Asymmetry of large-scale functional organization: heritable and phylogenetic profiles

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Introduction

- Asymmetry is a key organisational feature of the human brain and related to the hemispheric preference of functional processes, for example language. However, to what extent the functional organisation in the cerebral cortex is asymmetric, and whether this asymmetry is heritable is not known to date.
- The present study aims to investigate asymmetry of functional organization in healthy humans, study its heritability using a twin-sample, and analyse the asymmetry in non-human primates (i.e., macaque monkeys) to map phylogenetic conservation.

Methods

- Human data: HCP S1200 (n=1014) (www.humanconnectome.org/)
- Macaque data: PRIMATE-DE (n=19). (Milham et al., 2018)
- Functional connectivity (FC) included intra-hemispheric (left-left and right-right) and inter-hemispheric (left-right and right-left) patterns.
- Gradients of each FC pattern were computed using BrainSpace (Vos de Wael et al., 2020) and aligned to the template gradients (gradients of group mean left-left FC).
- Asymmetry index: left minus right hemisphere in the homologous regions.
- We computed heritability by means of family structure of HCP using SOLAR eclipse 8.4.1b (http://solar-eclipse-genetics.org/). Heritability $h^2 = \sigma^2_g$ (total additive genetic variance) / σ^2_p (phenotypic variance).
- Functions along the asymmetry axis was computed using projection of meta-analytical task-based activity generated by NeuroSynth (Chang et al., 2013) (https://neurosynth.org/).

