## Understanding (and mitigating) the impact of preprocessing pipelines on neuroimaging analyses (Can you\* reproduce neuroimaging analyses?)

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Code: https://github.com/neurodatascience/compare-surf-tools







#### INTRODUCTION

- Implementation choices in the computational workflow introduce variability in the neuroimaging analysis which impacts reproducibility of scientific findings.
- We highlight this issue with a sample sMRI dataset processed using several pipelines (see Fig. 1).
- We compare the processed features and the performance variation of statistical models for biological inference and individualize prediction.

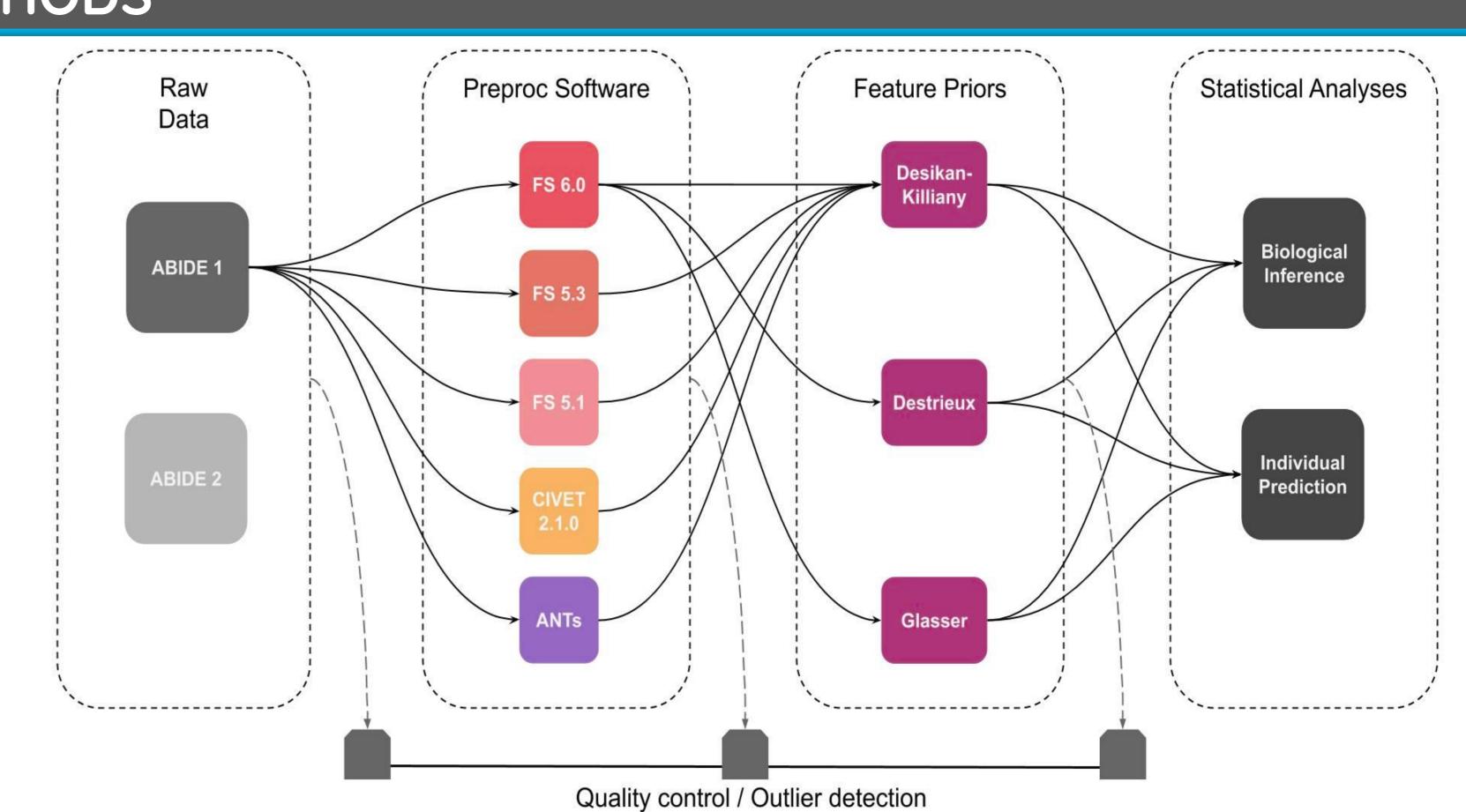
### **METHODS**

- Dataset: Autism Brain Imaging Data Exchange (ABIDE) Preprocessing project
- Phenotype: Cortical thickness

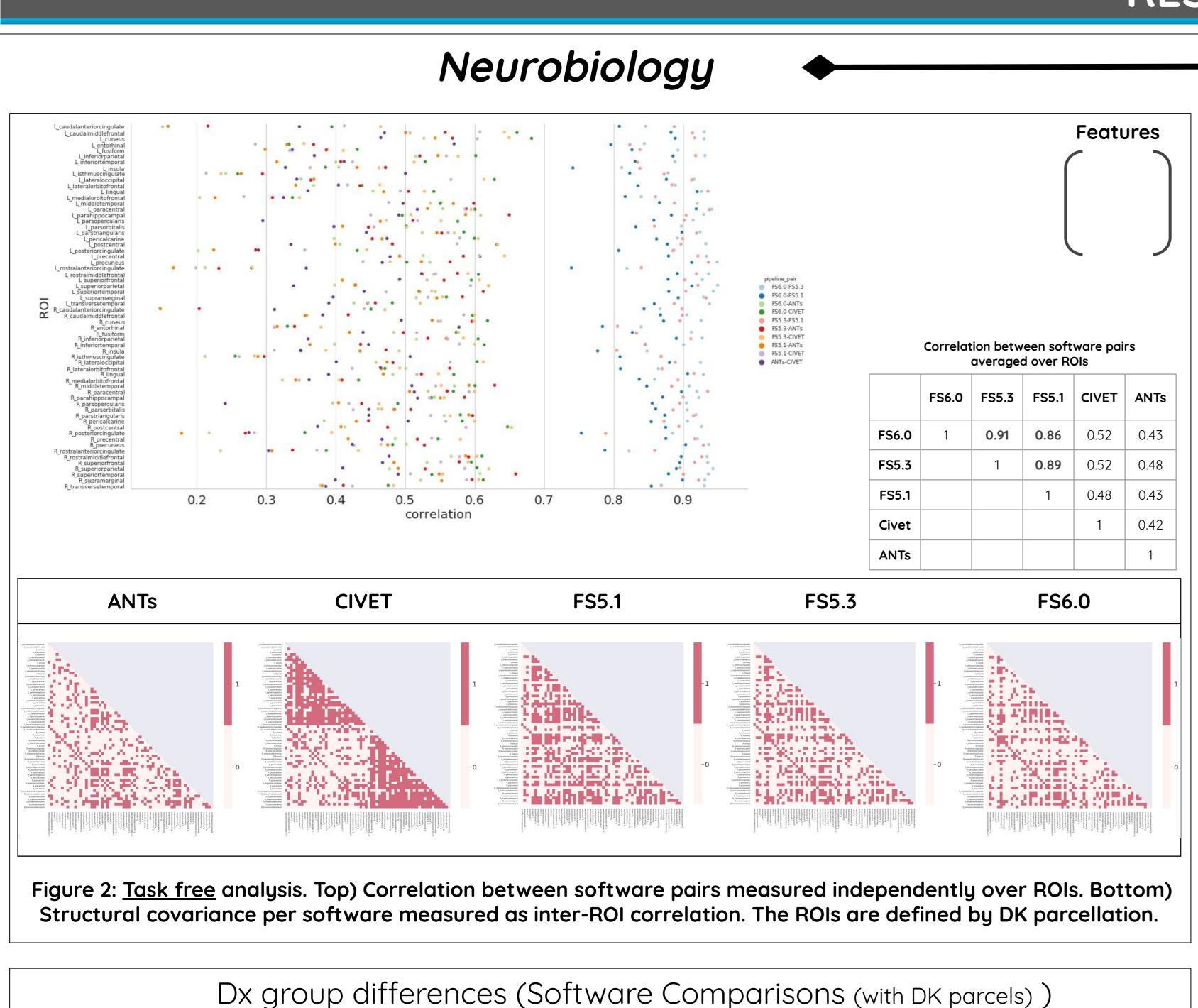
No QC (N= 778 CTRL: 415, ASD: 363)

