Development and Evaluation of Image Preprocessing Pipelines for the Centiloid Method

Weiquan Luo, MS[1], Davneet S Minhas, PhD[1], Ethan Rubenstein, BS[1], David Situ, BS[1], Sarah Royse[1], Beau M Ances, MD, PhD[2], Bradley T Christian, PhD[3], Ann D Cohen, PhD[1], Benjamin L Handen, PhD[1], William E Klunk, MD, PhD[1], Dana L Tudorascu, PhD[1], Shahid Zaman, MD, PhD[4], Charles M Laymon, PhD[1]

(1) University of Pittsburgh, Pittsburgh, PA, USA, (2) Washington University in St. Louis, St. Louis, MO, USA,
(3) University of Wisconsin-Madison Waisman Center, Madison, WI, USA (4) University of Cambridge, Cambridge, United Kingdom

Background

The Centiloid method (Klunk et al. Alzheimer's & Dementia 11 2015) provides a standardized procedure to quantify brain amyloid. The method entails registration of PET to MR and warping to a template and requires adequate MR and PET image quality.

We observe a higher Centiloid processing failure rate (Figure 1) in the Neurodegeneration in Aging Down Syndrome (NiAD) cohort compared to non-Down syndrome (DS) subjects, due to MR motion artifacts and brain morphology.

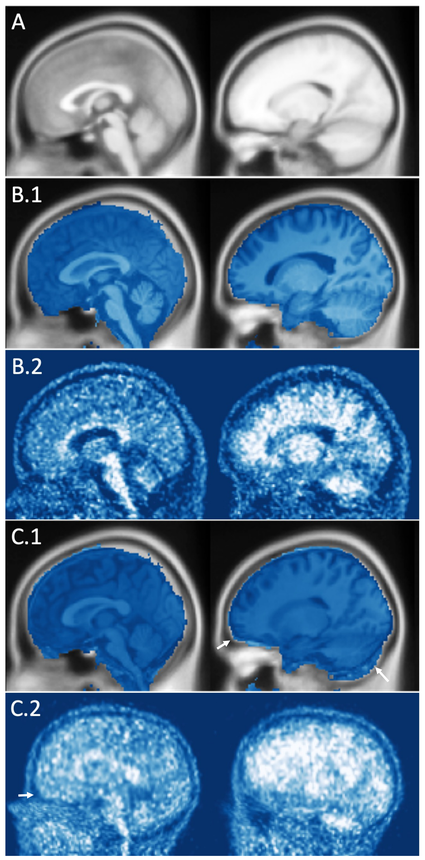

Figure 1. Examples for warped MR and PET images in MNI template space: MNI template (A); MR (B.1) with good normalization; PET (B.2) with good co-registration of a same subject; MR (C.1) failed normalization where the cerebellum was shrunk on normalization and extracerebral non-brain tissue was aligned to the template cerebellum; PET (C.2) failed registration where frontal lobe was pitched upward relative to the MRI and pointed to the frontal pole/orbitofrontal cortex.

Objective

Our goal was to improve the success rate of Centiloid on DS data by developing:

1. Rigorous quality-assurance (QA) criteria and
2. Alternative pipelines that are interchangeable with the standard pipeline.

Methods

New QA procedures were developed by characterizing the degree to which visually apparent registration/normalization deficiencies affect Centiloid score. All scans were randomly assigned to five raters for visual checks. The result were considered PASS when satisfying both of the following criteria:

- Template-MR: The boundary between grey matter-CSF are matched with the brain-only field of view in normalized MRI. Only a few segments of meninges are included. The whole cerebellum is included.
- MR-PET: Cerebellar, Corpus callosum, brainstem, ventricles are matched between MRI and PET. No LR, AP, IS shifts at edges of brain.

To improve the success rate, we developed 6 pipelines by adding 4 preprocessing steps to the standard pipeline:

- Automated MR/template origin matching (resetOrigin)
- N4 bias correction (n4)
- Co-registration using a smoothed PET image (smooth)
- MR skull-stripping (skullstrip)

All pipelines were run on standard Centiloid GAAIN (n=79) and NiAD PiB-PET and T1 MRI (n=319) datasets. Then, we performed the following analysis on the outputs:

- The registered images were rated as PASS/FAIL using the new QA procedures.
- Regression analysis between the Centiloid values obtained using the standard and modified pipelines were performed on passing scans.
- Following the reproducibility criteria of Klunk et al, regression results were evaluated to determine the compatibility of modified pipelines with the standard pipeline.

Results

The Linear regression parameters and R-squared values are presented in Table 1 and Figure 2.

