Hemispheric biases in automatic atlas-based cortical parcellations exaggerate surface area lateralization

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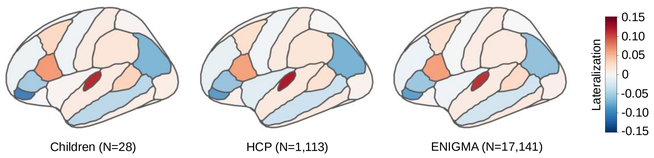
Summary

- Studies using automated surface-based parcellation and analysis packages (e.g., FreeSurfer) yield impossibly identical results when measuring lateralization of surface area, regardless of the size and distribution of samples.



- We used both original and left-right flipped MRI volumes to reveal hemispheric bias in automatic surface area parcellations.
- A step-by-step investigation of the automatic processing stream from FreeSurfer suggested that **the bias exists in the parcellation atlas**, rather than the surface reconstruction or registration.
- The atlas bias is carried into individual parcellations due to the algorithm's over-reliance on the atlas and underweight of individual curvature patterns.
- **Our results suggest that relying on the automatic parcellation provided by FreeSurfer can lead to misrepresentation of the degree of surface area lateralization in key structures that are important to audition and language.**

Methods

Participants: N = 55 adult participants (38 female, 17 male; age 19-32 years, M = 22.6 years).

MRI Acquisition: T1-weighted (T1w) multi-echo magnetization-prepared rapid gradient-echo anatomical volume (TR = 2,530ms, TE = [1.64, 3.50, 5.36, 7.22ms], TI = 1,400ms, flip angle = 7.0°, 1.0mm isotropic voxels, FOV = 256 × 256, 176 sagittal slices) and T2-weighted (T2w) anatomical volume (TR = 3,200ms, TE = 454ms, 1.0mm isotropic voxels, FOV = 256 × 256, 176 sagittal slices).

Surface Processing: Left-right directional encoding in unprocessed *NIfTI* files was reversed using the FreeSurfer command *mri_convert* to create flipped copies of the brains. For both the original and flipped brains, cortical reconstruction was performed using the default processing stream *recon-all* in FreeSurfer v6.0.0.

Lateralization and Bias: The lateralization index (λ) was computed as $(\text{left} - \text{right}) \,/\, (\text{left} + \text{right})$ per region for each measurement. Bias was computed as $\lambda_{orig} + \lambda_{flip}$. Leftward asymmetry in the original brains should be captured as rightward asymmetry in the flipped brains if the measurement is unbiased.

