Hemispheric biases in automatic cortical parcellations exaggerate surface area lateralization in primary auditory cortex and other key language areas

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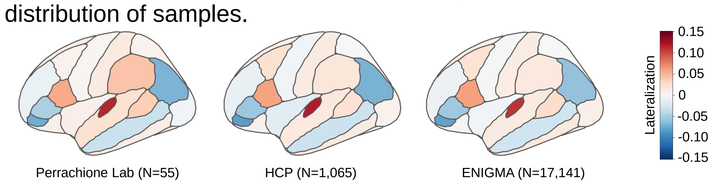
Summary

- 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.
- **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.

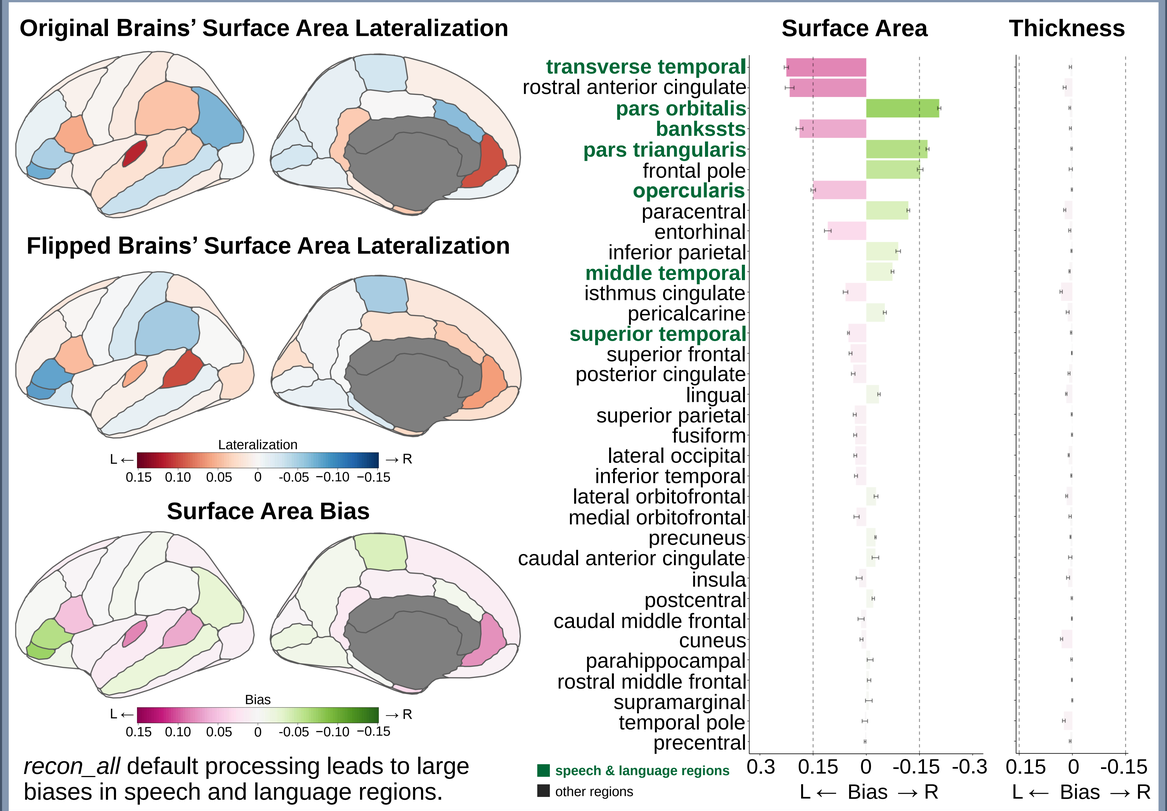
Lateralization and Bias: The lateralization index (λ) was computed as $(\text{left} - \text{right}) \,/\, (\text{left} + \text{right})$ per region for each measurement. Bias was computed as $\lambda_{orig} + \lambda_{flip}$. Leftward asymmetry in the original brains should be captured as rightward asymmetry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

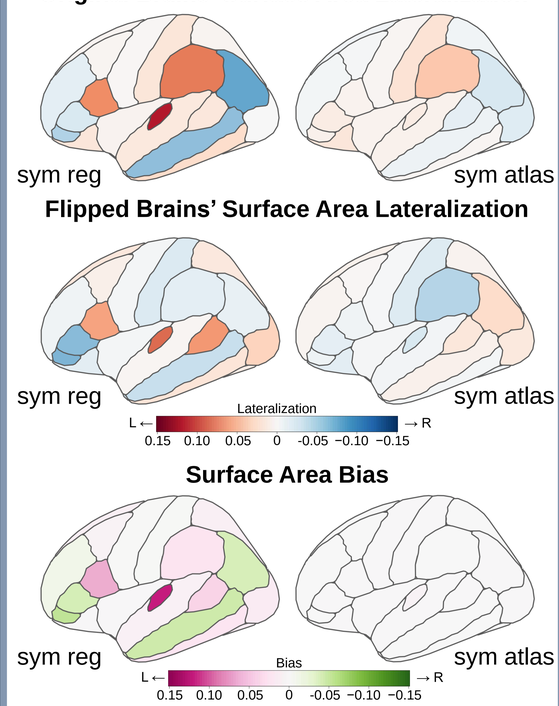
Symmetric Atlas Parcellation: We also applied one single atlas to parcellate both hemispheres after symmetric registration.

