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

Bin Wan[1,2,3,4], Seyma Bayrak[1,3,4], Ting Xu[6], H. Lina Schaare[1,4], Boris C. Bernhardt[7], Sofie L. Valk[1,4,5]

Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany[1]; International Max Planck Research School on Neuroscience of Communication: Function, Structure, and Plasticity, Leipzig, Germany[2]; Medical Faculty, Leipzig University, Leipzig, Germany[3]; Research Center Jülich, Jülich, Germany[4]; Institute of Systems Neuroscience, Heinrich Heine University Düsseldorf, Düsseldorf, Germany[5]; Child Mind Institute, New York, USA[6]; Montreal Neurological Institute, Montreal, Canada[7].

binwan@cbs.mpg.de, twitter: @wanb_psych

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 analyze the asymmetry in macaque monkeys to map phylogenetic conservation.

Methods

- **Data**
  Human: HCP S1200 (n=1014) (Van Essen et al. 2013)
  Macaque: PRIMATE-DE (n=19) (Milham et al., 2018; Xu et al., 2020)
- **Functional connectivity (FC) patterns**
  Intra-hemisphere (left-left LL and right-right RR)
  Inter-hemisphere (left-right LR and right-left RL)
- **Gradients of each FC pattern**
  Gradients were computed using BrainSpace (Vos de Wael et al., 2020)
  Firstly computed the template gradients (gradients of group mean LL FC)
  Then aligned the individual gradients of each FC pattern to the template gradients
- **Asymmetry index (AI)**
  Intra-hemisphere (LL-RR)
  Inter-hemisphere (LR-RL)
  (Left-right)/(left+right) was also computed to test the robustness
- **Heritability analyses**
  We computed heritability by means of family structure of HCP using SOLAR eclipse 8.4.1b. $h^2 = o^2_g$ (total additive genetic variance) / o^2_p (phenotypic variance) (Almasy and Blangero 1998)
- **Non-human primates**
  Macaques were similarly compted using Markov parcellation (Markov et al., 2014)
  Comparison between humans and macaques using a joint alignment (Xu et al., 2020)
- **Functional decoding**
  Along the asymmetry axis, functional decoding was computed using projection of meta-analytical task-based activity generated by NeuroSynth (Yarkoni et al., 2011)

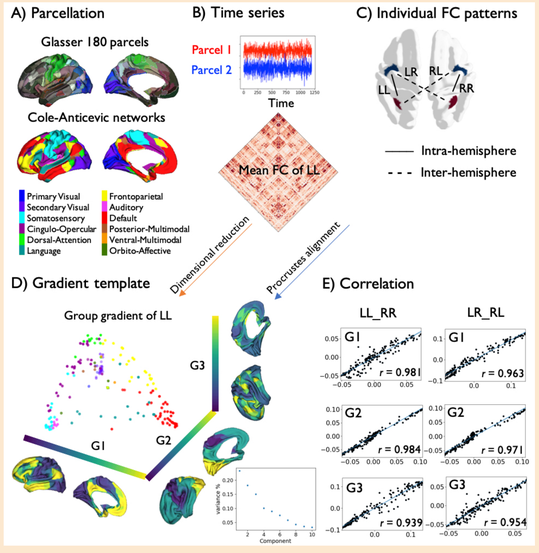

Fig 1. Processing of functional gradients. A) Parcellation using Glasser 180 atlas in each hemisphere and Cole-Anticevic networks. B) Time series of two parcels and mean functional connectivity (FC) matrix between left and left hemisphere (LL). C) Individual FC in each hemispheric pattern, i.e., (LL), 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. E) correlation between LL and RR, correlation between LR and RL. Color code of the scatter plot represents Cole-Anticevic Network. The asymmetry of intra- and inter-hemisphere was respectively highly similar.

