

# The Configurable Pipeline for the Analysis of Connectomes (C-PAC) 2020-21: Transitioning Out of Beta

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## Introduction

The Configurable Pipeline for the Analysis of Connectomes (C-PAC) is a configurable, open-source, Nipype(Gorgolewski et al., 2011)-based, automated processing pipeline for resting state functional MRI (R-fMRI) data, for use by both novice and expert users. C-PAC is designed to bring the power, flexibility and elegance of the Nipype platform to users in a plug and play fashion—without requiring the ability to program. Using an easy to read, text-editable configuration file or a graphical user interface, C-PAC users can rapidly orchestrate automated R-fMRI processing procedures, including: quality assessment measurements, image preprocessing based upon user specified preferences, generation of functional connectivity maps (e.g., seed-based correlation analysis), customizable extraction of time-series data, generation of graphical representations of the connectomes at various scales (e.g., voxel, parcellation unit), generation of local R-fMRI measures (e.g., regional homogeneity, voxel-matched homotopic connectivity, frequency amplitude measures). At the group level, C-PAC features Connectome-Wide Association Studies, Bootstrap Analysis of Stable Clusters, Intersubject Correlation Analysis (based on BrainIAK (Kumar et al., 2020)), and integrated group statistics using FSL/FEAT (Smith et al., 2004). Users can easily extract preprocessed time-series data and connectivity matrices for analysis with other packages.

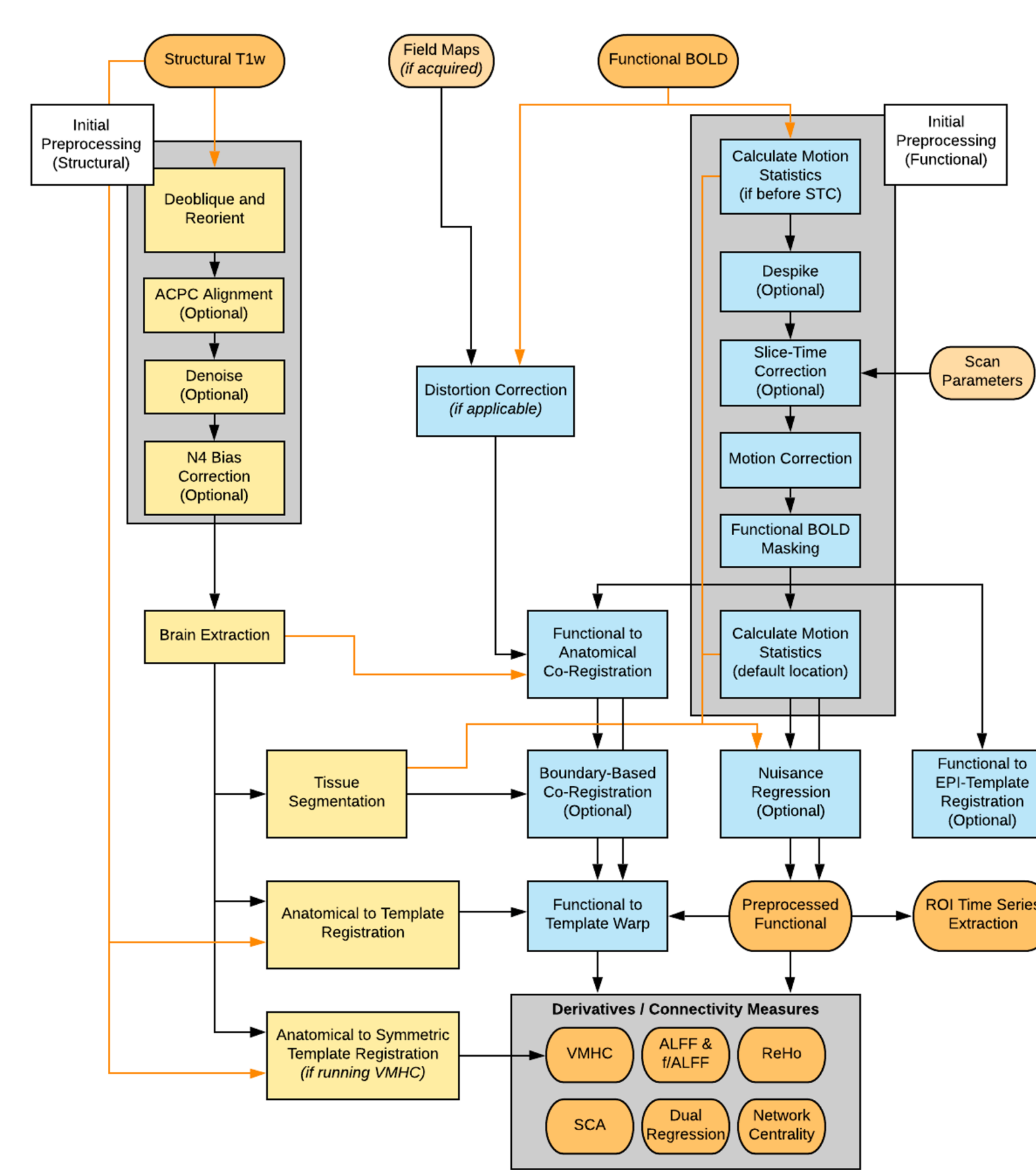
## Methods

Launched in 2012, C-PAC is implemented in Python using the Nipype pipelining library, which provides mechanisms to automatically detect and exploit parallelism in a pipeline, maintain provenance, iterate over parameter settings, and restart a pipeline without re-executing previously completed steps.

