AUTOMATED QUANTITATIVE ANALYSIS METHODS FOR THE DIAGNOSIS OF ALZHEIMER'S DISEASE WITH ^{11}C-PIB PET AND ^{18}F-FDG PET

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Introduction

Currently, quantitative methods for analyzing PIB data, including SUVR and DVR, require manual segmentation to generate the regions needed for reference and analysis. This manual segmentation is time consuming and suffers from a lack of reproducibility (subject to intra/interobserver variability).

Objectives

The purpose of this study is to evaluate automated methods for quantification of PIB including use of single and multisubject probabilistic anatomical brain atlases[1-3] (defined on high resolution MRI scans) for automatic volume of interest (VOI) generation for both reference and analysis regions, parametric voxel-based analysis (VBA), and cortical projection analysis (CP).

Materials and Methods

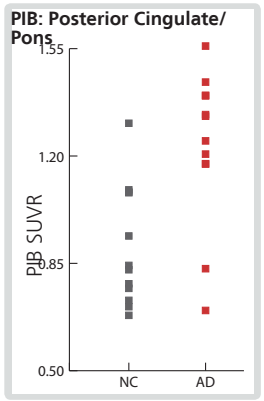
- C-11 PIB and FDG PET images were used from the Alzheimer's Disease Neuroimaging Initiative database for 12 AD and 12 normal controls (NC) from 10 institutions.
- The 40-60min interval PIB scans were co-registered to the FDG scans for each subject.
- The FDG scans were deformably registered to a template volume using the MIMneuro deformable registration[4] (MIMvista, Cleveland, OH).
- The PIB scans were registered to the template space by concatenating the deformable FDG registration with the rigid PIB-to-FDG registration.
- VOI's for reference and analysis were generated on the PIB and FDG scans using the single brain and multisubject probabilistic brain atlases.
- Both the cerebellum and pons were used as reference regions.
- T-tests were used to determine the atlas VOIs, VBA voxels, and CP pixels most accurate in distinguishing AD from NC.

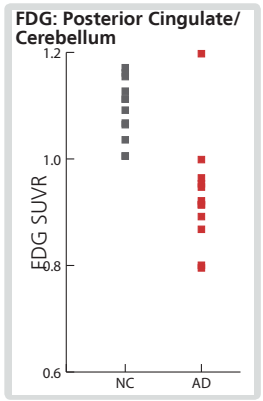
Results and Discussion

PIB VOI (Figure 1), VBA (Figure 2), and CP (Figure 3) each distinguished AD from NC with 87.5% accuracy (21/24). The most significant VOIs were generally in the sensorimotor cortex, but also included VOIs in the frontal and parietal lobes, posterior cingulate, basal ganglia, and amygdala. FDG VOI (Figure 1), VBA (Figure 2), and CP (Figure 3) each distinguished AD from NC with 95.8% (23/24) accuracy. The posterior cingulate, and VOIs in the temporal and parietal lobes were the most significant regions.

Problematic for all analyses were the PIB- AD and PIB+ NC subjects. Two AD subjects were PIB-, confirmed by visual inspection. FDG showed primary visual cortex hypometabolism consistent with DLB which could explain the PIB- result (Figure 4). The distribution in NC subjects was broad with at least one subject indistinguishable from AD (Figure 5). This is consistent with reports that a significant cohort of clinically normal subjects can be PIB+ in aged populations.

Figure 1
VOI SUVR Distribution for Posterior Cingulate Gyrus

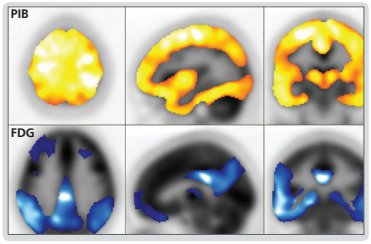




Posterior cingulate PIB SUVR is able to distinguish AD from NC with 87.5% (21/24) accuracy. Note the two PIB- patients diagnosed with AD and the PIB+ normal control. Several additional normal controls are outliers from the main cluster, with one appearing indistinguishable from PIB+ AD. These results are typical for many brain regions.