Results

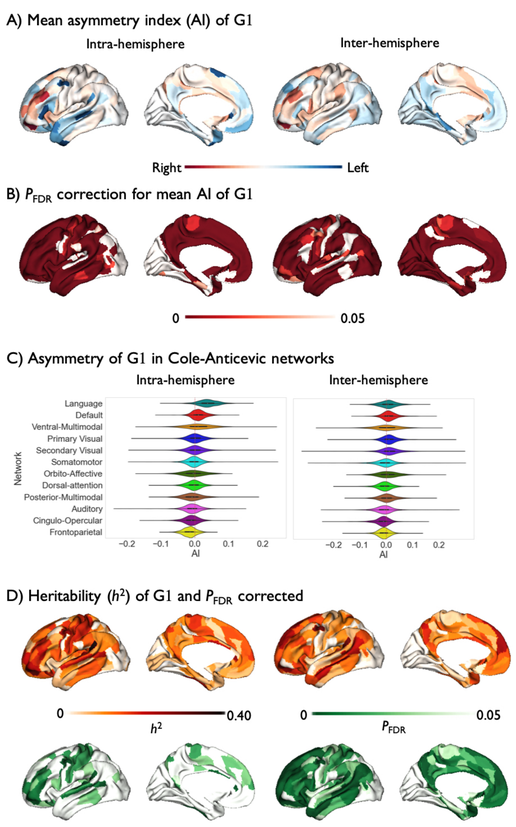

Fig 2. Asymmetry of functional gradients in humans. A) Mean asymmetry index (AI) of intra-hemispheric pattern and inter-hemispheric pattern in humans. B) FDR correction for the *p*-value of AI. C) Asymmetries of the principal gradient using Cole-Anticevic networks. D) Heritability of G1 and FDR correction for related *p*-value. Aears including 11l, p9-46v, 9-46d were the most three rightward areas and TGv, STSdp, and 55b were the most three leftward areas in the intra-hemispheric pattern. The top six areas included 11l, 46, 9-46v, p9-46v, PreS, and PHA2 for the inter-hemispheric pattern. Language network showed the peak left-ward asymmetry and heritability.

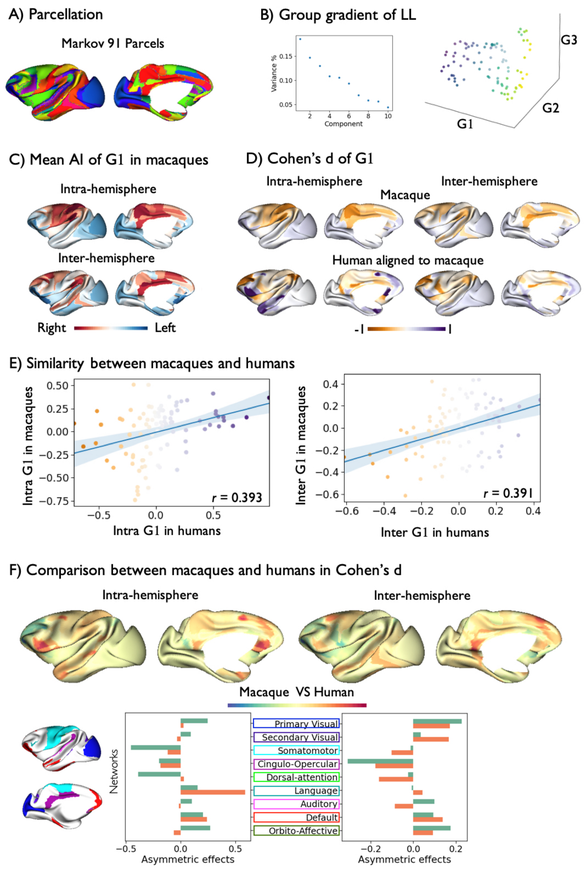

Fig 3. Asymmetry of functional gradients in macaques. A) Parcellation used Markov 91 atlas in macaques. B) Template gradients. C) Mean asymmetry index of G1 in macaques. D) Asymmetric effects (Cohen's d) of the G1 in macaques and humans aligned to macaques. E) Similarity of G1 in humans with G1 in macaques. F) Comparison between macaques and humans in Cohen's d of G1. Asymmetry in macaques was not significant. After aligning humans to macaques, asymmetric pattern in macaques was similar with that in humans. Qualitative comparison showed that humans showed great asymmetry in language network but small in visual networks.

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 availability

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

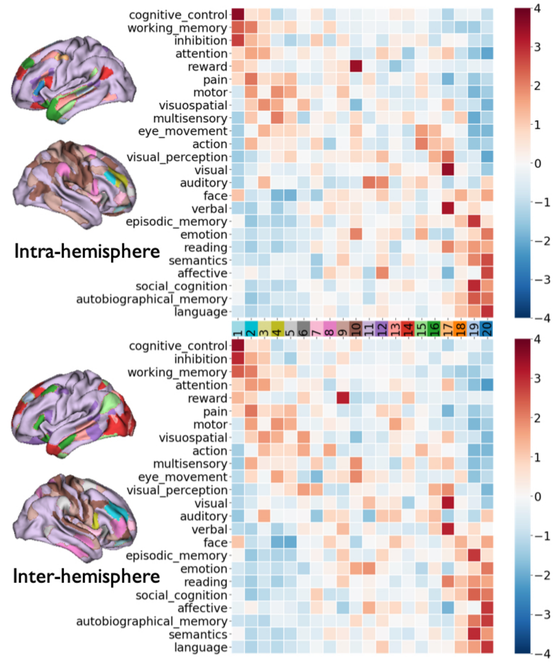

Fig. 4. Projection of meta-analytical task-based function along asymmetric effects of G1. Right panel is the functional decoding of the intra-hemispheric pattern and the left panel is the inter-hemispheric pattern. It revealed regions showing leftward asymmetry associated with language processing, whereas rightward asymmetry in organization related to cognitive control.

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