**Introduction**

Classification of subjects as Amyloid-Positive (Aβ+) or Amyloid-Negative (Aβ-) based on Amyloid positron emission tomography (PET) scans is increasingly utilized in research studies and clinical practice. While qualitative, visual assessment is currently the gold-standard approach, automated classification techniques possess the inherent advantages of being objective, reproducible, and efficient. The goal of this work was to develop a statistically-driven approach, based on a vertexwise discriminant analysis (VDA), that will facilitate automated classification of subjects based on conventional [18F]florbetapir PET scans. This novel approach provides an objective method for determination of the optimal Stat-ROI and associated threshold for automated discrimination between Aβ+ and Aβ- subjects. Future studies should assess the applicability of our empirically-derived Stat-ROI and threshold to other subject populations (e.g., healthy elders, Alzheimer’s disease). Ultimately, automated subject classification may complement or supplant visual reads in clinical practice and for eligibility assessment in AD clinical trials.

**Methods**

[18F]florbetapir PET and 3D T1-weighted MRI scans were obtained from ADNI-GO/-2 study subjects classified as MCI (n=200). The PET volumes were registered to a customized MRI template in MNI stereotaxic space, and SUVR images were generated using Biospective’s fully-automated PIANOTM image processing software. An iterative approach was then employed to determine the optimal statistical region-of-interest (Stat-ROI) (see details in Flowchart). This process was initialized based on visual assessment of the Amyloid PET images, and the VDA employed a leave-one-out strategy.

**Results**

The resulting Stat-ROI from Iteration #1 (Figure 1) included few small regions of the default mode network (DMN), including the precuneus and medial frontal cortex. Receiver operating characteristic (ROC) analysis based on this Stat-ROI produced an optimal cut-off of 1.31, which resulted in 18 subjects shifting from the initial Aβ- group to the Aβ+ group (Figure 2 and Table 1). The Stat-ROI from Iteration #2 consisted of more spatially expansive regions of the DMN (Figure 3), which yielded increased accuracy, sensitivity, and specificity. The process was found to converge at Iteration #2 and resulted in an optimal threshold of 1.31.

**Conclusions**

This novel approach provides an objective method for determination of the optimal Stat-ROI and associated threshold for automated discrimination between Aβ+ and Aβ- subjects. Future studies should assess the applicability of our empirically-derived Stat-ROI and threshold to other subject populations (e.g., healthy elders, Alzheimer’s disease). Ultimately, automated subject classification may complement or supplant visual reads in clinical practice and for eligibility assessment in AD clinical trials.

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