Original vs. Flipped Brains



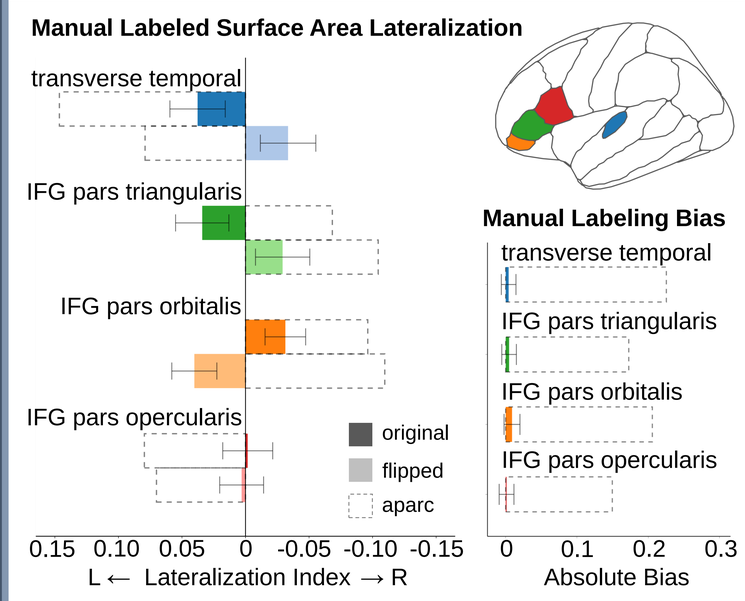
recon_all default processing leads to large biases in speech and language regions.

Registration vs. Atlas

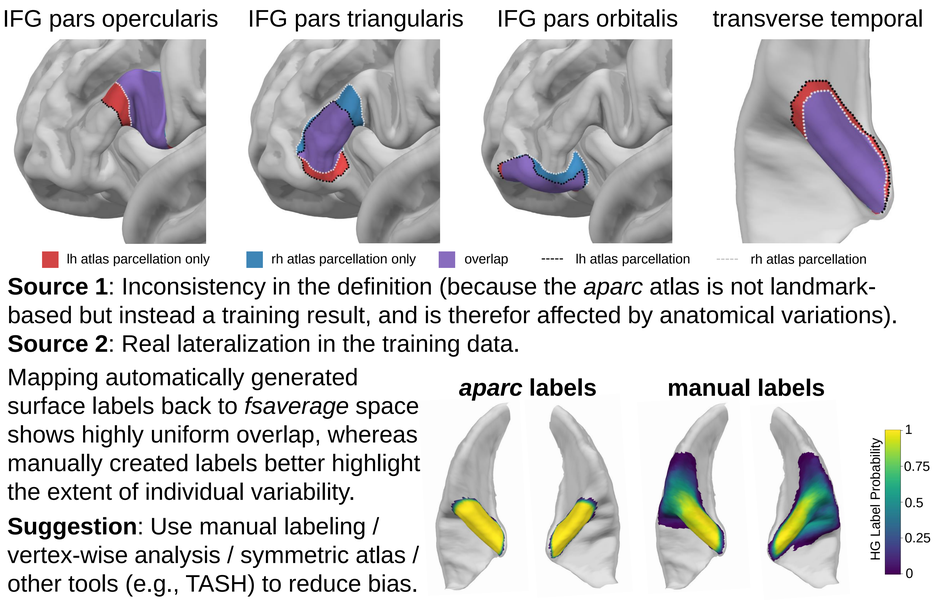


Symmetric registration does not reduce the bias but applying a symmetric atlas does.

Manual Labeling



Sources of Bias in the Atlas



Source 1: Inconsistency in the definition (because the *aparc* atlas is not landmark-based but instead a training result, and is therefor affected by anatomical variations).
Source 2: Real lateralization in the training data.

Mapping automatically generated surface labels back to *fsaverage* space shows highly uniform overlap, whereas manually created labels better highlight the extent of individual variability.

Suggestion: Use manual labeling / vertex-wise analysis / symmetric atlas / other tools (e.g., TASH) to reduce 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*.