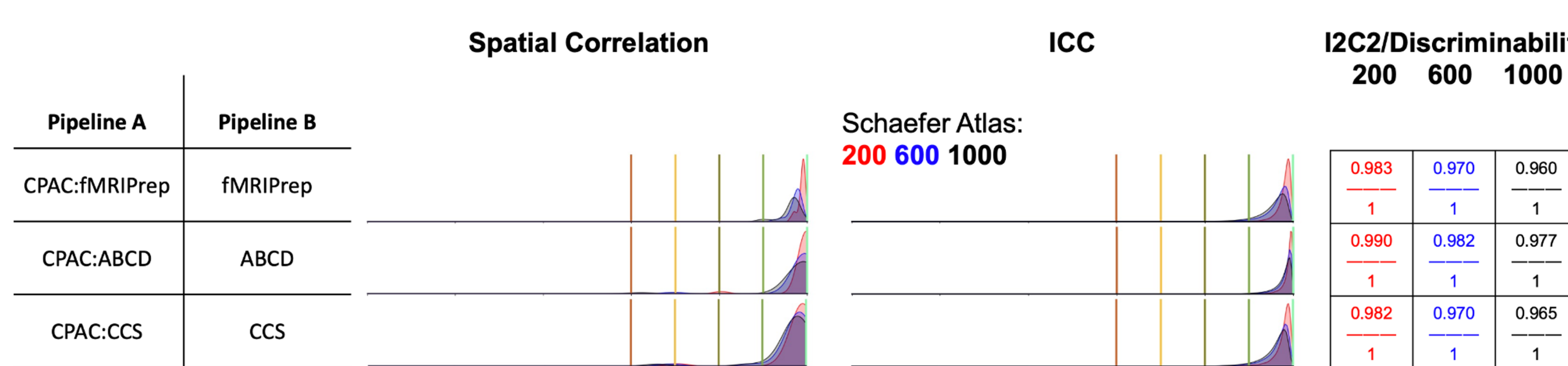
C-PAC extends Nipype functionality by providing workflows specific to connectivity analyses, functional connectivity derivatives and analyses not present in other neuroimaging packages. The C-PAC workflows are built from AFNI (Cox, 1996) and FSL (Smith et al., 2004) tools, as well as algorithms coded in Python using SciPy (Virtanen et al., 2020), NumPy (Harris et al., 2020) and scikit-learn (Pedregosa et al., 2011). C-PAC is designed to seamlessly interact with shared memory (multi-core) and cluster-based (e.g. Slurm, Sun Grid Engine) high performance computing environments to minimize computation time. Over the past two years, inspired by the needs of the BRAIN Initiative, the C-PAC team has placed an increased emphasis on implementing customizations to support nonhuman primate, rodent and longitudinal (including pre/post) studies.

