INTRODUCTION

• We compare results of differing PET scanner spatial resolution on effect size between group differences of standard uptake value ratio (SUVR) measurements in Florbetapir (AV45) and FDG images from the ADNI database. Most reported ADNI analyses use “Level 4” preprocessed data [Koeppe 2009] smoothed to a uniform isotropic resolution of 8mm FWHM, but there is the potential that the unsmoothed data captures more sensitive information.

METHODS

• Freesurfer was used to obtain an ROI parcellation on T1 MRI data from 458 subjects (175 Normal, 92 EMCI, 153 LMC niche, 38AD) Florbetapir and FDG data from two time points approximately 24 months apart were registered to the MRI data in T1 native space, and SUVR’s were computed at each time point. Results were obtained from both ADNI level 4 smoothed data, and from unsmoothed images (ADNI level 3) [Koeppe 2009]. Cross sectional effect sizes between AD, EMCI, LMC and Normal groups were evaluated using Cohen’s d. Effect size of longitudinal change in each group was also compared. Eight reference regions (described below) were evaluated for both the Florbetapir and FDG data. Cortical ROIs for the AV45 SUVR calculation followed the [Landau 2013] method, and FDG cortical ROI selection was based on individual region effect size (Figure 1).

SUVR Reference Regions for AV45 and FDG Analysis

• Numerous potential reference regions were evaluated:
  • Brainstem (BS)
  • Cerebellar Grey (CG)
  • Whole Cerebellum (WC)
  • Cerebellar White Matter (WMcereb)
  • Subcortical White Matter (WM)
  • Eroded Subcortical White Matter (WMeroded)
  • Whole Brain (WB)
  • Average of BS, WMeroded, WC (AvgRef)

Comparison Metric

• Cohen’s d effect size is the metric used for comparison of methods:

  Cross-sectional:
  \[ d = \frac{\text{Mean}_{\text{Group 1}} - \text{Mean}_{\text{Group 2}}}{\text{SD}_{\text{Pooled}}} \]

  Longitudinal:
  \[ d = \frac{\text{Mean}_{\text{Initial}} - \text{Mean}_{\text{Follow-up}}}{\text{SD}_{\text{Whole Brain}}} \]

RESULTS

• Unsmoothed data consistently showed slightly higher effect size in both the cross sectional and longitudinal analyses of the Florbetapir data, regardless of the reference region used. This trend was not seen in the FDG data, where there was little difference between the smoothed and unsmoothed data.

• Cross sectional and longitudinal effect sizes in the Florbetapir analysis were largest using a reference regions including subcortical white matter for both the smoothed and unsmoothed data.

• Cross sectional and longitudinal effect sizes in FDG data including subcortical white matter generally show a decreased effect size compared to both smoothed and unsmoothed data, indicating that these reference regions are not optimal for FDG analyses. The decreased effect size of FDG SUVRs using white matter reference regions also imply that tracer uptake in adjacent grey and white matter regions included in the SUVR calculation are positively correlated.

CONCLUSIONS

• There appears to be a trend for increasing effect size in longitudinal and cross sectional SUVR analyses of Florbetapir PET data using unsmoothed compared to smoothed data, but not in FDG data. In a clinical trial setting, this could imply that longitudinal studies of Florbetapir can obtain greater sensitivity to detecting therapeutic effects by using PET scanners with higher resolution.

• Use of unsmoothed data in the FDG analysis did not show the advantages that were seen in the Florbetapir analysis. One possible reason for this could be due to likely correlation between adjacent grey and white matter uptake in FDG images. In this case, the partial volume effect in the smoothed data would not tend to decrease any signal that might be present in differentiating AD from N patient subgroups. Conversely, for the Florbetapir data, it is the differentiation of grey matter uptake that distinguishes diseased from normal subjects. In this case, there is an advantage to higher spatial resolution, less smoothed data.

REFERENCES

1. Koeppe et al. ADNI PET Preprocessing 2009 [http://adni.loni.usc.edu/methods/pet-analysis/pre-processing/]

Figure 1: Brain regions used for reference in the AV45 data and SUVR calculation.

Figure 2: AV45 SUVR Effect Size of Smoothed vs Unsmoothed Images

(LEFT) Cross-sectional Results (LEFT) and Longitudinal Results (RIGHT). Effect size is consistently larger for unsmoothed compared to smoothed data, regardless of the reference region used in the SUVR calculation.

Figure 3: FDG Cross-Sectional Effect Size

Smoothed vs Unsmoothed (AD vs N)

Figure 4: FDG Longitudinal Effect Size

Smoothed vs Unsmoothed (AD vs N)

Figure 5: Comparing AV45 PET spatial resolution using different reference regions for unsmoothed data in the AV45 dataset, regardless of the reference region used in the SUVR calculation. Apparently, because of the partial volume effect, it appears that there is an advantage to using unsmoothed data for cross-sectional and longitudinal quantitative SUVR analyses. AV45 reference regions in order of longitudinal effect size included eroded white matter (WMeroded), subcortical white matter (WM), whole brain (WB), an average of WMeroded, WC and BS (AvgRef), cerebellar grey (CG), whole cerebellum (WC), cerebellar white matter (WMeroded) and brainstem (BS).