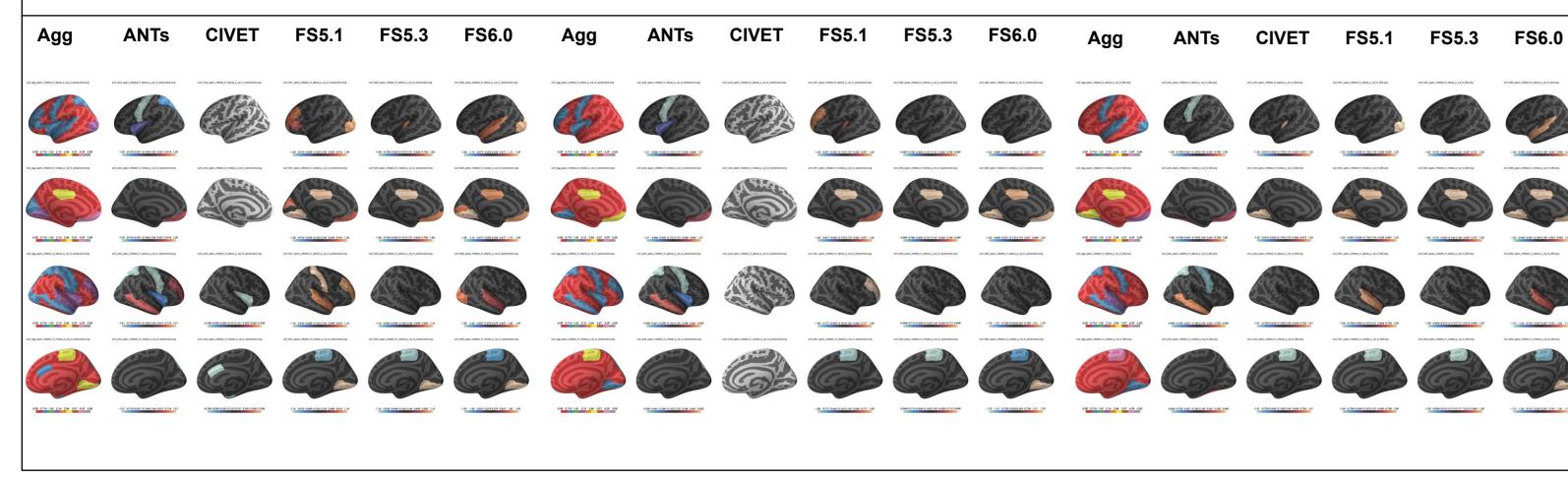
- Comparisons
  - Software: Freesurfer (6.0, 5.3, 5.1) , CIVET (2.1.0), ANTs (RRID:SCR\_004757)
  - Parcellations: Desikan-Killiany Atlas (31x2), Destrieux (74x2), Glasser (180x2)
  - Quality control (QC): manual, automatic outlier detection
- Analyses
  - Neurobiological inference: diagnostic group differences
  - Individualized prediction: Dx, Age prediction

Figure 1: Computational workflow building blocks and potential permutations for typical structural MR image analyses. Only a subset of possible pipelines analyzed in this work is shown with connected arrows.



