Optimizing Lifespan Normative Models for Regional Subcortical Volume, Cortical Thickness, and Surface Area

Ruiyang Ge[1], Yuetong Yu[1], Yi Xuan Qi[1], Yunan Fan[1], Faye New[2], Shalaila Haas[2], Paul Thompson[3], Sophia Frangou[1,2]

[1]Department of Psychiatry, University of British Columbia, Canada; [2]Department of Psychiatry, Icahn School of Medicine at Mount Sinai, USA;

[3]Imaging Genetics Center, Mark and Mary Stevens Neuroimaging and Informatics Institute, Keck School of Medicine, University of Southern California, USA

BACKGROUND

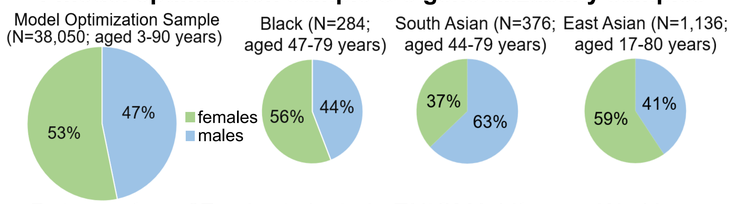
- Normative brain modeling has recently been used to derive individual-level deviation in quantitative neuroimaging phenotypes.[1,2,3]
- Choice of algorithms lacks empirical support from direct comparative benchmarking.

OBJECTIVES

- evaluate commonly used normative modeling algorithms in building normative neuroanatomical models
- establish the minimum sample size required for reliable model performance
- present normative neuroanatomical models of high generalizability & an open-access web portal to the research community

METHODS

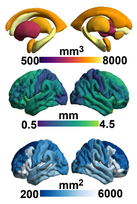
- **1 model optimization sample & 3 generalizability samples**



⊖ Data are from 87 cohorts include ENIGMA-Lifespan Working Group[4], ABCD[5], UK-Biobank[6] etc.

⊖ Only participants considered free of psychiatric disorders, medical and neurological morbidity, and cognitive impairment at the time of scanning are included.

- **150 FreeSurfer[7] measures**

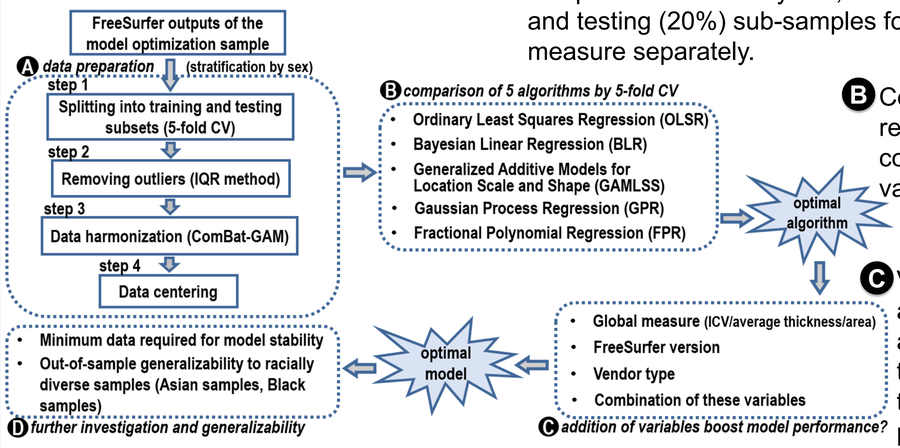


14 subcortical volumes

68 cortical thickness measures

68 surface area measures

- **Data analysis procedures**



A Each FreeSurfer measure of the model optimization sample are stratified by sex, and split into training (80%) and testing (20%) sub-samples for each anatomical measure separately.

B Comparisons between 5 regression approaches are conducted by 5-fold cross-validation (CV).

C Variables are sequentially added to the optimal algorithm in procedure (B) to assess if inclusion of them would boost model performance.