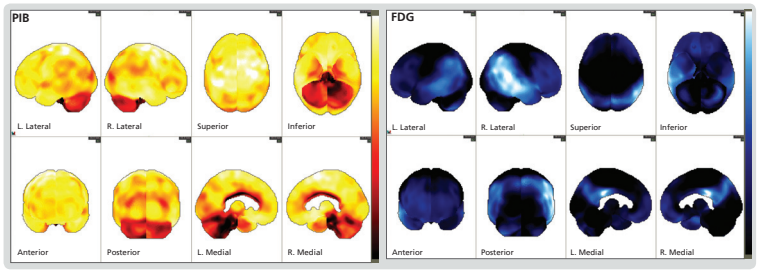
Posterior cingulate FDG SUVR is able to distinguish AD from NC with 95.8% (23/24) accuracy.

Figure 2
VBA T-test



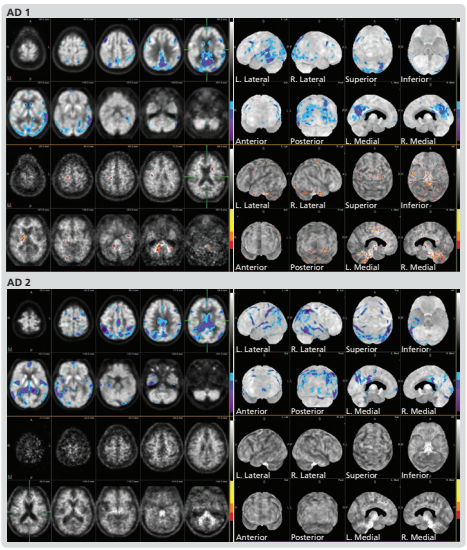
PIB SUVR showing areas of increased uptake in AD patients (t-test). FDG SUVR showing areas of decreased uptake in AD patients (t-test).

Figure 3
Cortical Projection T-test



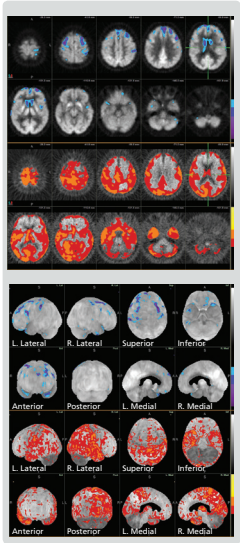
PIB SUVR showing areas of increased uptake in AD patients (t-test). FDG SUVR showing areas of decreased uptake in AD patients (t-test).

Figure 4
PIB- AD Patients



PIB- patients with AD diagnosis. Z-Score comparisons are to the database of 12 normal controls. FDG z-scores are consistent with patterns expected for Dementia with Lewy Bodies.

Figure 5
PIB+ Normal Control



PIB+ normal control. Z-score comparisons are to the database of 12 normal controls. The PIB pattern could not be distinguished from AD.

Conclusion

Automated quantitative analysis provides objective, robust, and reproducible SUVR calculation and parametric Automated quantitative analysis provides objective, robust, and reproducible SUVR calculation and parametric analysis. The utility of these tools has previously been demonstrated for FDG PET. Future PIB studies and clinical interpretation may both benefit from the automated and reproducible analysis offered by these methods.

Acknowledgments

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References

1 Nelson AS, Piper JW, Friedland RP, Freeman B. Probabilistic Human Brain Atlas for functional imaging: Comparison to single brain atlases. J Nucl Med. 2007;48 Suppl 2:S403

2 Piper JW, Nelson AS. Probabilistic Human Brain Atlas: Part 1, a surrogate for manual VOI definition. J Nucl Med. 2008;49 (Supplement 1):378p.

3 Piper JW, Nelson AS. Probabilistic Human Brain Atlas: Part 2, validation with ADNI data. J Nucl Med. 2008;49 (Supplement 1):379p.

4 Piper JW. Quantitative comparison of Spatial Normalization Algorithms for 3D PET brain scans. J Nucl Med. 2007;48 Suppl 2:S403.