Regional Study of the Genetic Influence on the Sulcal Pits

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Challenge

- Sulcal pits representing the putative first cortical folds are assumed to be under tight genetic control [1] and their spatial pattern was found more consistent in monozygotic twins than unrelated individuals [2, 3].
- We propose to assess this genetic control by *first* evaluating the robustness our sulcal pits extraction method [4] in a huge cohort (HCP) and *second* estimate the heritability of the sulcal pit depth in each group-level sulcal basin with a high group density of pits.

Materials & Methods

Imaging

- HCP cohort composed of **897 subjects** with T1 & T2 MR Images (0,7 mm iso).
- Extract each subject white mesh with HCP Freesurfer pipeline.
- Individual sulcal pits extraction procedure and group cluster-regions definition (**Fig. 1**) [4].

Pedigree and heritability analysis

- **Pedigree**: 114 monozygotic and 65 dizygotic twin pairs, 423 siblings, 25 half-siblings, 87 unpaired individuals.
- covariance matrix: $\Omega = 2 \cdot \Phi \cdot \sigma_g^2 + I \cdot \sigma_e^2$

With σ_g^2: **genetic variance due to the additive genetic factors**, Φ: kinship matrix representing the pair-wise kinship coefficients among all individuals, I: identity matrix, σ_e^2: individual-specific environmental effects, σ_p^2: phenotype variance.

- **Narrow-sense heritability**: $h^2 = \sigma_g^2 / \sigma_p^2$.