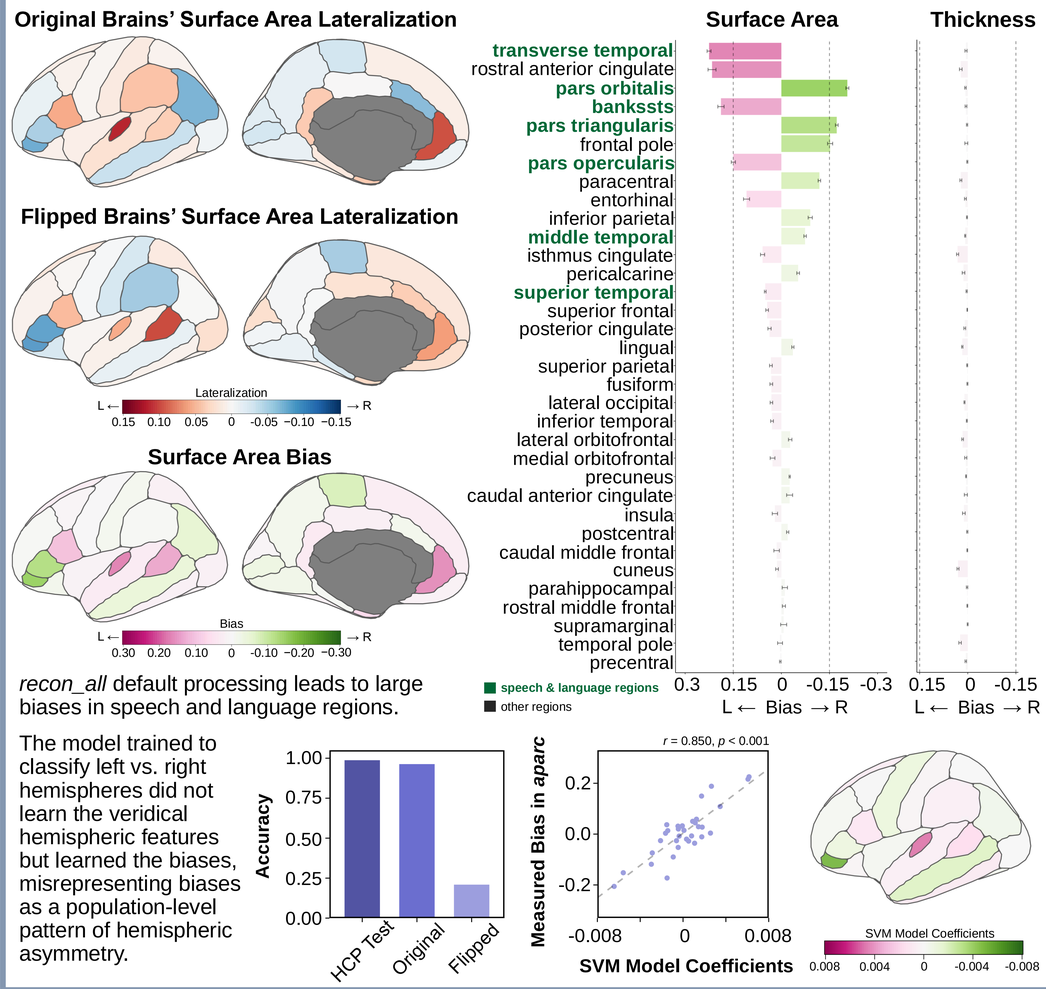
Manual Labeling: We manually labeled transverse temporal gyrus and subregions of inferior frontal gyrus (IFG pars opercularis, pars triangularis, and pars orbitalis) using the individual pial and inflated surfaces for each hemisphere per participant.

Symmetric Registration: The source of bias in the default processing pipeline can originate from asymmetric registration to the template and/or asymmetric atlas-based parcellation. To examine the source of bias, all surfaces were registered to the symmetric template *fsaverage_sym* using Xhemi and then parcellated by the respective left or right *aparc* atlas using *mris_ca_label*.

Symmetric Atlas Parcellation: We applied one single atlas to parcellate both hemispheres after symmetric registration.

Support Vector Machine: We trained a SVM model to classify left vs. right hemispheres based on default surface area measurements on HCP S1200 datasets (training: testing = 7:3) and applied the trained model to our original and flipped brains.

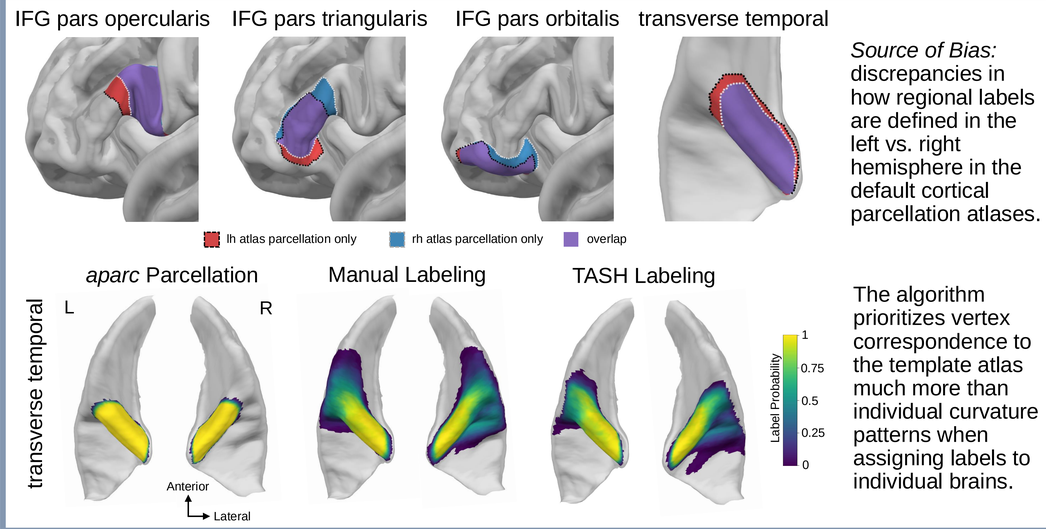
Original vs. Flipped Brains



recon_all default processing leads to large biases in speech and language regions.