## Results

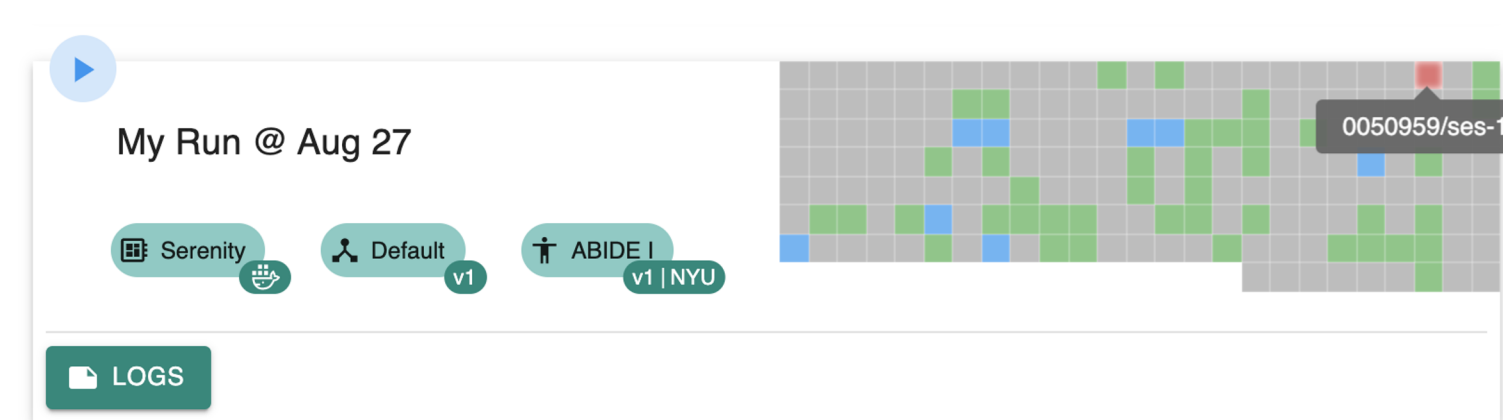
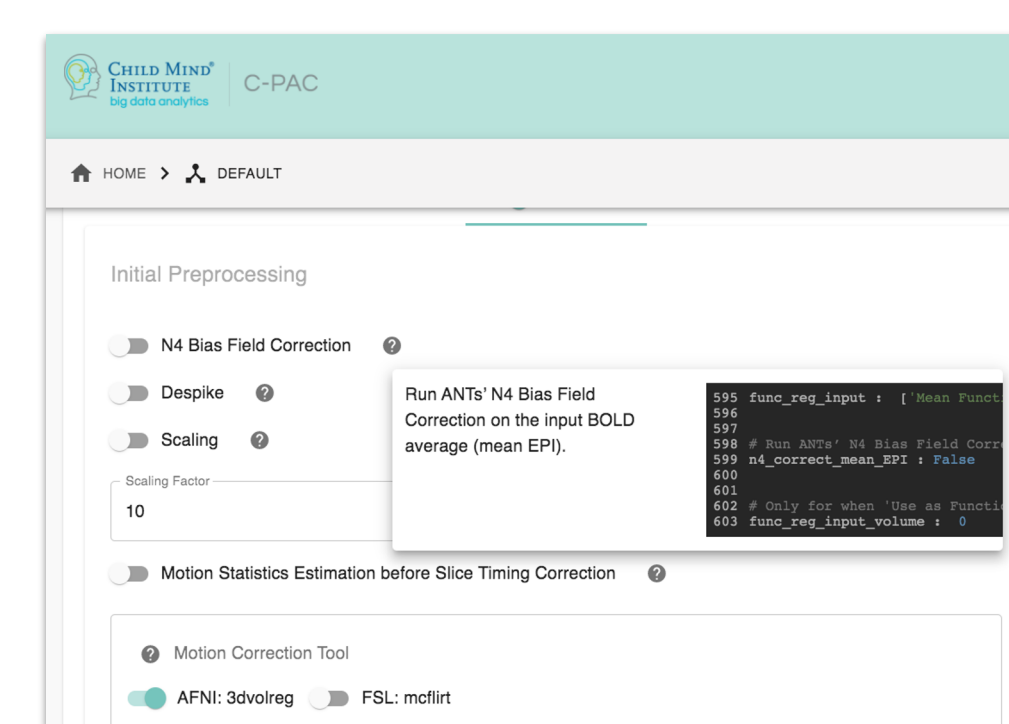
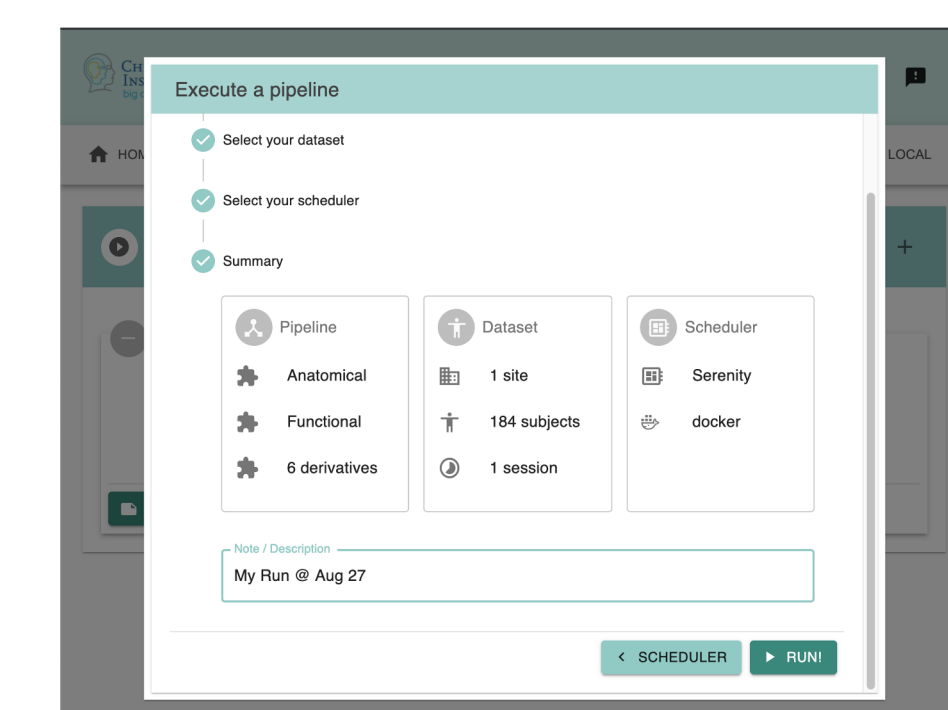
### Comprehensive Pipeline



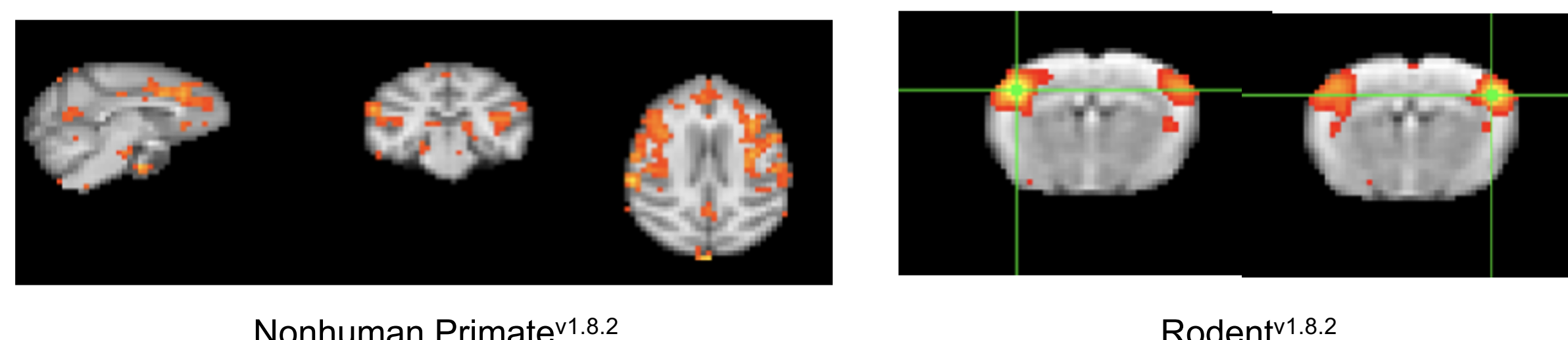
### Harmonized Minimal Preprocessing Configurations



