ROIs were derived from MRI images using FreeSurfer/BIRN procedures. PET activity was averaged within each ROI and normalized to the brainstem activity. Regression analyses were then performed to examine group differences while controlling for age. Cortical surface maps were generated to analyze average differences in activity between diagnostic groups. To generate these maps, normalized PET activity for each subject was sampled onto their respective cortical surface. Surface-registered activity within each diagnostic group was averaged in spherical atlas space.

RESULTS: We observed significant activity reductions in AD and MCI groups in the left hippocampus and left entorhinal cortex (AD vs. NC $p<.001$; AD vs. MCI $p<.005$; MCI vs. NC $p<.01$) as well as in the right (AD vs. NC $p<.001$; AD vs. MCI $p<.05$; MCI vs. NC $p<.05$). We also found reductions in AD groups compared to NCs in the left inferior temporal ($p<.001$), right inferior temporal ($p<.005$), left inferior parietal ($p<.001$), right inferior parietal ($p<.005$), left precuneus ($p<.001$), right precuneus ($p<.005$), left posterior cingulate ($p<.01$), right posterior cingulate ($p<.05$) and left fusiform ($p<.001$) gyri. Results for some of these ROIs are shown in Figure 1. In addition, we found greater asymmetry of regional metabolism in AD vs. NCs. Specifically, we found that the ratio of left to right hemisphere activity is lower in AD groups compared to NCs in the inferior parietal ($p<.05$), inferior temporal ($p<.005$), fusiform ($p<.01$) and posterior cingulate ($p<.005$) gyri, (data not shown). Lastly, average cortical activity maps show large bilateral reductions in activity (> 20%) between NCs and ADs in widespread temporoparietal regions, consistent with the ROI data presented above (Figure 2).

CONCLUSIONS: Significant bilateral differences were found between the NC and AD groups in temporoparietal regions. The slight hemispheric asymmetry of these regional differences in AD vs. NC suggests that the disease process underlying AD may preferentially affect the left hemisphere. Overall, these findings are in general agreement with previous studies of reduced metabolism in temporoparietal regions. Furthermore, the pattern of reduced metabolic activity is highly consistent with the pattern of cortical thinning in the same group comparisons in ADNI and previous studies. The present results demonstrate the feasibility of using automated MRI-derived, ROI-based analyses for evaluation of structure-specific metabolism in large-scale clinical trials.

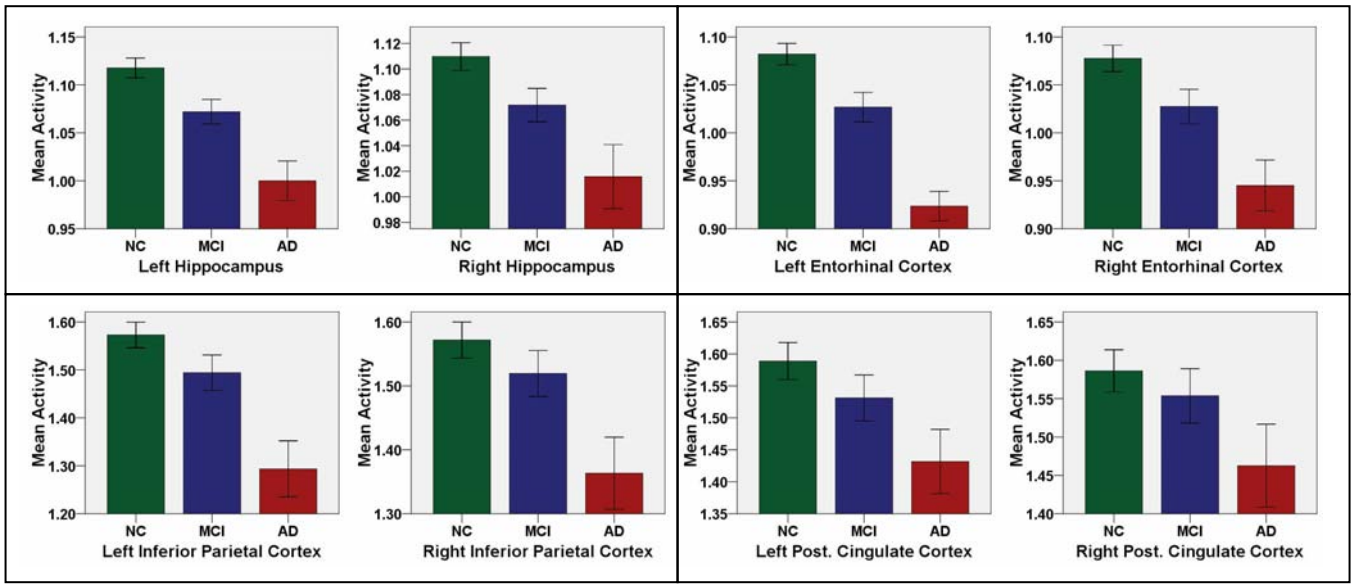

Figure 1: ROI mean activity: Activity normalized to brainstem. Error bars: +/- 1 SE. Y-axes scaled to data.

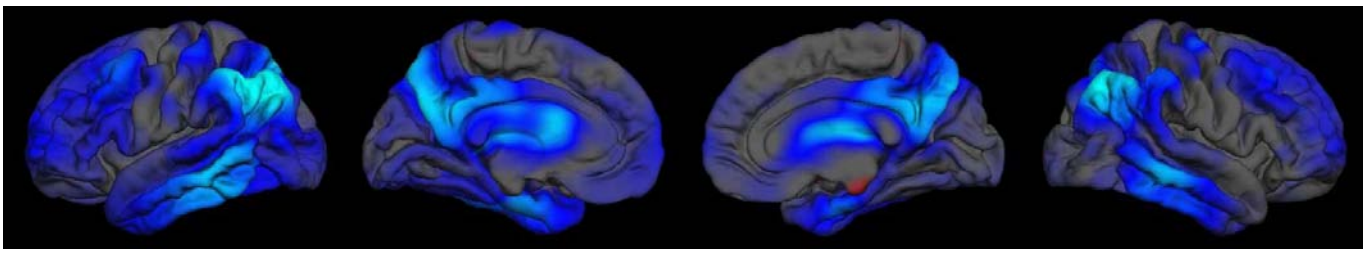

Figure 2: Cortical surface maps of average differences in activity between AD and NC. The scale ranges from -20% (blue/cyan) to +20% (red/yellow). From left to right: left hemisphere, lateral view; left hemisphere, medial view; right hemisphere, medial view; right hemisphere, lateral view.