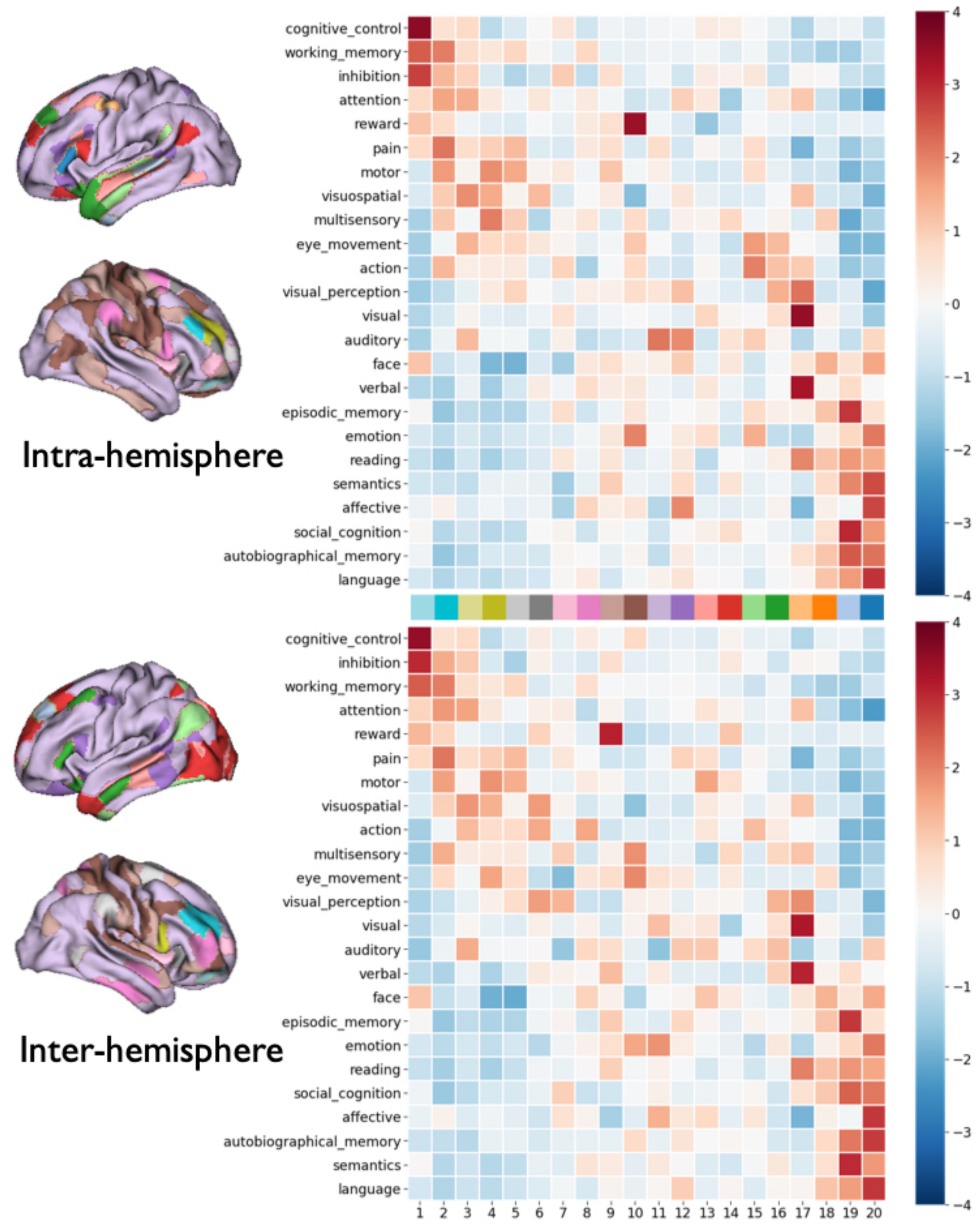

Fig. 4. Projection of meta-analytical task-based function along asymmetry effects of G1. Right panel is the functional decoding of the intra-hemispheric pattern and the left panel is the inter-hemispheric pattern.