### Graphical User Interface & Dashboard<sup>v2.0</sup>

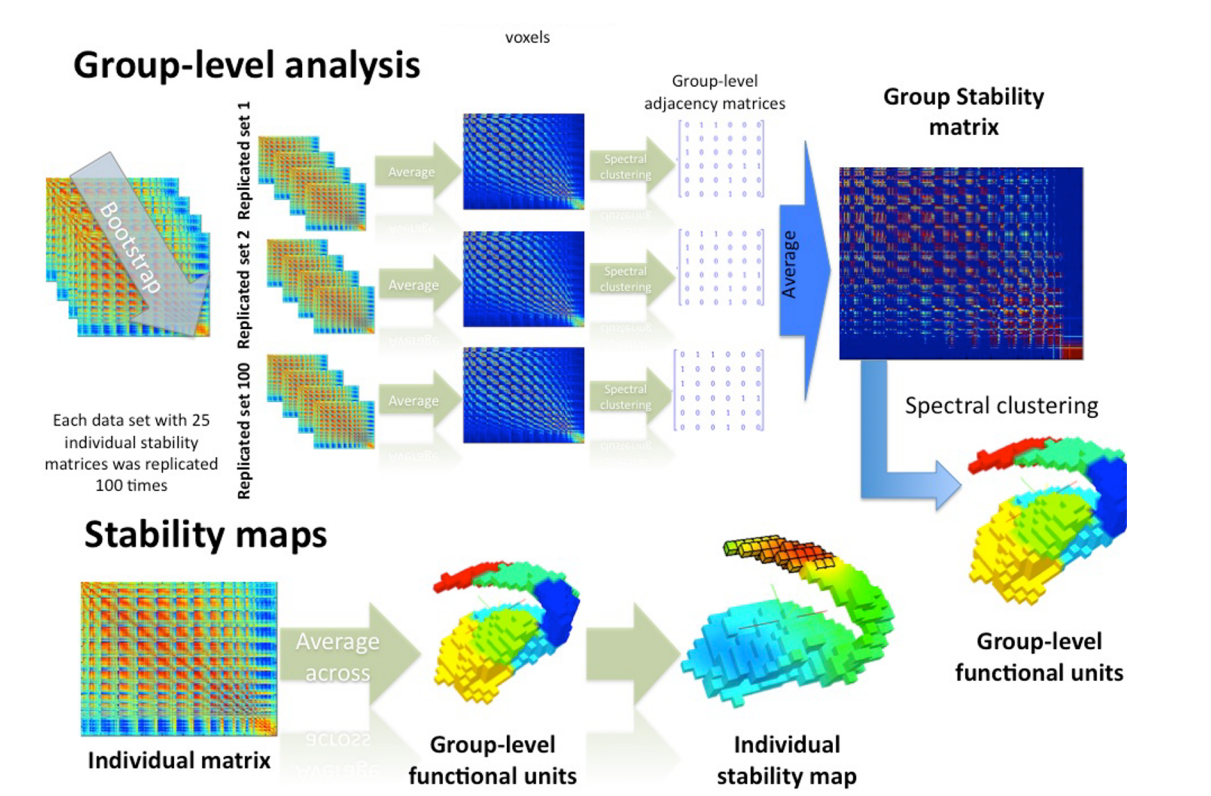


### Optimized Nonhuman Pipelines



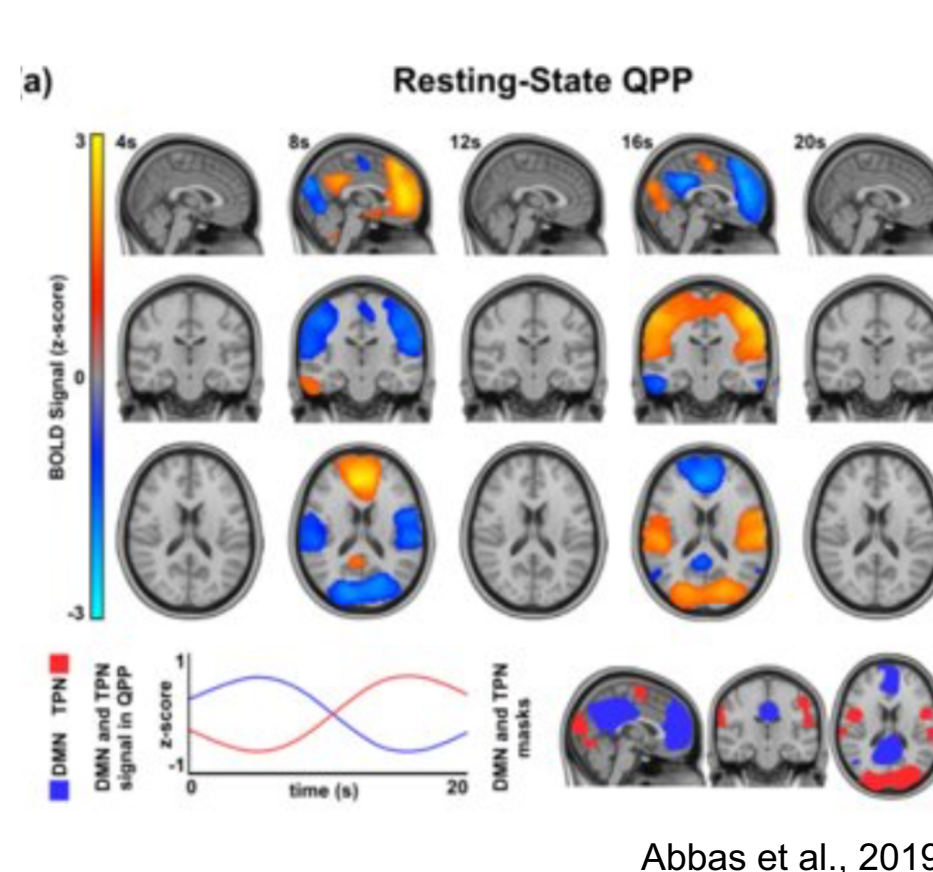
### Innovative Analyses

#### Bootstrap Analysis of Stable Clusters (BASC)



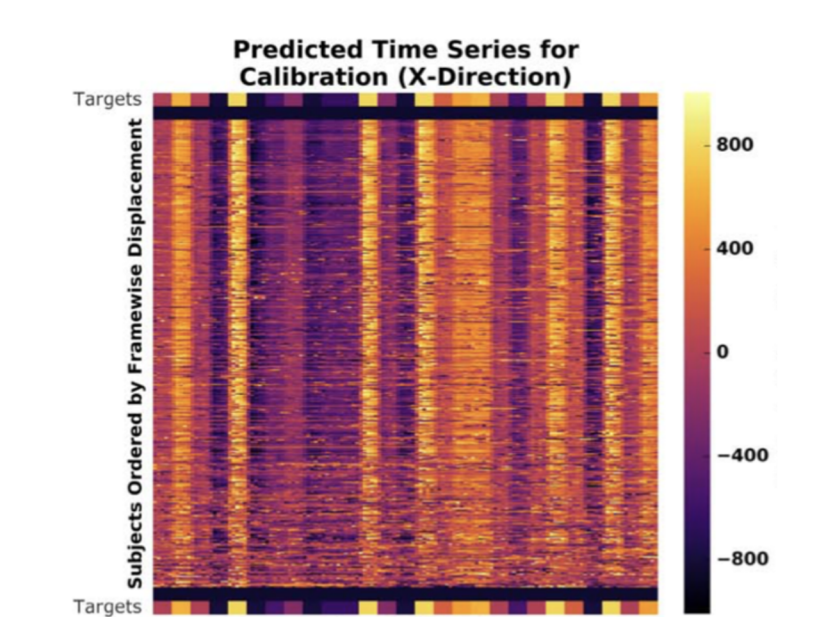
Bellec et al., 2010  
[pyproject.org/project/pyBASC](https://pyproject.org/project/pyBASC)