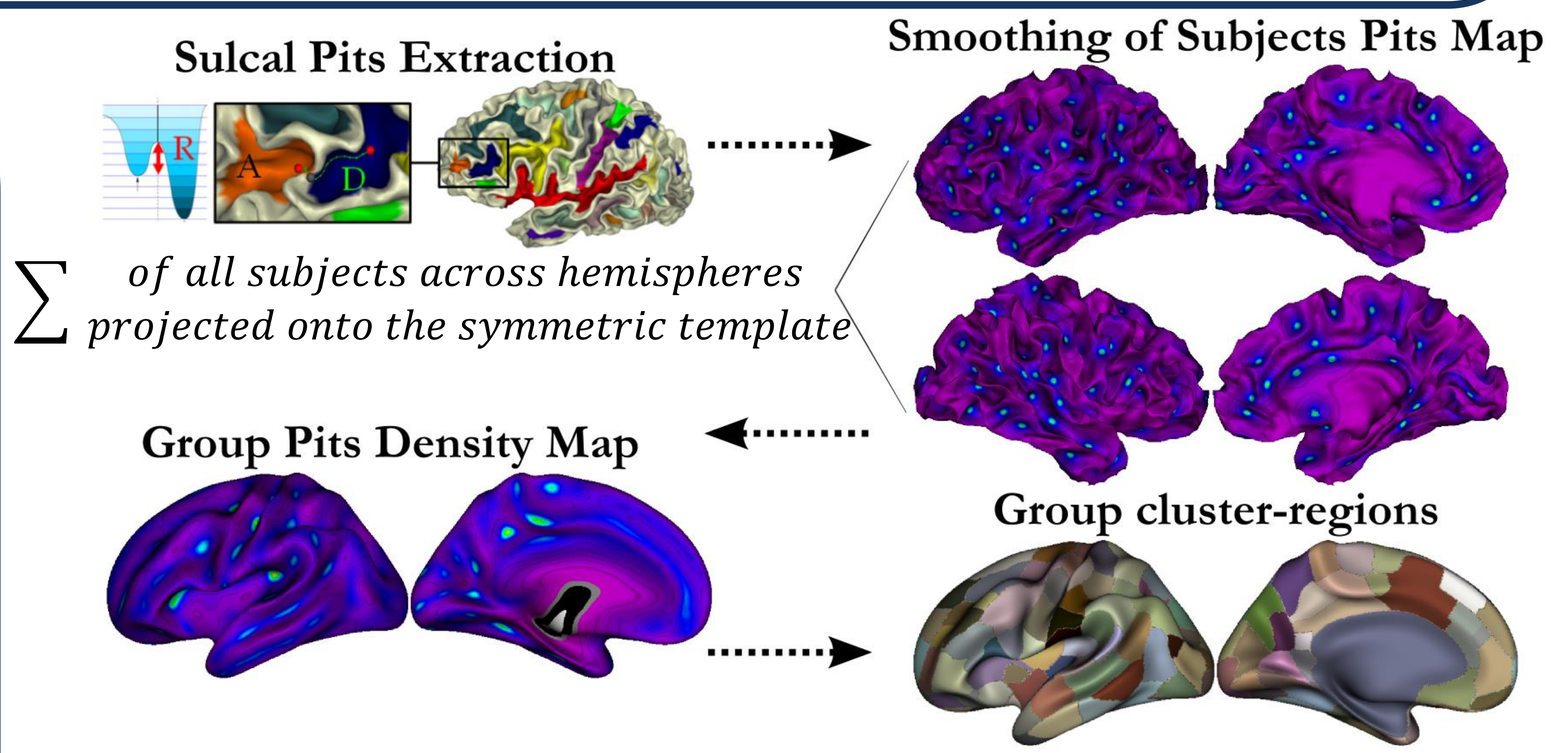

Fig. 1 Summary of the sulcal pits extraction procedure and methodological steps to obtain the group-level sulcal basins by performing a group watershed on the density map.

