Evaluating the sensitivity of Centiloid quantification to pipeline design and image resolution

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AMYPAD Amyloid imaging to prevent Alzheimer's Disease

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Introduction

- Centiloid (CL) scale is used for improving the comparability of amyloid PET quantification
- Alternative pipelines to the Standard Centiloid one (MNI space, predefined cortical and reference region VOIs) may perform better for specific applications

Aim

- ***Evaluating the impact of pipeline design options on Centiloid values***
- ***Evaluating the impact of effective image resolution on global Centiloid***

Methods

- **32 Different** combination of Centiloid pipeline were designed

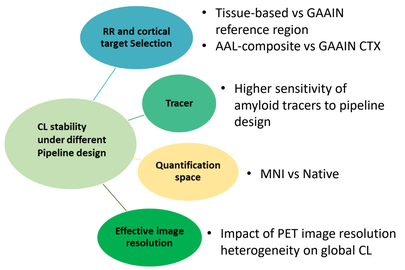

Figure1. Schematic of different factors included in 32 pipelines

- **659** subjects from **AMYPAD PNHS and DPMS group**
- PET images were smoothed with Gaussian filter to achieve an effective image resolution of 8mm
- SUVr and CL calculated for 32 alternative design of CL pipeline for harmonized and original PET images

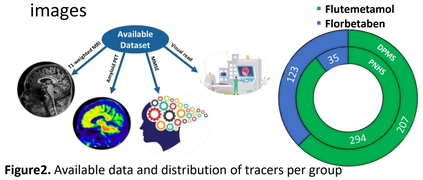

Figure2. Available data and distribution of tracers per group

Statistical analysis

- General estimation equation (GEE) for comparing the CL values across all pipeline combinations

DPMS group

Centiloid~ Intercept + Space + Tracer + Target Type +Reference region+ Reference region type+ visual read + MMSE

PNHS group

Centiloid~ Intercept + Space + Tracer + Target Type +Reference region+ Reference region type+ visual read

- Comparing CL values before/after harmonization was done using **correlation** and **Bland-Altman** plots

Results

Demographic	PNHS	DPMS
Age (Mean±SD)	68.4±7.51	70.52±7.23
Sex (Female%)	282 (85.71%)	138 (41.8%)
MMSE (Mean±SD)	28.99±1.22	25.67±4.14
Clinical status	Cognitively unimpaired	SCD+(110, 33%) MCI (134, 40.6%), & Dementia (86, 26.1%)
Centiloid	14.28±24.17	46.33±48.86

Table 1. Demographic information of PNHS and DPMS group

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Results

Tests of Model Effects for DMPS group			
Source	Type III		
	Wald Chi-Square	df	P-value
(Intercept)	71.684	1	<0.001
Visual read	516.25	1	<0.001
MMSE	19.076	1	<0.010
Reference region	164.191	3	<0.001
Reference region type (GAAIN vs tissue-based)	84.601	1	<0.001
Target (GAAIN vs AAL-composite)	36.668	1	<0.001
Space (MNI vs Native)	9.564	1	0.002
Tracer	0.321	1	0.571

Table 2. GEE model results for DPMS group. **RR and RR type had highest impact on CL values. Tracer has no effect on CL.**

Marginal means estimates				
Reference region	Mean	Std. Error	95% Wald Confidence Interval	
			Lower	Upper
Whole cerebellum	42.115	1.504	39.167	45.0633
Cerebellum grey matter	45.480	1.590	42.362	48.598
Whole cerebellum+Brainstem	39.066	1.467	36.190	41.942
Pons	29.688	1.612	26.527	32.848
Tissue-based reference region	37.299	1.479	34.398	40.200
GAAIN reference region	40.875	1.481	37.972	43.778
AAL composite target	40.329	1.507	37.375	43.283
GAAIN CRTX target	37.845	1.456	34.991	40.699
MNI space	38.481	1.415	35.707	41.255
Native space	39.693	1.543	36.669	42.718
Flutemetamol	38.280	1.873	34.608	41.952
Florbetaben	40.051	2.583	34.989	45.114

Table 3. Comparing marginal means for each predictor. **Pons produced lowest CL values among other RR. GAAIN RR and AAL-composite target produced higher marginal mean values (~3 CL)**

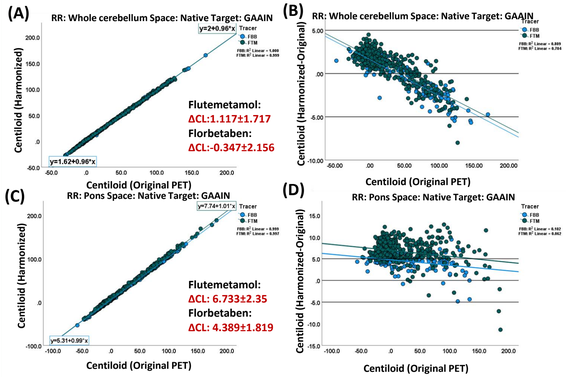

Figure 3. Correlation between CL values (A,C)Bland Altman plots comparing CL changes (B,D) before and after harmonization using whole cerebellum and pons as RR

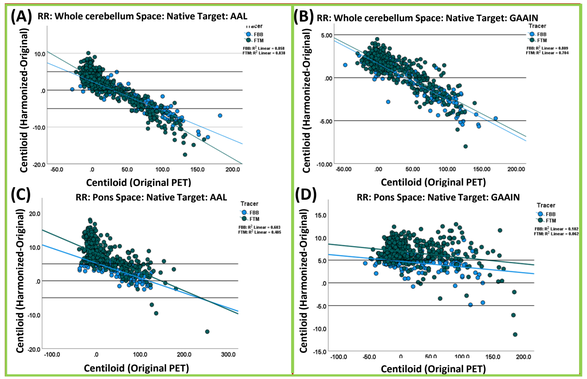

Figure4. Bland Altman plots comparing CL changes before and after harmonization (A&B) using whole cerebellum as RR and AAL composite and GAAIN CTX respectively (C&D) using pons as RR and AAL composite and GAAIN CTX respectively

Conclusion

- ✓ Main GEE model was developed in the DPMS cohort, and it was replicated in PNHS group with different criteria
- ✓ Reference region had the strongest impact on CL values
- ✓ Pons produced significantly lower CL values (10-15 CL)
- ✓ Other factors had lower impact (2-3 CL)
- ✓ No effect of Tracer
- ✓ Low sensitivity of CL to image resolution using whole cerebellum as RR and GAAIN cortical target
- ✓ Increasing the sensitivity of CL to image resolution using AAL-composite target irrespective of selected reference region
- ✓ Highest sensitivity of CL to image resolution observed using pons (~7 CL) and cerebellum grey matter (~5 CL) as RR irrespective of cortical target

Take home message

- ✓ **Using whole cerebellum as reference region is recommended for Centiloid scaling**
- ✓ **Using whole cerebellum and GAAIN cortical target is recommended for robustness against differences in image resolution**

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