The model trained to classify left vs. right hemispheres did not learn the veridical hemispheric features but learned the biases, misrepresenting biases as a population-level pattern of hemispheric asymmetry.

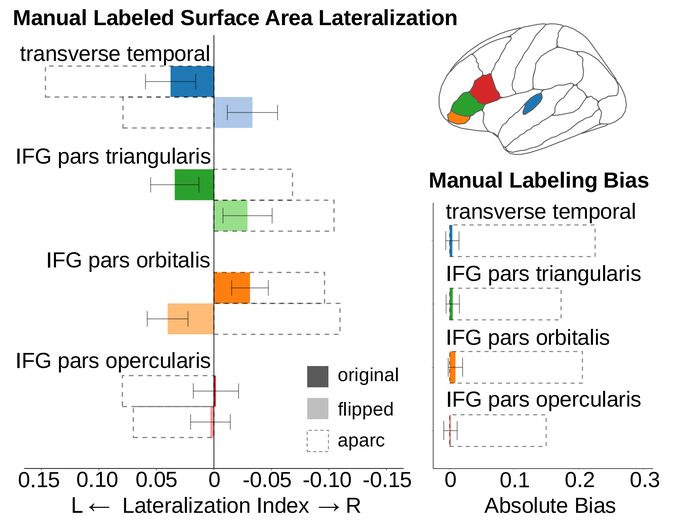
Source of Bias



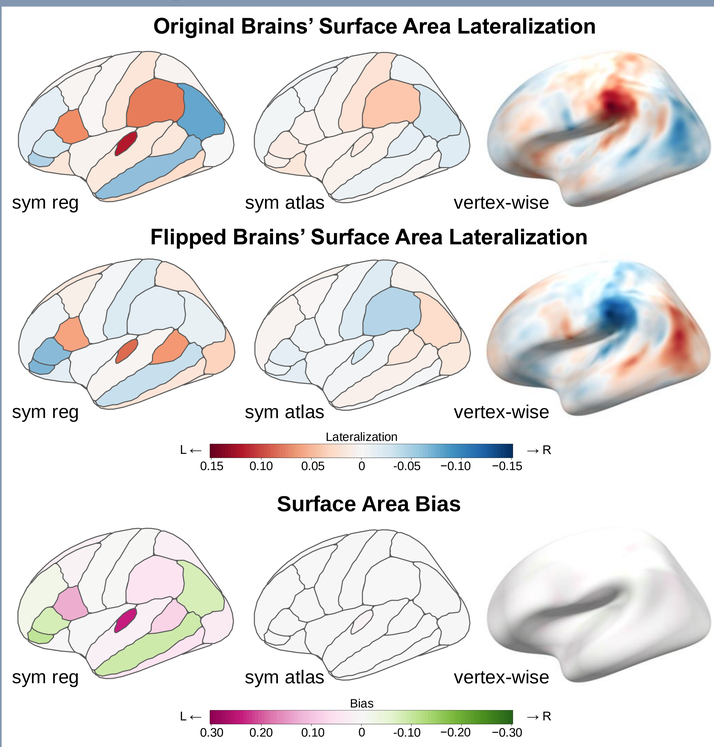
Source of Bias: discrepancies in how regional labels are defined in the left vs. right hemisphere in the default cortical parcellation atlases.

The algorithm prioritizes vertex correspondence to the template atlas much more than individual curvature patterns when assigning labels to individual brains.

Manual Labeling



Registration vs. Parcellation



Suggestion: Use manual labeling / vertex-wise analysis / symmetric atlas / curvature-based parcellation tools (e.g., TASH for HG) to ameliorate the bias.

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References: [1] Dalboni da Rocha et al. (2020). *Sci. Rep.* [2] Desikan et al., (2006). *NeuroImage.* [3] Fischl et al., (2004). *Cerebral Cortex*. [4] Greve et al., (2013). *J. Cog. Neuro*. [5] Kong et al. (2018). *PNAS.*