

rPOP: Robust PET-only processing and quantification of community-acquired amyloid-PET from the IDEAS Study

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Abstract

Background: The Imaging Dementia-Evidence for Amyloid Scanning (IDEAS) Study collected over 15,000 community-acquired amyloid-PET scans, without structural MRI and with different acquisition times, tracers and scanners. Here we describe and validate rPOP (robust PET-Only Processing), a pipeline for ¹⁸F-Florbetapir (FBP), ¹⁸F-Florbetaben (FBB) and ¹⁸F-Flutemetamol (FLUTE) scans collected in IDEAS.

Method: Each image undergoes automatic origin reset to center of mass, spatial normalization based on weighted PET templates (with SPM12) and data-driven differential smoothing (with AFNI). We received n=740 (514 FBP, 182 FBB, 44 FLUTE) amyloid-PET scans from the IDEAS-Brain Health Registry substudy (IDEAS-BHR), with amyloid-PET local visual reads available for N=663 scans. We performed semi-quantification via rPOP and estimated neocortical Centiloids after tracer-specific calibrations using the GAAIN VOIs with whole cerebellum reference. Centiloids were calculated for clinical groups (MCI or dementia), to compare rPOP-based amyloid-status (centiloids \geq 24.4) with visual reads. The pipeline was validated with n=1518 ADNI scans (n=1249 FBP, n=269 FBB), using MRI-based amyloid-status as a reference and testing the associations between rPOP- and MRI-based centiloids.

Result: rPOP successfully processed N=2233/2258 (98.9%) scans in the first pass, with N=24/25 warping-related failures rescued with a manual reorientation and origin reset prior to warping. In IDEAS-BHR, we observed the expected centiloids distribution (Figure 1A-B) both according to visual reads and also stratifying by clinical stage amyloid-negative, i.e. mean \pm sd Centiloids MCI/Dementia: 2 \pm 23/-5 \pm 27; amyloid-positive: MCI/Dementia: 65 \pm 42/80 \pm 37. There was high concordance (Table 1) between rPOP-based amyloid status and both local visual reads (IDEAS-BHR, Cohen's k=0.72 [0.7-0.74], ~86% concordance). Very high concordance was also observed in the ADNI dataset (k=0.88 [0.87-0.89], ~94% concordance), with rPOP- and MRI-based Centiloids being strongly linearly associated (R²:0.95, p<0.001), with a tighter relationship in images with better resolution (β = -0.016, p<0.001).

Conclusion: With rPOP, we successfully derived Centiloids quantification from heterogeneous IDEAS amyloid-PET scans and validated the pipeline with ADNI scans acquired in a research setting. These data show that community-acquired amyloid-PET scans can be successfully analyzed, enabling joint efforts by clinical sites and research centers.

Figure 1. Distribution of rPOP Neocortical Centiloids in the IDEAS-BHR dataset

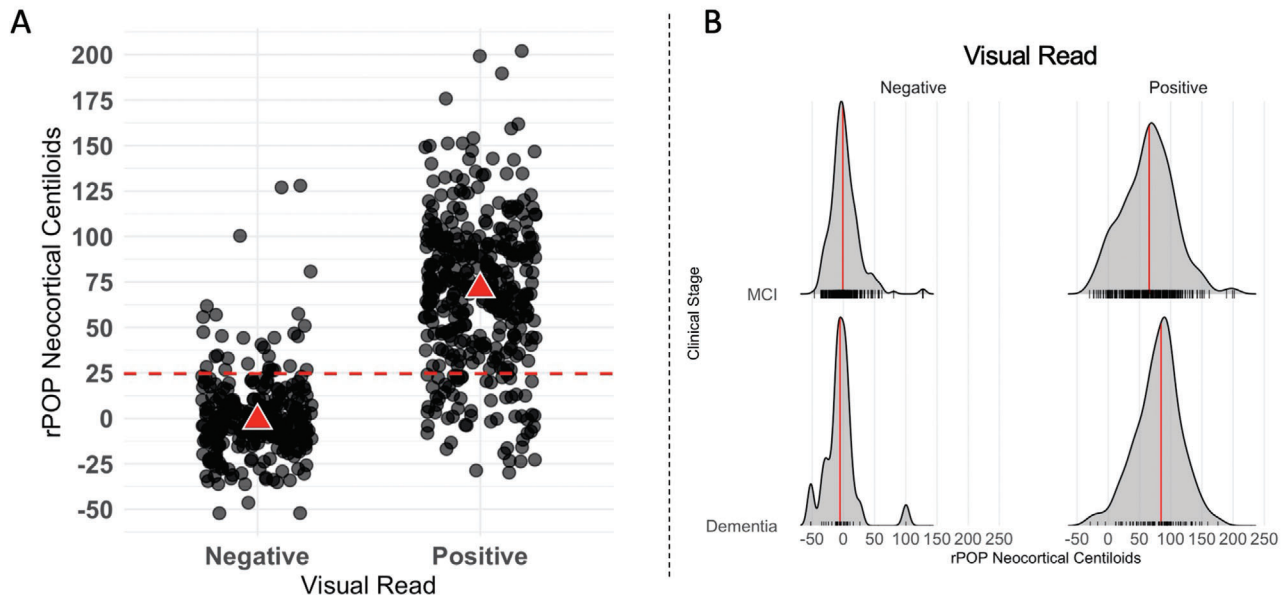


Figure showing relationships between rPOP Neocortical Centiloids and local visual reads in IDEAS-BHR (A) and ridgeplots showing density of rPOP Neocortical Centiloids by clinical stage and local read (B). Red dashed line in panel A represents an a priori threshold of 24.4 to define (semi)quantification-based amyloid-status.

FIGURE 1

TABLE 1**Table 1. Performance of rPOP-based quantification**

Cohort	IDEAS-BHR	ADNI
Reference standard	Local visual reads	MRI-based quantification
Total N	663	1518
TP/TN/FP/FN	328/244/30/61	704/725/10/79
Sensitivity	0.84 (0.80-0.88)	0.90 (0.88-0.92)
Specificity	0.89 (0.85-0.92)	0.99 (0.98-0.99)
Accuracy	0.86 (0.83-0.89)	0.94 (0.93-0.95)
Positive Predictive Value	0.92 (0.88-0.94)	0.99 (0.97-0.99)
Negative Predictive Value	0.80 (0.75-0.84)	0.90 (0.88-0.92)
Cohen's k	0.72 (0.70-0.74)	0.88 (0.87-0.89)

Legend: IDEAS-BHR= Imaging Dementia: Evidence for Amyloid Scanning – Brain Health Registry substudy, ADNI=Alzheimer's Disease Neuroimaging Initiative, N=Number, TP=True Positive, TN=True Negative, FP=False Positive, FN=False Negative