- Using the GAAIN dataset, all modified pipelines met reproducibility criteria.
- Using the NiAD data, 5 out of 6 pipelines met reproducibility criteria based on 2 significant digits, whereas the 6th pipeline's slope was off by 0.007.
- By combining the results from 5 verified pipelines, the success rate for processing NiAD scans increased from 61.4% (n=196, standard pipeline only) to 95.6% (n=305).

Table 1: Linear regression parameters and R-squared between the standard pipeline and each of the modified pipelines for the GAAIN dataset and the NiAD dataset. For the NiAD data, regression was performed using those scans that passed the QA procedure. Green entries indicate that the reproducibility criteria described in Klunk at al, 2015 were met: slope between 0.98 and 1.02, intercept between -2 and 2, and R-squared greater than 0.98.

	GAAIN79			NiAD319 (QA)		
Modified Pipelines as y	Slope	Intercept	R2	Slope	Intercept	R2
resetOrigin_register_normalize	1.002	-0.005	0.999	1.001	-0.004	1.000
resetOrigin_smooth_register_normalize	1.001	-0.023	0.999	0.977	-0.335	0.999
n4_resetOrigin_register_normalize	0.999	0.311	0.998	1.016	0.281	0.999
n4_resetOrigin_smooth_register_normalize	0.997	0.283	0.998	0.992	0.123	0.999
n4_resetOrigin_register_skullstrip_normalize	0.996	0.390	0.997	1.003	0.345	0.998
n4_resetOrigin_smooth_register_skullstrip_normalize	0.994	0.366	0.997	0.973	0.093	0.998

Conclusion

Compatibility of the standard and five modified pipelines has been established. Additional preprocessing steps significantly improve the success rate of Centiloid processing for DS imaging.

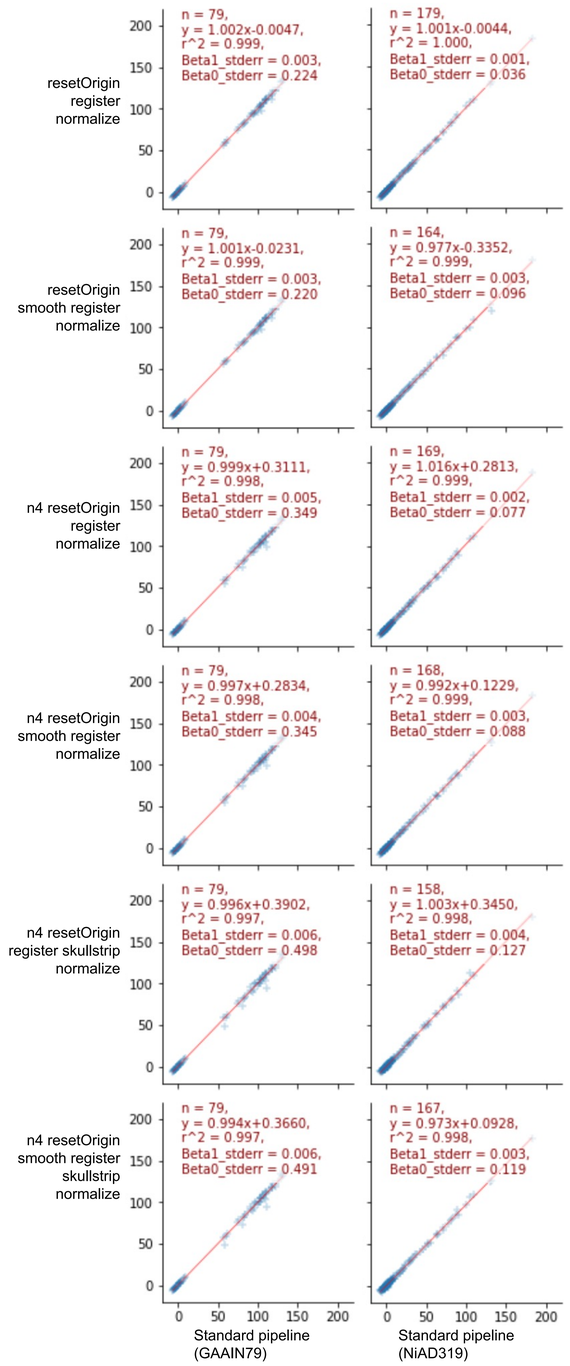

Figure 2: Linear regression results comparing Centiloid values from the standard pipeline (x-axis) to the each of modified pipelines (y-axis). Results are shown for GAAIN dataset (first column) and NiAD dataset (second column). The regression models are presented in each subplot with additional statistics: sample size (n), r squared (r^2), standard error of estimate slope (Beta1_sterr) and intercept (Beta0_sterr).