Results

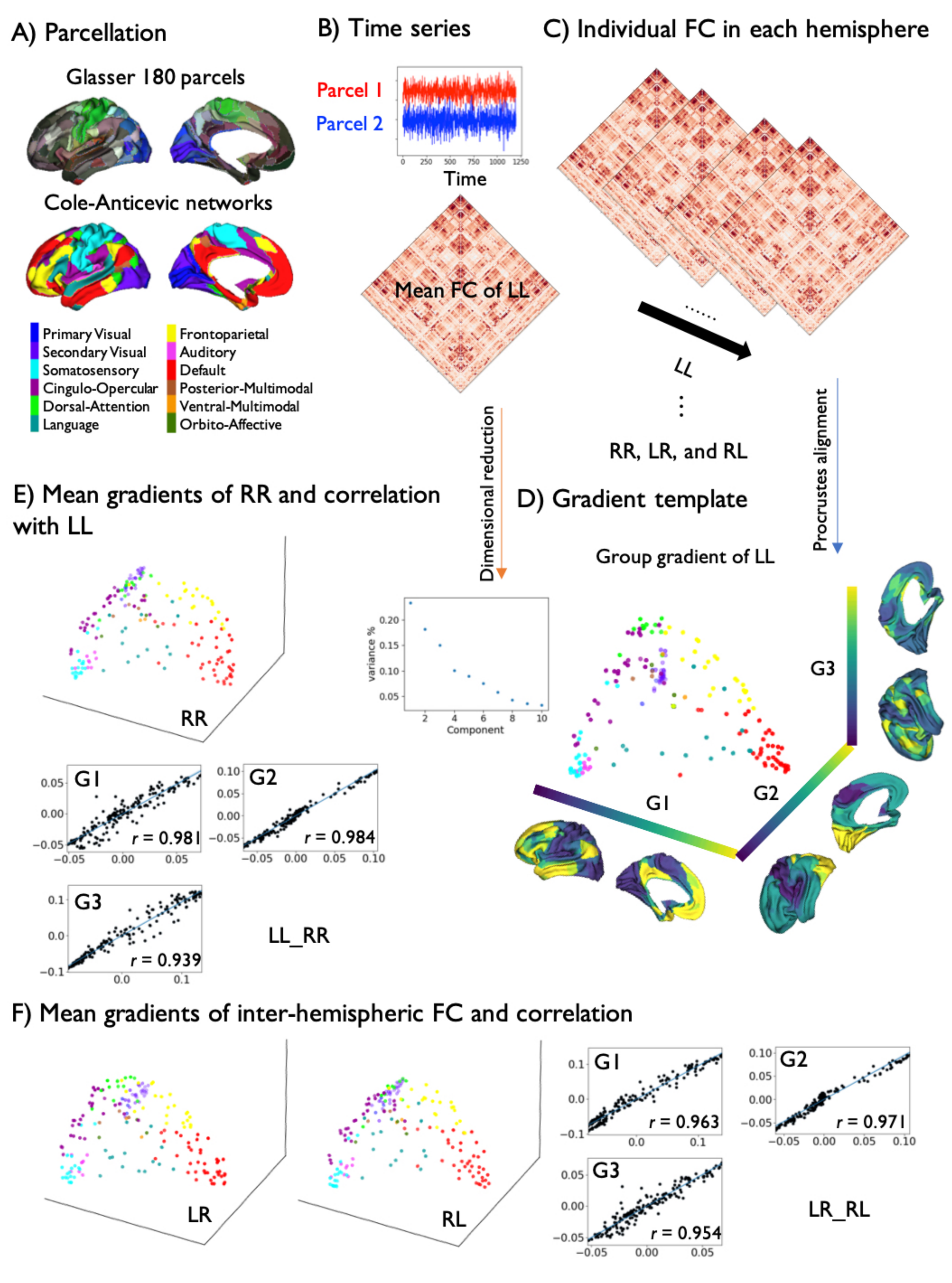

Fig 1. Processing of functional gradients. A) Parcellation using Glasser 180 atlas in each hemisphere and Cole-Anticevic networks. B) Time series of two parcels and mean functional connectivity (FC) matrix between left and left hemisphere (LL). C) Individual FC in each hemispheric pattern, i.e., (LL), right-right (RR), left-right (LR), and right-left (RL). D) Gradient template using group level gradient LL. E) Mean gradients of RR and correlation with LL F) Mean gradients of inter-hemispheric FC and correlation. Color of dots in 3D plotting means Cole-Anticevic networks.

