

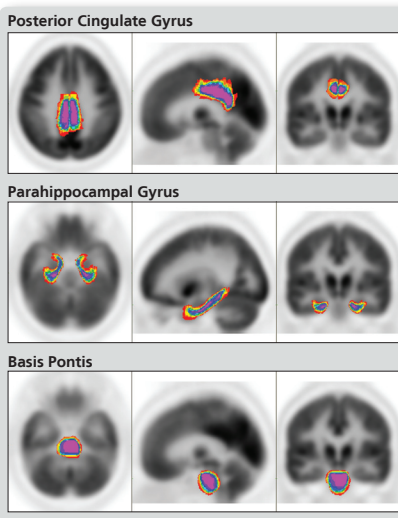
Purpose and Objectives

Many of the studies which have reported diagnostic accuracies of FDG-PET for Alzheimer's Disease (AD) have used qualitative diagnostic criteria and have been performed with single institution data. Here we propose and validate an Artificial Neural Network Computer-Aided Diagnosis (ANN-CAD) scheme for the diagnosis of AD with multi-center data using the registration and region-based statistics generated by MIMneuro^{1,2} (MIMvista Corp., Cleveland, OH).

Materials and Methods

FDG-PET images were acquired as part of the Alzheimer's Disease Neuroimaging Initiative using a variety of imaging protocols, reconstructions, and cameras from 36 different imaging centers for 128 subjects: 61 with clinically diagnosed AD and 67 normal controls³. Each brain was spatially registered to a standard template volume to reduce the anatomical variability, and region-based statistics were computed using both a single-brain atlas and a multi-subject probabilistic atlas which affords tunable anatomic sensitivity and specificity. A three input single-level ANN was chosen for the CAD system and the inputs were selected for their ability to distinguish the groups. The ANN was then trained and tested using a leave-one-out scheme.

Figure 1
Probabilistic Brain Atlas



The multi-subject probabilistic atlas allows considerable flexibility for region-based analysis. Regions can be selected which are highly specific, highly sensitive, or anywhere in between. Each color of the 10 step color scale represents a different probabilistic level ranging from 10% (red) where the VOI is comprised of all of the voxels that at least 1 out of 10 subjects had in common to 100% (purple) where the VOI is made of all of the voxels that 10 out of 10 subjects had in common.

Table 1
Artificial Neural Network Predictive Accuracy and Consistency

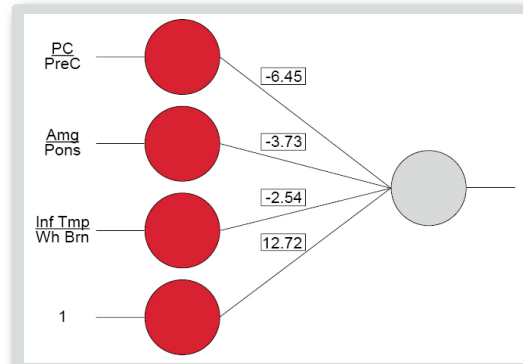
		Sensitivity	Specificity	Accuracy
Single Brain Atlas	Fitted	94.5%	91.6%	93.0%
	Predictive	91.8%	89.6%	90.6%
Both Atlases	Fitted	95.9%	96.3%	96.1%
	Predictive	93.4%	95.5%	94.5%
Specificity Tuned	Predictive	86.9%	98.5%	93.0%
Sensitivity Tuned	Predictive	95.1%	80.6%	87.5%

Average sensitivities, specificities, and accuracies for the ANNs. Fitted statistics are averaged for the training sets and predictive statistics are averaged for the testing sets. Results are displayed for the ANN based on the single-brain atlas alone, both the single-brain with the probabilistic atlas, both atlases with the ANN trained for higher specificity, and both atlases with the ANN trained for higher sensitivity. Training the ANN for higher specificity was more successful than sensitivity.

Results and Discussion

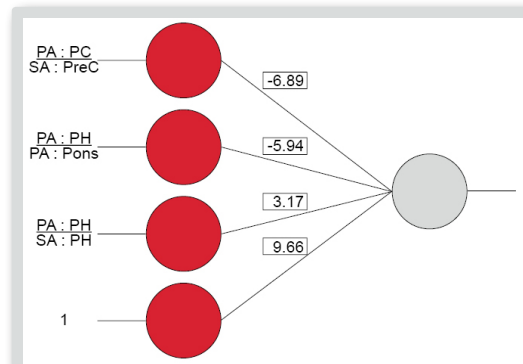
Using the single-brain atlas only, the selected ANN resulted in 91.8% sensitivity, 89.6% specificity, and 90.6% accuracy. With the addition of the probabilistic atlas, the ANN provided increased predictive power at 93.4% sensitivity, 95.5% specificity, and 94.5% accuracy.

Figure 2
Artificial Neural Network Using Single-Brain Atlas



A typical three input single level ANN for the leave-one-out training sets with inputs extracted from automatic single-brain atlas region-based analysis provided by MIMneuro. The inputs were median intensities for bilateral posterior cingulate gyrus (PC) normalized to bilateral precentral gyrus (PreC), bilateral amygdala (Amg) normalized to the basis pontis (Pons), the left inferior temporal gyrus (Inf Tmp) normalized to the whole brain (Wh Brn), and a constant term which serves to threshold the output. Predictive accuracy for these ANNs averaged 90.6%.

Figure 3
Artificial Neural Network Using Probabilistic Atlas



A typical three input single level ANN for the leave-one-out training sets with inputs were extracted from both automatic single and probabilistic brain atlas region-based analysis provided by MIMneuro. The inputs were median intensities for bilateral 90% probability posterior cingulate gyrus (PA: PC) normalized to single-brain bilateral precentral gyrus (SA: PreC), bilateral 10% probability parahippocampal gyrus (PA: PH) normalized to the 10% probability basis pontis (PA: Pons), the bilateral 100% parahippocampal gyrus (PA: PH) normalized to the single-brain parahippocampal gyrus (SA: PH), and a constant term which serves to threshold the output. Predictive accuracy for these ANNs averaged 94.5%.

Conclusions

To our knowledge, the diagnostic accuracy of 94.5% is the best result reported for AD using FDG-PET from multiple imaging centers. The ANN-CAD scheme used also allows for considerable flexibility during the training stage and could be tuned to increase either sensitivity at the expense of specificity or vice versa. The flexibility of the MIMneuro probabilistic atlas allows for significantly better results than a single brain atlas alone.

References

- 1) Piper. Quantitative comparison of spatial normalization algorithms for 3D PET brain scans. J Nucl Med. 2007; 48 (Supplement 2):403P.
- 2) A.S. Nelson, J Piper, R Friedland, B Freeman. Probabilistic human brain atlas for functional imaging: Comparison to single brain atlases. J Nucl Med. 2007; 48 (Supplement 2):403P.
- 3) A list of funding sources for the ADNI can be found at: http://www.loni.ucla.edu/ADNI/Application/ADNI_License.jsp

Note: the CAD scheme is not available in MIMneuro.