Evaluating and Improving Cross-Pipeline Reproducibility in Functional Connectomics: A Case Study

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Introduction

The past decade has witnessed the emergence of a growing array of openly shared functional MRI image processing pipelines. Unfortunately, while each of the pipelines are similar to one another with respect to the basic processing steps, they can vary substantially in the specific procedures included as well as their implementation.

Here, we provide a case study based on two pipelines - fMRIPrep[1], which is a one click pipeline that focuses on the preprocessing of fMRI data and generation of nuisance covariates for usage in later packages, and the Configurable Pipeline for the Analysis of Connectomes (C-PAC)[2], which focuses on providing a highly configurable, end-to-end solution for functional connectomics. The central challenge we took on was to evaluate the comparability of registrations, nuisance covariates and fMRI signals, generated by the two packages, and then expanding the range of configurable options in C-PAC to improve reproducibility.

Methods

Dataset 30 participants' scans (session #1) from Hangzhou Normal University (HNU) test-retest dataset[3]

Benchmark Methods We first surveyed methods employed by fMRIPrep and C-PAC for key steps (see Table 1) and identified methods that could not be matched using the configurable options in C-PAC. We next implemented additional configuration options in C-PAC to enable a C-PAC configuration that closely matches fMRIPrep (referred to as CPAC:fMRIPrep). To evaluate the impact of our changes on end-results, we ingressed each of our three preprocessing pipeline outputs (fMRIPrep, CPAC:Default, CPAC:fMRIPrep) into the eXtensible Connectivity Pipeline (XCP), which was originally designed to take fMRIPrep outputs. End-to-End preprocessing in C-PAC was also carried out (CPAC:F/X).

Evaluation Methods Each pipeline was run twice on the same data to establish within-pipeline test-retest similarity. To evaluate the reproducibility of findings, we calculated the spatial correlation of the connectivity matrix produced by each pairing of pipelines for a given dataset.

Key Steps	C-PAC New Features
Anatomical Preprocessing	
Initial Preprocessing	Non-local Means Filtering, N4 Bias Correction
Brain Extraction	ANTs-NiWorkflows
Tissue Segmentation	Thresholding, Erosion
Functional Preprocessing	
Motion Estimation	Estimation Order Option, FSL MCFLIRT
Brain Extraction	FSL BET + AFNI 3dAutoMask
Co-registration	N4 Correction on Mean EPI
Nuisance Signal Regression	Cosine Filter, Ventricle Mask Option, Brain Mask Erosion, Polynomial Regression