#### Quasi-Periodic Pattern Analysis (QPP)



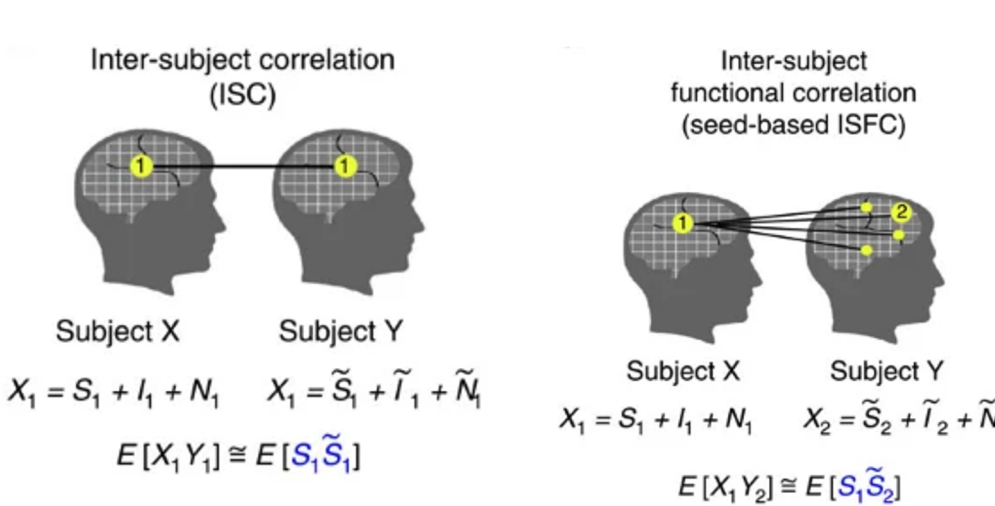
Abbas et al., 2019

#### Predictive Eye Estimate Regression (PEER)



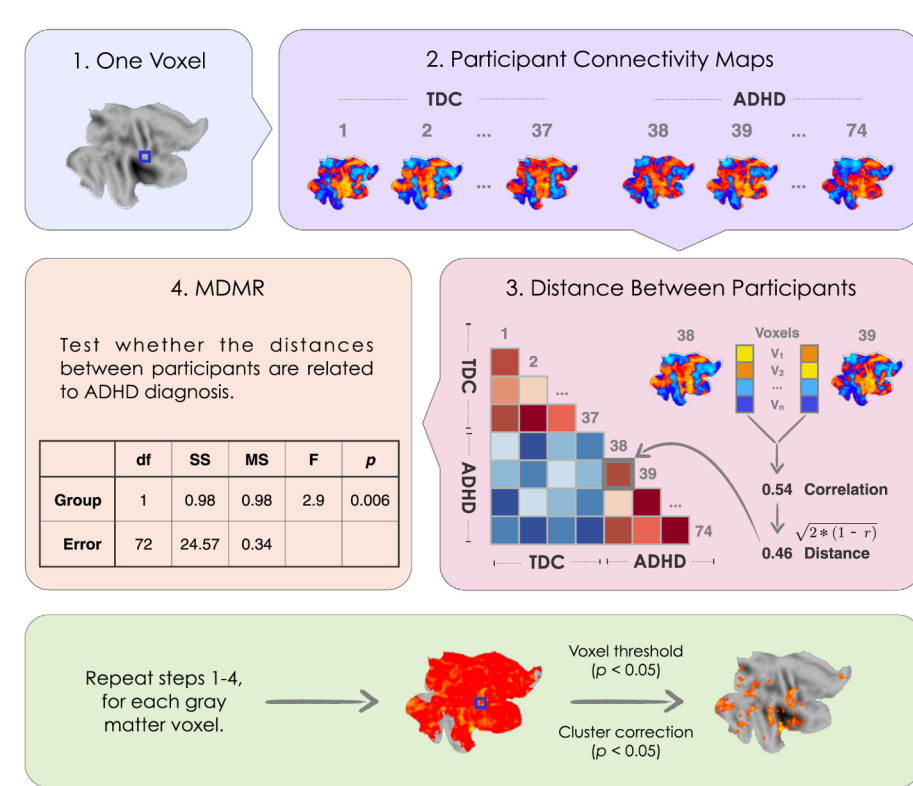
Son et al., 2019

#### Intersubject Correlation Analyses



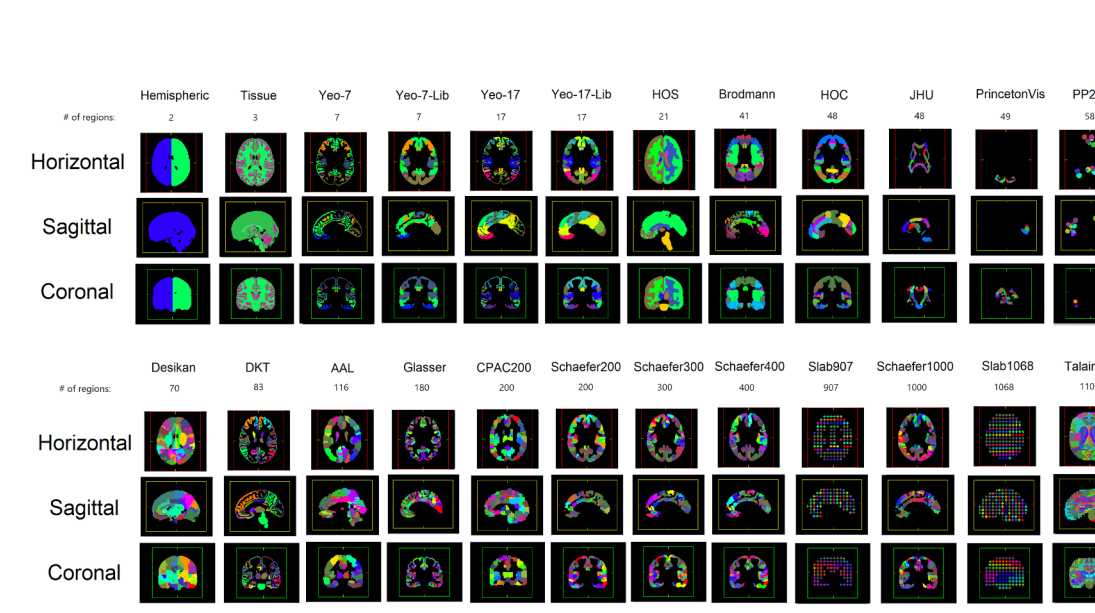
Simony et al., 2016  
[brainiak.org](https://brainiak.org)