## RESULTS





Manual QC (N=748 CTRL: 407, ASD: 341)

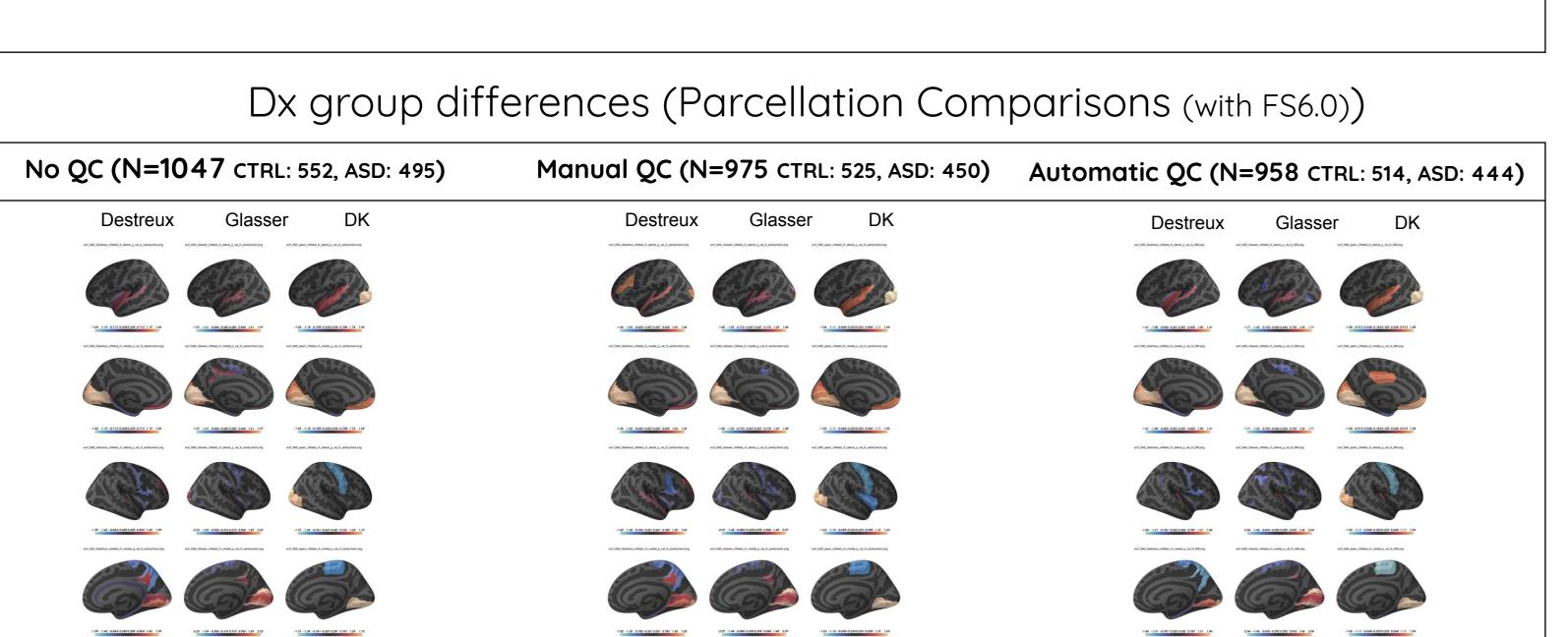


Figure 3: Task driven analysis. Top) Significantly ROI differences with various software and QC levels. The 'agg' column represents ranking based on overlap across pipelines. Bottom) Significantly ROI differences with various parcellations and QC levels. The ROI colors denote beta values.