Table 1. C-PAC fMRIPrep-options configuration

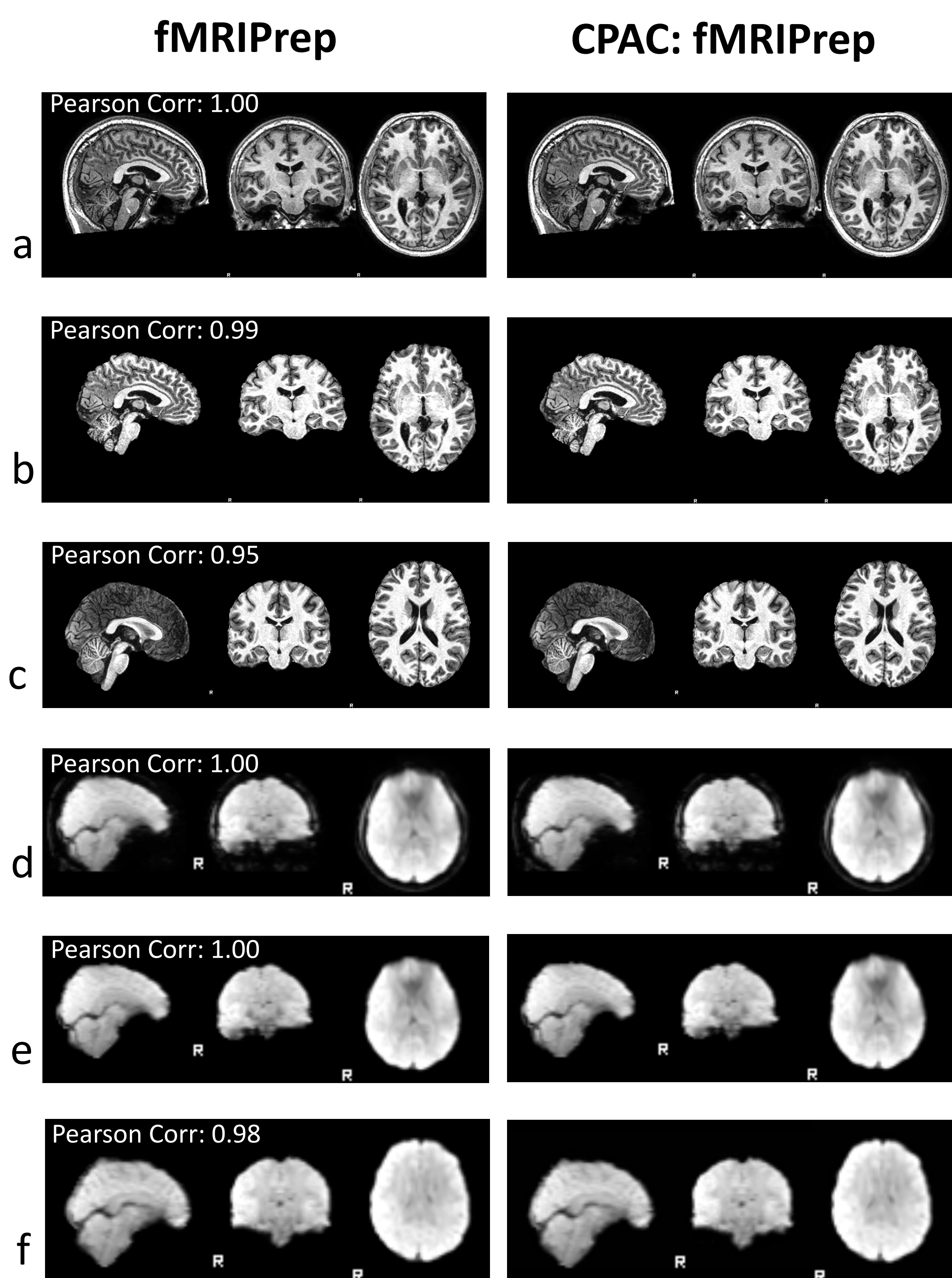## Results: Key Step Visualization

Figure 1. Key step output visualization and comparison.
a. original anatomical image; b. anatomical brain in native space; c. anatomical brain in template space; d. original functional image; e. functional brain in native space; f. functional brain in template space.
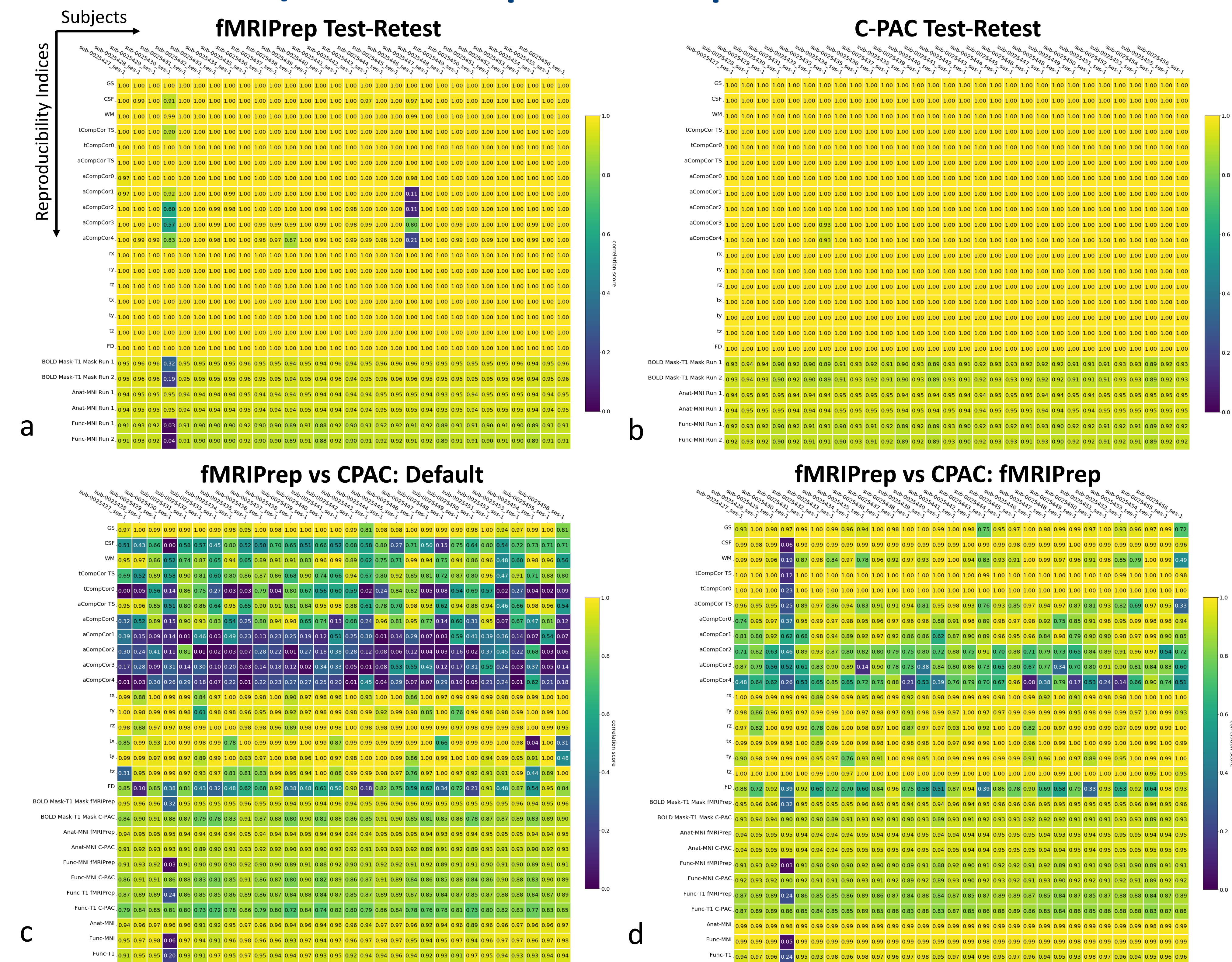
Results: Within/Between Pipeline Comparison

Figure 2. Within/between pipeline comparison. Value depicts Pearson correlation.
a. fMRIPrep test-retest similarity; b. C-PAC test-retest similarity; c. fMRIPrep vs C-PAC with the fMRIPrep-options configuration; d. fMRIPrep vs C-PAC with the default configuration.
GS: global signal; CSF: cerebrospinal fluid; WM: white matter; aCompCor TS: 1D timeseries for aCompCor extraction; FD: framewise displacement