#### Multivariate Distance Matrix Regression (MDMR)



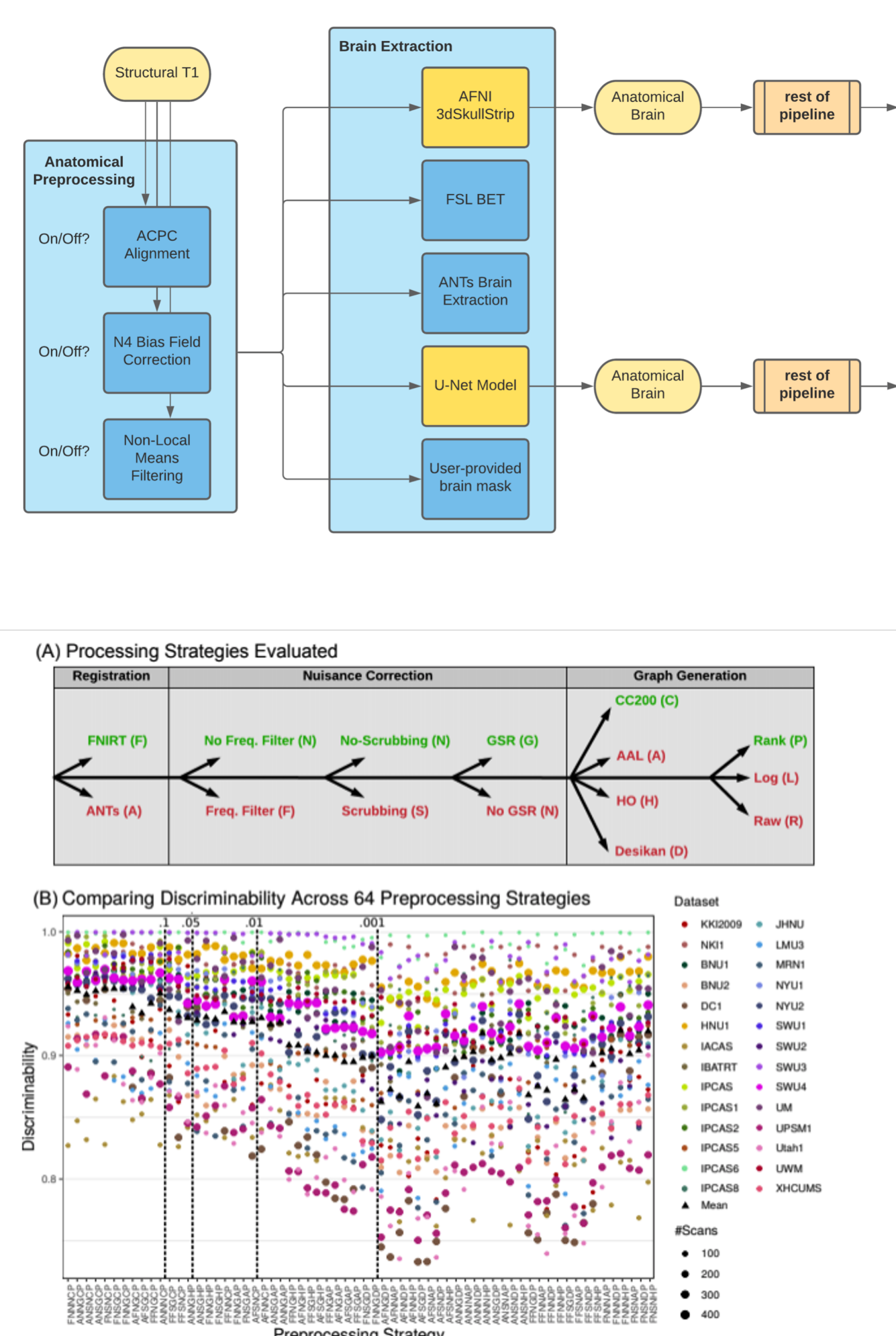
Shehzad et al., 2014

#### Automated Atlas Extraction (Neuroparc Library)



NeuroData, 2020

### Pipeline Forking and Iterables



Bridgeford et al., in press

### Extensive Registration Options

- Unbiased longitudinal registration
- EPI-Template based registration
- Anatomical surface registration
- End-to-end surface registration<sup>v1.82</sup>

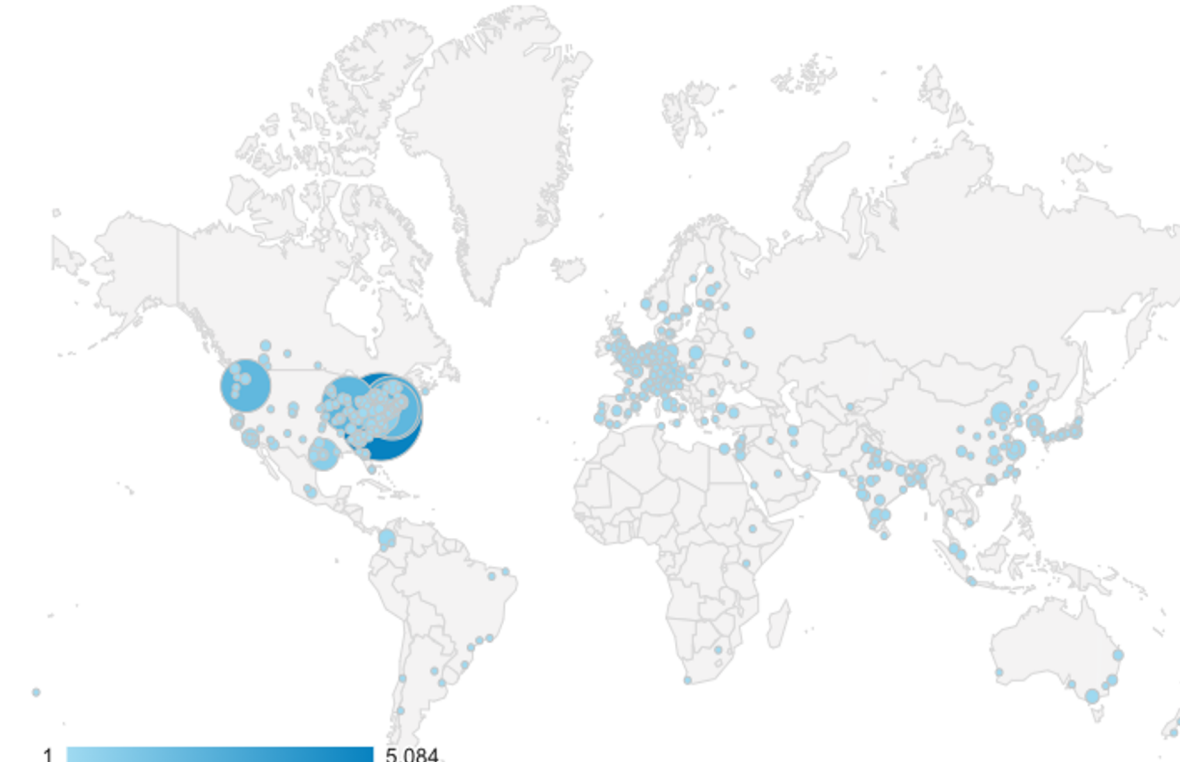
### BIDS Compatibility

- Inputs: BIDS Format
- Outputs: BIDS Derivatives
- Gorgolewski et al., 2016
- [bids-specification.readthedocs.io](https://bids-specification.readthedocs.io)

### Simplified Access



### Broad Adoption



|     |                | 30,340<br>% of Total: 100.00% (30,340) |
|-----|----------------|----------------------------------------|
| 1.  | United States  | 20,843 (68.74%)                        |
| 2.  | Germany        | 1,102 (3.63%)                          |
| 3.  | China          | 947 (3.12%)                            |
| 4.  | United Kingdom | 841 (2.77%)                            |
| 5.  | India          | 763 (2.50%)                            |
| 6.  | Canada         | 595 (1.96%)                            |
| 7.  | Netherlands    | 589 (1.93%)                            |
| 8.  | Japan          | 442 (1.45%)                            |
| 9.  | Italy          | 349 (1.14%)                            |
| 10. | South Korea    | 342 (1.12%)                            |

Google Analytics report for C-PAC runs by region.  
 Runs with `--tracking_opt-out` flag are not tracked.

## Conclusions

Following an iterative development process and multiple efforts to update the capabilities of the C-PAC project, the functional connectomics-focused pipeline configuration and execution platform is readying to exit its beta phase. We believe that the extended maturation process has allowed us to deliver the software needed to meet the ambitions and scale of cutting edge functional connectomics efforts.