# Individuals

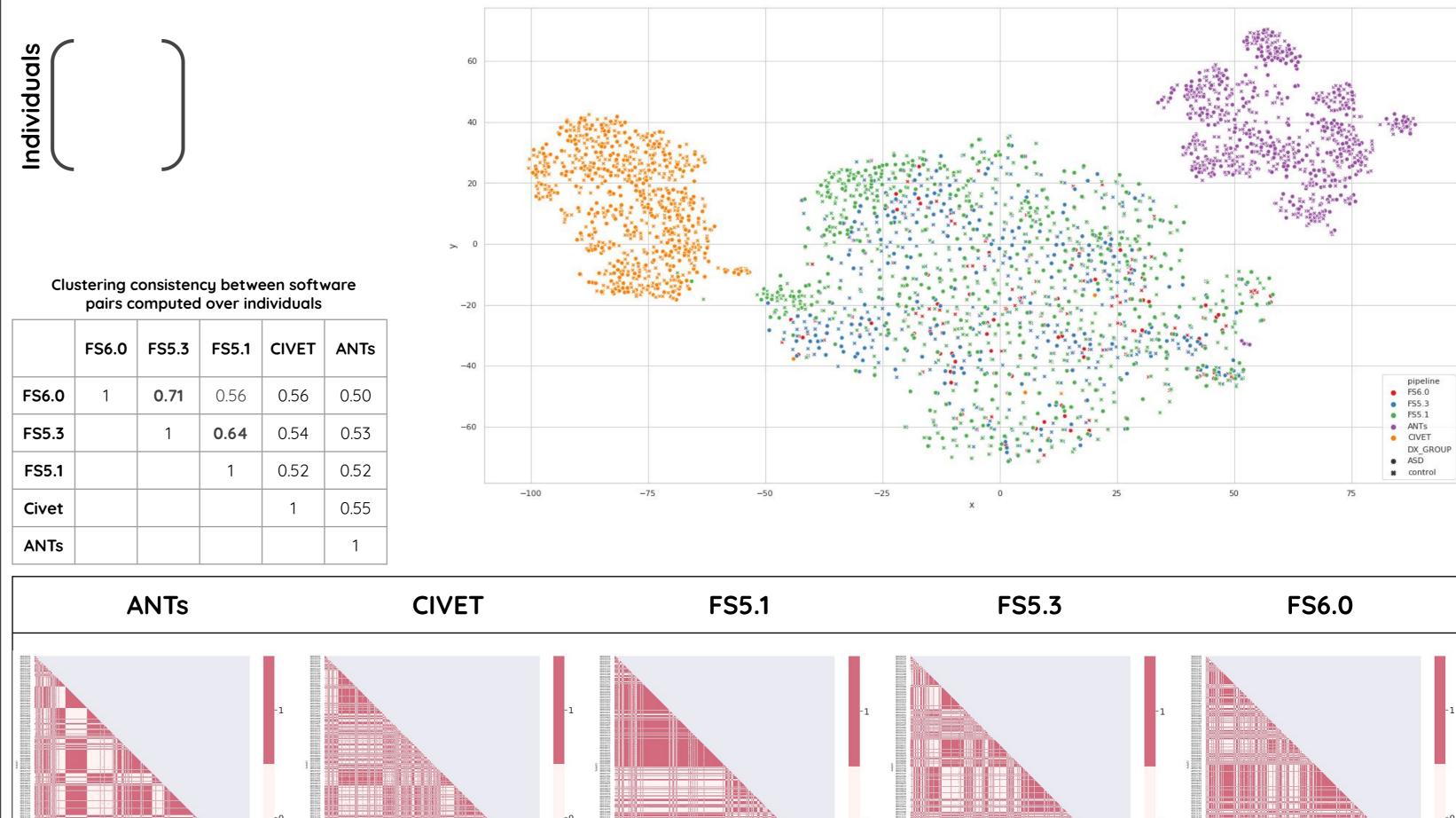