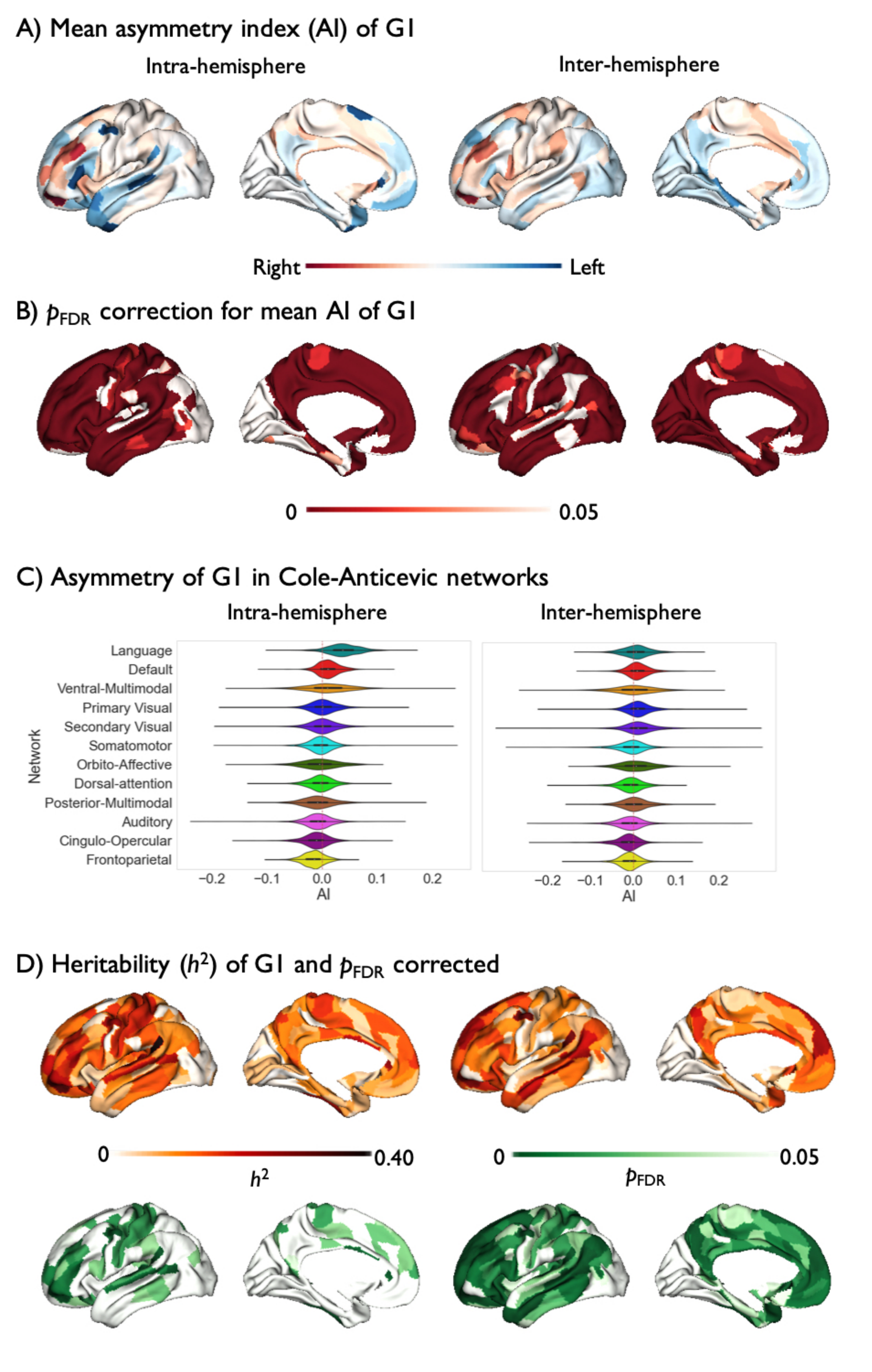

Fig 2. Asymmetry of functional gradients in humans. A) Mean asymmetric index (AI) of intra-hemispheric pattern and inter-hemispheric pattern in humans. B) FDR correction for the p value. C) Asymmetries of the first gradient in Cole-Anticevic networks. D) Heritability of G1 and FDR correction for p value.