## References

- Abbas, A., Belloy, M., ... Keilholz, S. (2019). Quasi-periodic patterns contribute to functional connectivity in the brain. *NeuroImage*, 191, 193–204. [doi:10.1016/j.neuroimage.2019.01.076](https://doi.org/10.1016/j.neuroimage.2019.01.076)
- Bellec, P., Rosa-Neto, P., ... Evans, A. C. (2010). Multi-level bootstrap analysis of stable clusters in resting-state fMRI. *NeuroImage*, 51(3), 1126–1139. [doi:10.1016/j.neuroimage.2010.02.082](https://doi.org/10.1016/j.neuroimage.2010.02.082)
- Bridgeford, E. W., Wang, S., ... Vogelstein, J. T. (2020). Eliminating accidental deviations to minimize generalization error and maximize reliability: Applications in connectomics and genomics. *BioRxiv*, 802629. [doi:10.1101/802629](https://doi.org/10.1101/802629)
- Cox, R. W. (1996). AFNI: Software for Analysis and Visualization of Functional Magnetic Resonance Neuroimages. *Computers and Biomedical Research*, 29(3): 162–173. [doi:10.1006/cbmr.1996.0014](https://doi.org/10.1006/cbmr.1996.0014)
- Esteban, O., Markiewicz, C. J., ... Gorgolewski, K. J. (2019). fMRIprep: A robust preprocessing pipeline for functional MRI. *Nature Methods*, 16(1), 111–116. [doi:10.1038/s41592-018-0235-4](https://doi.org/10.1038/s41592-018-0235-4)
- Gorgolewski, K., Burns, C. D., ... Ghosh, S. S. (2011). Nipype: A Flexible Lightweight and Extensible Neuroimaging Data Processing Framework in Python. *Frontiers in Neuroinformatics*, 5. [doi:10.3389/fninf.2011.00013](https://doi.org/10.3389/fninf.2011.00013)
- Gorgolewski, K. J., Auer, T., ... Poldrack, R. A. (2016). The brain imaging data structure, a format for organizing and describing outputs of neuroimaging experiments. *Scientific Data*, 3(1), 160044. [doi:10.1038/sdata.2016.44](https://doi.org/10.1038/sdata.2016.44)
- Harris, C. R., Millman, K. J., ... Oliphant, T. E. (2020). Array programming with NumPy. *Nature*, 585(7825), 357–362. [doi:10.1038/s41586-020-2649-2](https://doi.org/10.1038/s41586-020-2649-2)
- Kumar, M., Anderson, M. J., ... Norman, K. A. (2020). BrainIAK: The Brain Imaging Analysis Kit. *OSF Preprints*. [doi:10.31219/osf.io/db2ev](https://doi.org/10.31219/osf.io/db2ev)
- Li, X., Ai, L., ... Milham, M. (2021). Putting Pipeline Implementation-related Variation into Perspective for Functional Connectomics. 27th Annual Meeting of the Organization for Human Brain Mapping (OHBM) 2021, poster # 2405.
- NeuroData. (2020). *Neuroparc* (v1.0). GitHub. [github.com/neurodata/neuroparc/tree/v1.0](https://github.com/neurodata/neuroparc/tree/v1.0)
- Pedregosa, F., Varoquaux, G., ... Duchesnay, E. (2011). Scikit-learn: Machine Learning in Python. *Journal of Machine Learning Research*, 12(85), 2825–2830. [jmlr.org/papers/v12/pedregosa11a.html](https://jmlr.org/papers/v12/pedregosa11a.html)
- Shehzad, Z., Kelly, C., ... Milham, M. P. (2014). A multivariate distance-based analytic framework for connectome-wide association studies. *NeuroImage*, 93, Pt 1, 74–94. [doi:10.1016/j.neuroimage.2014.02.024](https://doi.org/10.1016/j.neuroimage.2014.02.024)
- Simony, E., Honey, C. J., ... Hasson, U. (2016). Dynamic reconfiguration of the default mode network during narrative comprehension. *Nature Communications*, 7(1), 12141. [doi:10.1038/ncomms12141](https://doi.org/10.1038/ncomms12141)
- Smith, S. M., Jenkinson, M., ... Matthews, P. M. (2004). Advances in functional and structural MR image analysis and implementation as FSL. *NeuroImage*, 23, S208–S219. [doi:10.1016/j.neuroimage.2004.07.051](https://doi.org/10.1016/j.neuroimage.2004.07.051)
- Son, J., Ai, L., ... Milham, M. (2020). Evaluating fMRI-Based Estimation of Eye Gaze During Naturalistic Viewing. *Cerebral Cortex*, 30(3), 1171–1184. [doi:10.1093/cercor/bhz157](https://doi.org/10.1093/cercor/bhz157)
- Sturgeon, D., Earl, E., ... Snider, K. (2021). *ABCD-HCP BIDS fMRI Pipeline*. GitHub. [doi:10.5281/zenodo.4571051](https://doi.org/10.5281/zenodo.4571051)
- Virtanen, P., Gommers, R., ... van Mulbregt, P. (2020). SciPy 1.0: Fundamental algorithms for scientific computing in Python. *Nature Methods*, 17(3), 261–272. [doi:10.1038/s41592-019-0686-2](https://doi.org/10.1038/s41592-019-0686-2)
- Xu, T., Yang, Z., ... Zuo, X.-N. (2015). A Connectome Computation System for discovery science of brain. *Science Bulletin*, 60(1), 86–95. [doi:10.1007/s11434-014-0698-3](https://doi.org/10.1007/s11434-014-0698-3)