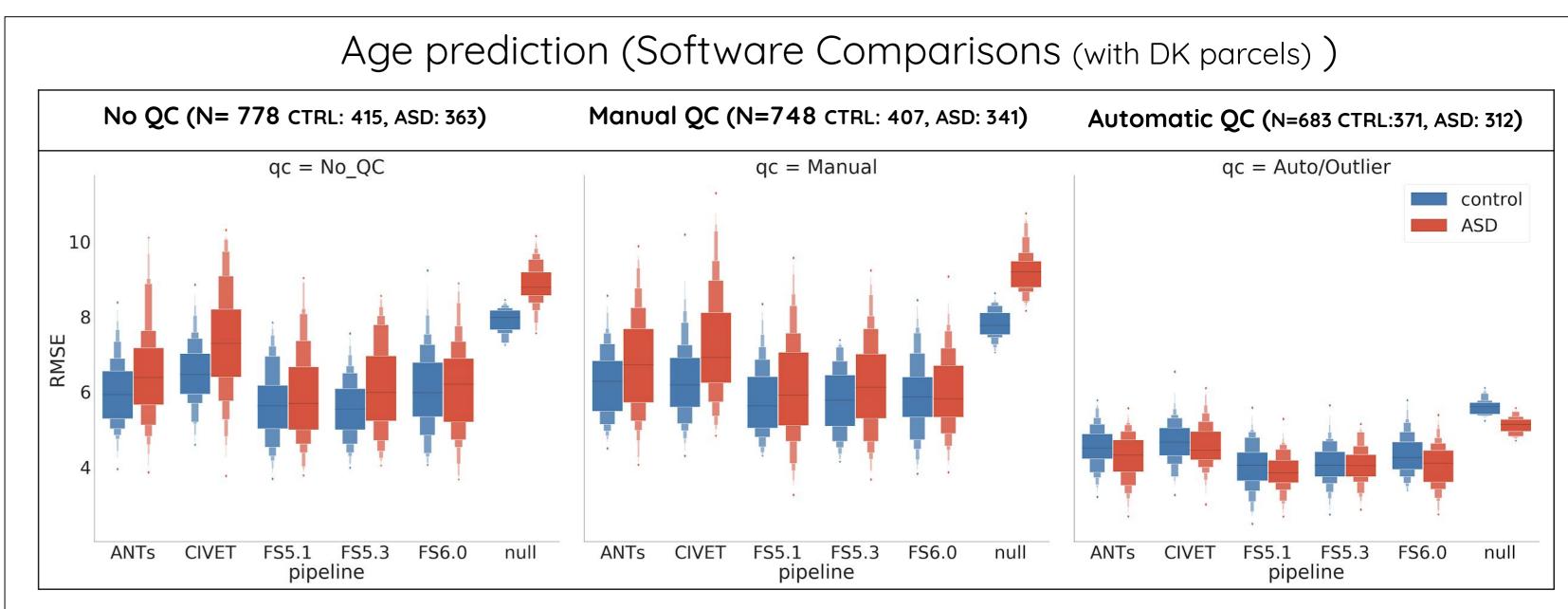