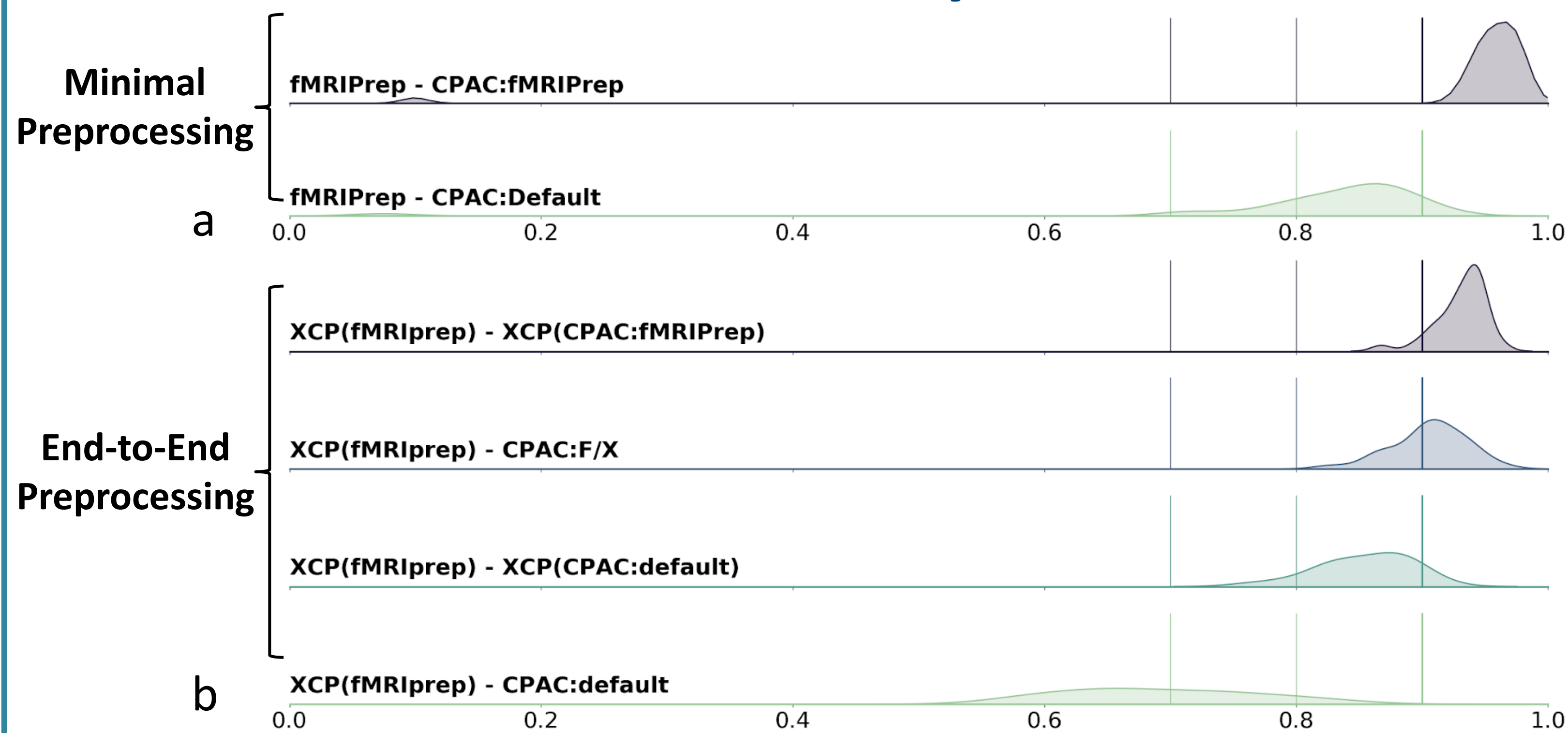## Results: Functional Connectivity Correlation

Figure 3. Functional connectivity correlation using Schaefer 200 atlas[4]. a. minimal preprocessing; b. end-to-end preprocessing (including nuisance regression and filtering)
XCP(*) indicates XCP result using preprocessed output from * pipeline

Results Summary

- Figure 1 visualizes key step outputs and shows high correlations between fMRIPrep and C-PAC with the fMRIPrep-options configuration.

- Figure 2 illustrates the generally high within-pipeline test-retest similarities in both pipelines and reveals notable improvements in between-pipeline similarity following an extension of C-PAC configurability options to enable a fMRIPrep-options configuration - particularly, as a result of increased matching of segmentation outputs, motion estimation parameters, registrations and nuisance signals (CompCors etc.).

- Figure 3 illustrates the distribution of correlation scores across datasets and demonstrates significant increase in functional connectivity correlation between fMRIPrep and C-PAC with the fMRIPrep-options configuration in both minimal preprocessing and end-to-end pipelines.

Conclusions

The present work demonstrates the importance of comparing independent pipeline packages and implementing the capabilities to improve inter-package reliability. Improving reliability between packages is a means of increasing the reproducibility of findings across studies and allows for independently preprocessed data to be aggregated. The ability to reproducibly launch a plurality of pipelines in C-PAC differing on key pipeline decisions, makes the comprehensive comparisons a relatively simple and reproducible process. Importantly, while high reliability does not guarantee accuracy, it is a critical requirement.

Reference

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