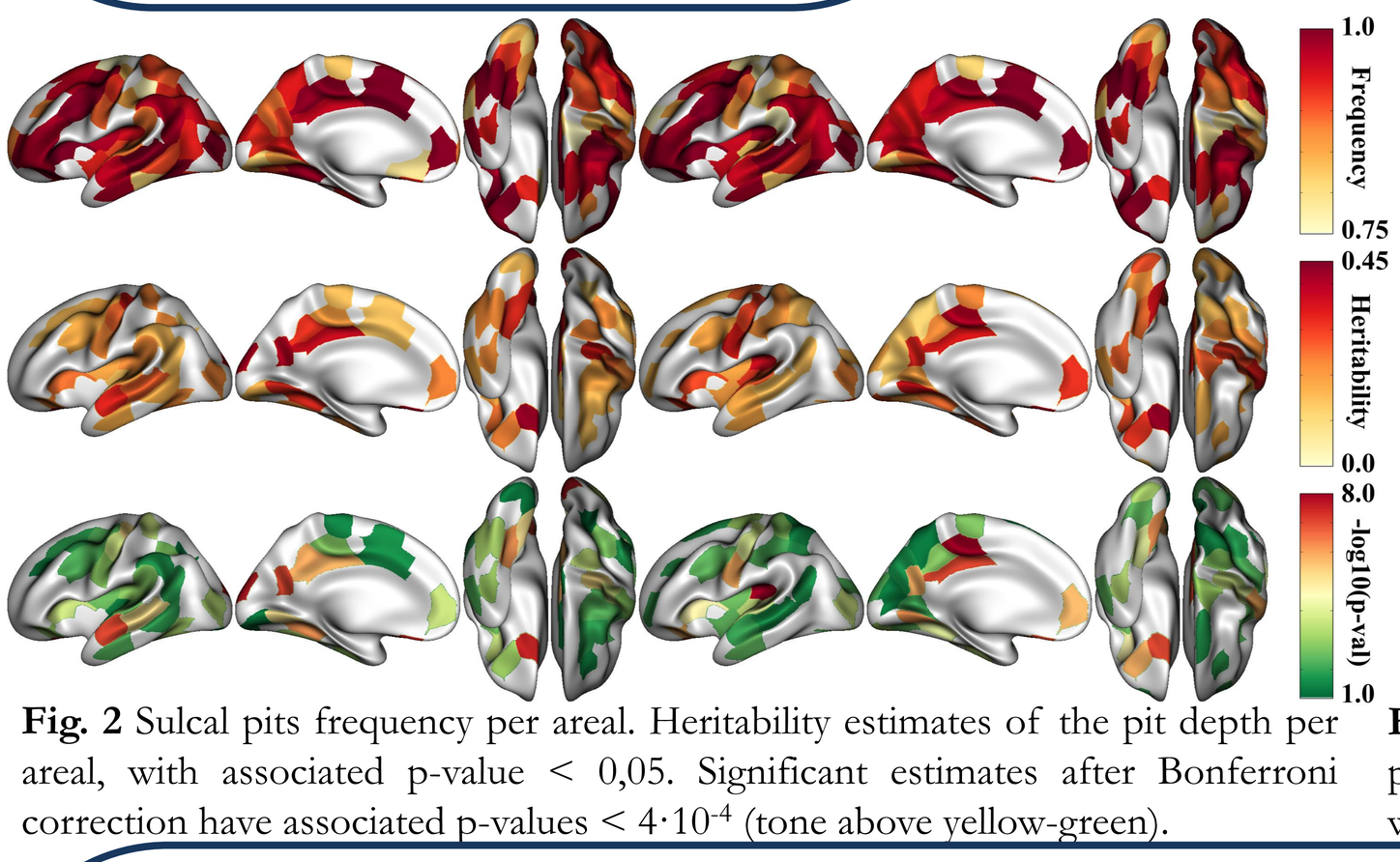

Fig. 2 Sulcal pits frequency per areal. Heritability estimates of the pit depth per areal, with associated p-value < 0,05. Significant estimates after Bonferroni correction have associated p-values < $4 \cdot 10^{-4}$ (tone above yellow-green).