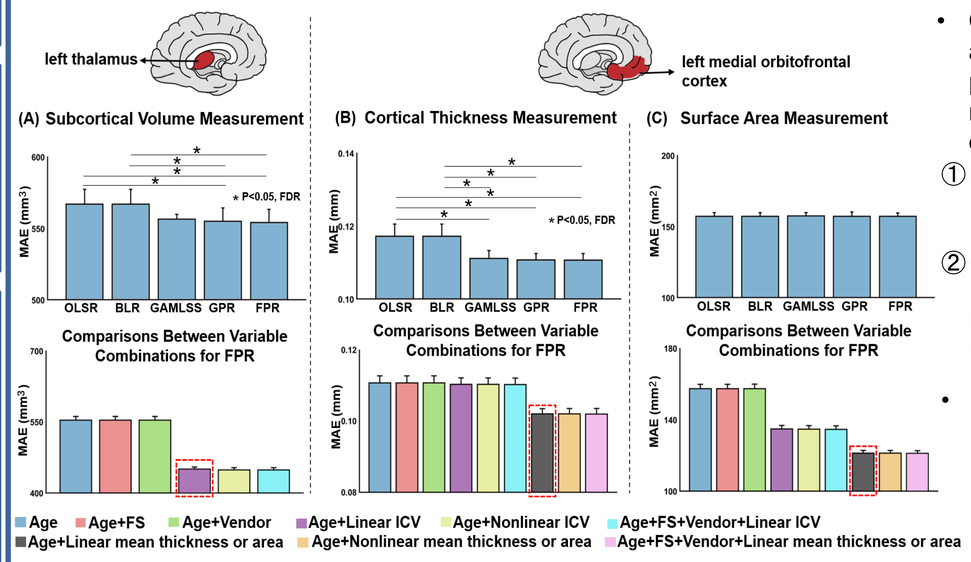
D After confirming the optimal model (optimal algorithm + optimal variable combination), two further questions are investigated.

① minimum sample size for a stable model

② test the generalizability of the pre-trained model to 3 racially diverse samples

RESULTS & CONCLUSIONS

- Results of female participants are presented in this section, and all conclusions can be generalized to males.



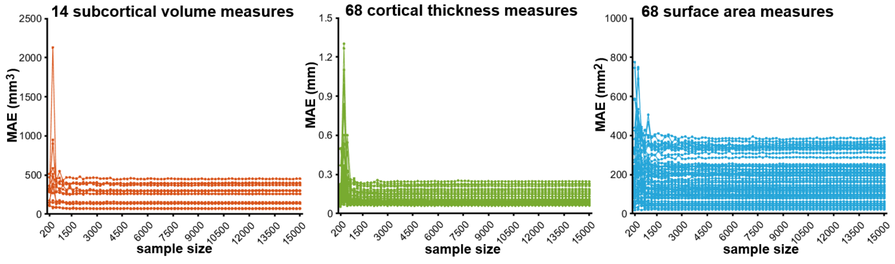
- **Optimal algorithm: FRP algorithm with its best predictive performance and reasonable computational efficacy**

① predictive performance, **MAE** (mean absolute error): FPR≈GPR≈GAMLSS<OLSR≈BLR

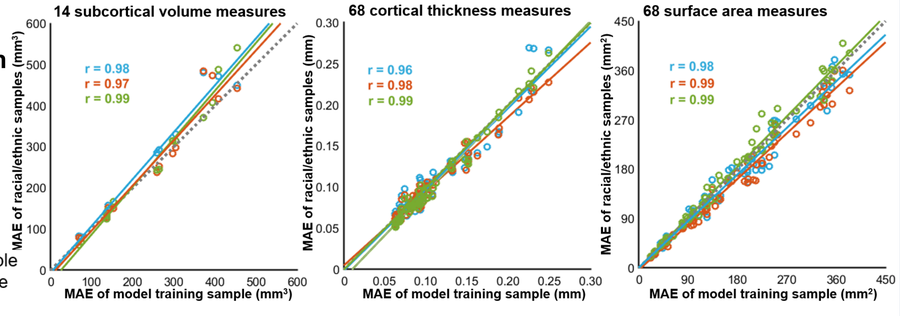
② CPU time: OLSR≈10ms, FPR≈500ms, BLR≈GAMLSS≈5,000ms, and GPR>30minutes.

- **Optimal model: FPR algorithm with the nonlinear fractional polynomials of age and linear global measure of the corresponding anatomical measure.**

- **Samples below 1,000 are likely to yield unreliable normative models.**
- **Collectively, a sample size above 3,000 is a decent size to generate a robust normative model.**



- **The pre-trained model for each anatomical measure has very high generalizability for all 3 samples with different races/ethnicities.**



- **We present an open-access web portal with:** https://centilebrain.org

① pre-trained sex-specific normative neuroanatomical models

② a functionality to generate individual-level normalised deviations of user data

③ full scripts for generating normative models in any user-specified T1-weighted MRI datasets

REFERENCE

1. T. Wolfers, N.T. Doan, et al., JAMA Psychiatry, 2018.
2. R. Bethlehem, J. Seidlitz, et al., Nature, 2022.
3. R. Saige, F. Charlotte, et al., Elife, 2022.
4. S. Frangou, A. Modabbernia, et al., Human Brain Mapping, 2022.
5. B.J. Casey, T. Cannonier, et al., Developmental Cognitive Neuroscience, 2018.
6. K. Miller, F. Alfaro-Almagro, et al., Nature Neuroscience, 2016.
7. B. Fischl, NeuroImage, 2012.