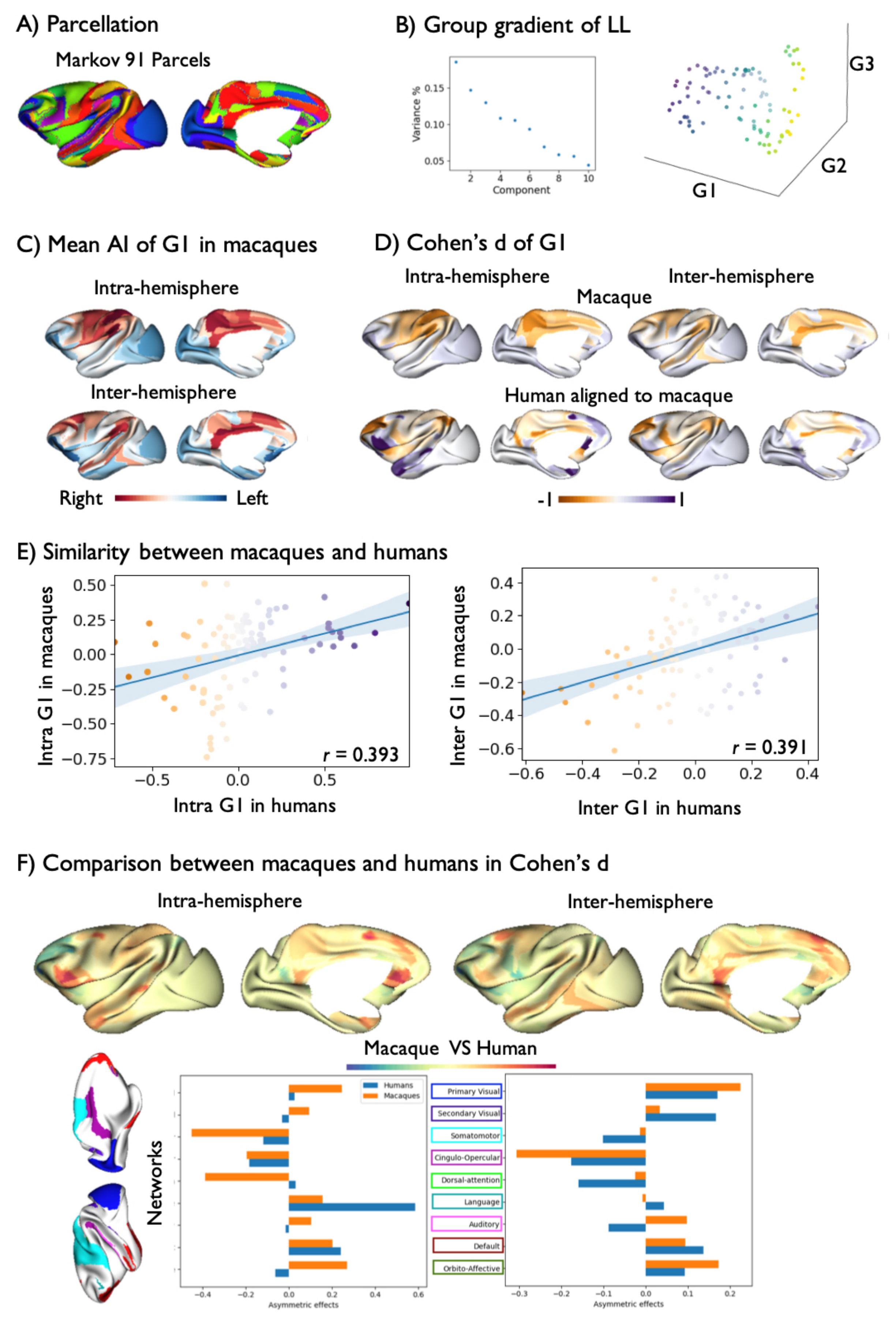

Fig. 3. Asymmetry of functional gradients in macaques. A) Parcellation used Markov 91 atlas in macaques. B) Template gradients. C) Mean asymmetry index of G1 in macaques. D) Asymmetric effects (Cohen's d) of the G1 in macaques and humans aligned to macaques. E) Similarity of G1 in humans with G1 in macaques. F) Comparison between macaques and humans in Cohen's d of G1.

Discussion

- For the intra-hemispheric pattern, transmodal systems showed great asymmetry (e.g., language, DMN, FPN), but unimodal systems showed small or no asymmetry (e.g., visual). For the inter-hemispheric pattern, we did not observed strong patterns of asymmetry (particularly in primary cortex). It indicates that neurons involved in higher order cognition are asymmetrically organized within hemisphere, but the asymmetric organization decreases when it needs corpus callosum to be connected.
- Excluding visual cortex, asymmetry of of both intra and inter-hemispheric asymmetry was significantly heritable, indicating that asymmetry of functional gradients may be under genetic control. As noted, heritability of asymmetry of Wernicke's area peaked among the cortex, indicating that lateralized language relies on the genetics.
- No significant asymmetry was observed in macaques. However, the asymmetric pattern was kind of similar with humans. It implicates the similar evolutionary origins of brain function between humans and non-human primates, and some unique function (e.g., language) occurring in humans.
- Functional decoding further provides the evidence that the lateralized function is asymmetrically organized in the brain.

Code avaliability

Scripts and data will be available at https://github.com/wanb-psych

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OHBM, 2021