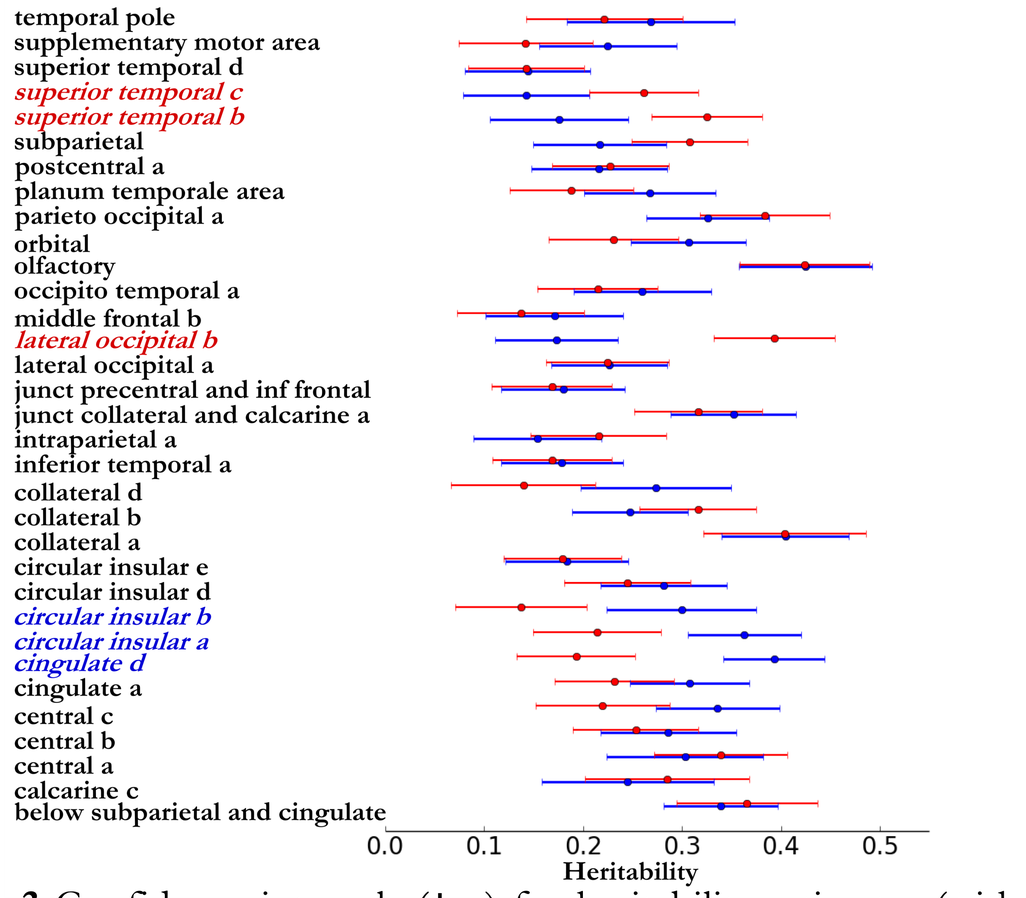

Fig. 3 Confidence intervals (± σ) for heritability estimates (with p <0,05 uncorrected) in the right and left hemisphere. Areals with asymmetric estimates (67% confidence) in *italic* and color.

Conclusion

- High pits frequency obtained in most areals along the sulci, emphasizing the **robustness of the sulcal pits extraction in a large dataset** with the method detailed in [4].
- Significant heritability estimates between 0.2 and 0.5. This range suggests pits depth and thus the cortical structure shape is primarily influenced by nongenetic factors, even though the genetic control over the formation of the gyral pattern is significant.
- **Overall symmetric genetic control with a noticeable exception in the superior temporal sulcus**. Asymmetric heritability might suggest genetic cues to increase the genetic control in the lay down of the cortex organization in regions involved in language functions.

Perspective

- Several studies have already emphasized the feasibility of using the sulcal pits as biomarkers to distinguish healthy subjects from diseased ones. (Ex: quantitatively describe the abnormal sulcal pattern in polymicrogyria [5]; or characterize the atypical sulcal pattern in children with developmental dyslexia [6] by using sulcal graph matching). Understanding the genetic underpinnings would provide insight into neuro-developmental disorders.

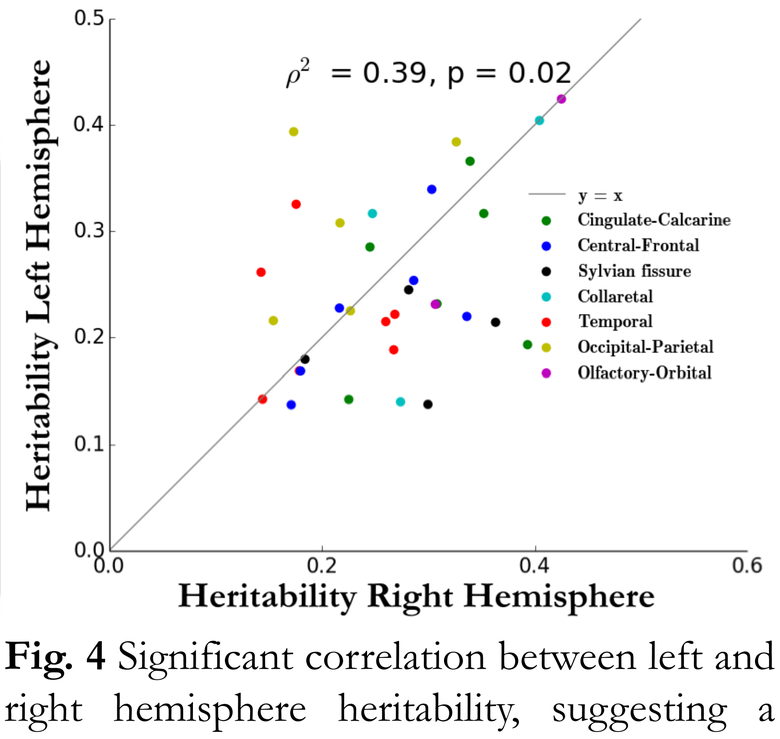

Fig. 4 Significant correlation between left and right hemisphere heritability, suggesting a symmetric genetic influence in most areals.

References & Acknowledgment

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