Figure 4: Task free analysis. Top) t-SNE representation of all individuals Bottom) Pairwise cluster-membership of all individuals. Binary membership is assigned based on two clusters derived from hierarchical clustering.



Age prediction (Parcellation Comparisons (with FS6.0))

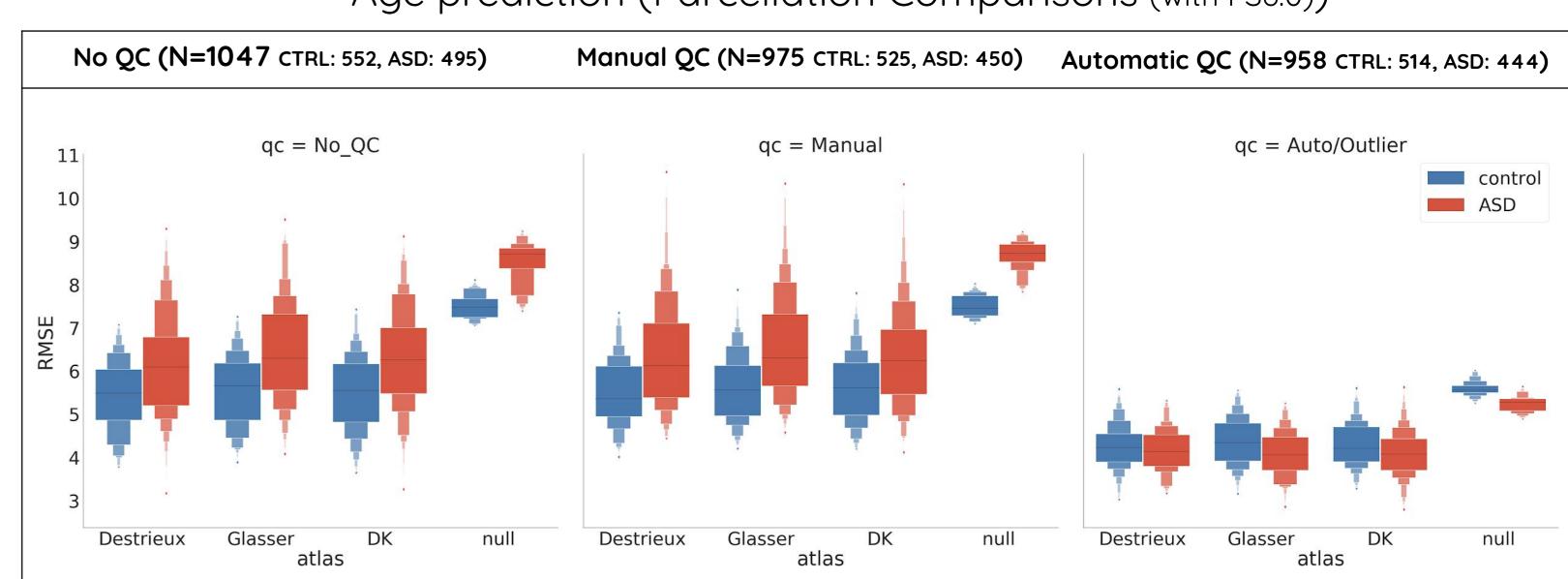


Figure 5: <u>Task driven</u> analysis. Top) Individual age prediction for different software and QC levels stratified by diagnosis. Bottom) ) Individual age prediction for different parcellations and QC levels stratified by diagnosis. Performance is validated using a Random Forest model over 100 shuffle-split iterations stratified by Dx.

### CONCLUSIONS

• Large differences across software produce weakly correlated features and offer poor clustering consistency across individuals.

Automatic QC (N=683 CTRL:371, ASD: 312)

- Consensus across parcellations can improve the confidence and specificity of biomarkers; however no significant impact is seen on individual predictions.
- QC procedure has strong impact on biological and individual findings, as well as the underlying null distributions.
- We encourage reporting of variation in scientific findings with respect to implementation choices of software, priors (e.g. parcellations), and QC filtering.

### **ACKNOWLEDGMENTS**

### REFERENCES

- Craddock, R. Cameron, and Pierre Bellec. 2015. "Preprocessed Connectomes Project: Abide." Available Online at:
- Http://preprocessed-Connectomes-Project. Github. Io/abide. http://preprocessed-connectomes-project.org/abide/. 2. Dickie, Erin, Steven M. Hodge, R. Cameron Craddock, Jean-Baptiste Poline, and David N. Kennedy. 2017. "Tools Matter: Comparison of Two Surface
- Analysis Tools Applied to the ABIDE Dataset." Riogrande Odontologico 3 (May): e13726. 3. Tustison, Nicholas J., Philip A. Cook, Arno Klein, Gang Song, Sandhitsu R. Das, Jeffrey T. Duda, Benjamin M. Kandel, et al. 2014. "Large-Scale Evaluation of ANTs and FreeSurfer Cortical Thickness Measurements." Neurolmage.

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