Summary of SPM Processed Images Uploaded to LONI
Banner Alzheimer's Institute, Arizona

The Banner Alzheimer's Institute (Arizona) of the ADNI PET Core analyzes the FDG-PET data using the computer package *SPM5* (http://www.fil.ion.ucl.ac.uk/spm/) to examine the progression that correlate with changes in cognition and to evaluate cross-sectional differences among three diagnostic groups: patients with AD, patients with MCI and normal healthy controls. All PET from the post-processed group-4 images (coregistered dynamic, averaged, standardized image and voxel size and smoothed to uniform resolution of 8mm) were downloaded from the LONI website in NIFTI format. Each image was re-centered to correspond to the center of the SPM MNI template. From the SPM procedure, two images are generated for each scan of each subject. Descriptions of the image types are provided (parts A and B below). In addition, the statistical procedures are also described (C).

A, Realignment (coregistration) between followup and baseline scans For analyses involving follow-up scans, the followup FDG-PET images were first realigned to the baseline scan in each subject. The realignment was in each patient's native coordinate space resulting the same voxel-size and matrix dimension as for the baseline scan.

B, Spatial normalization to the SPM template space and smooth

SPM5 default settings were used to linearly and non-linearly deform each baseline PET image to the coordinate space of the SPM brain template, and the left-right orientation of each image was confirmed. The deformation parameters estimated for the baseline PET scan were then applied to the coregistered followup images. The resulting images were in the coordinate space of the SPM template with 2 cubic mm voxel size and 79×95×69 (in x y z) matrix dimension. The images were further smoothed by a Gaussian kernel with the full width at half maximum of 12 mm in all x, y and z directions. This smoothing is on top of the scanner specific smoothing described in the introduction.

C, Voxel-by-voxel statistical analyses

For all analyses, the global brain counts were computed by the SPM sub-routine spm_global and normalized using proportional scaling. Then appropriate statistics were calculated on a voxel-by-voxel basis to characterize and compare regional glucose hypometabolism in the three subject groups.

Analysis of variance (ANOVA) was performed to compare baseline measurements in the three subject groups. Within the framework of the ANOVA, Student t-tests were performed to compare AD patients versus MCI patients, AD patients versus controls and MCI patients versus controls.

For 6-month longitudinal analyses, ANOVA with repeated measures was used to examine the decline for each of the three diagnostic groups, and to contrast the decline differences among these three groups.

To estimate the number of subjects needed to evaluate the effectiveness of a putative treatment using data from multi-center study conducted over 6-moth period, simple paired t-tests were performed in independent analyses of the AD and MCI groups.

For all analyses, maps were generated using a statistical threshold of $P<0.001$, uncorrected for multiple comparisons for visual inspection. To address the statistical problem of multiple comparisons, the small volume correction method in SPM was used within each of the posterior cingulate/precuneus, parietal, temporal and prefrontal regions functionally defined in our previous cross-sectional comparison of AD cases and controls (Alexander et al, 2002). We further addressed this problem using the bootstrap method to examine the reliability of the detected AD/MCI hypometabolism regions with different type-I error rates ($p=0.005$, 0.001, 0.0005 and 0.0001). We then adopted the variable threshold approach originally proposed by Thomas Nichols to correct for the multiple comparisons accounting for the variation of the reliability of the brain regions affected by AD or MCI.