

Transmodal decoupling of human cortical microstructure and function is under genetic control

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Introduction

How does a relatively stable human brain structure produce function and ultimately cognition that allow the flexible navigation through a complex culturally-rich social landscape? Although brain structure ultimately constraints function, structure-function relationships are increasingly recognized to not be uniform across the cortex. This observation leads to the hypothesis that the relationship between structure and function may enable specific forms of higher-order cognition particularly in humans. By combining heritability and phylogenetic approaches to probe structure-function associations within a single study, we hope to understand processes that underpin flexible cognition in our species and to identify uniqueness of human structure-function coupling and decoupling.

Methods

Human participant data were obtained from the **Human Connectome Project** (S1200 release; Van Essen, 2013). The sample was composed of monozygotic and dizygotic twins, siblings and unrelated individuals.

T1w/T2w values along 12 equidistant layers between the GM/WM and GM/pial surfaces for each cortical region, and inter-regional profile correlations (Paquola, 2019), creating MPC. Pre-processing steps for resting-state were based on standard HCP protocols (van Essen, 2013)

Both layer-based MPC and intrinsic functional connectivity (rsFC) were extracted for 400 parcels (Schaefer, 2018), to construct an MPC and rsFC matrix. We measured MPC-rsFC coupling as the row-wise correlation of both metrics.

We computed heritability of MPC and rsFC by means of the family structure of HCP using solar eclipse 8.4.0. (<http://solar-eclipse-genetics.org>)

We then measured using the correlation between heritable and mean patterns of each row in MPC and rsFC respectively, and associated these patterns of genetic coupling with structure-function coupling.

For non-human primate analysis, we used the macaque MRI data included in **PRIME-DE** (http://fcon_1000.projects.nitrc.org/indi/indiPRIME.html); cohorts Davis. MPC and rsFC were computed using Freesurfer, and resampled on the Markov parcellation.

To identify the macroscale organization of MPC and rsFC, we used **diffusion embedding**, a nonlinear dimensionality reduction technique that resolves the principle axes of differentiation (Vos De Wael, 2020; Coifmann, 2005)

The maps were spatially correlated to functional communities (Yeo, 2011), cytoarchitectural classes (Mesulam, 2000), 24 selected Neurosynth paradigms (Yarkoni, 2013), phylogenetic maps (Xu, 2020; Pandya, 2015), and Allen Human Brain Atlas (Hawrylycz, 2012).

Fig 1. Coupling and heritability microstructural profile covariance and functional connectivity.

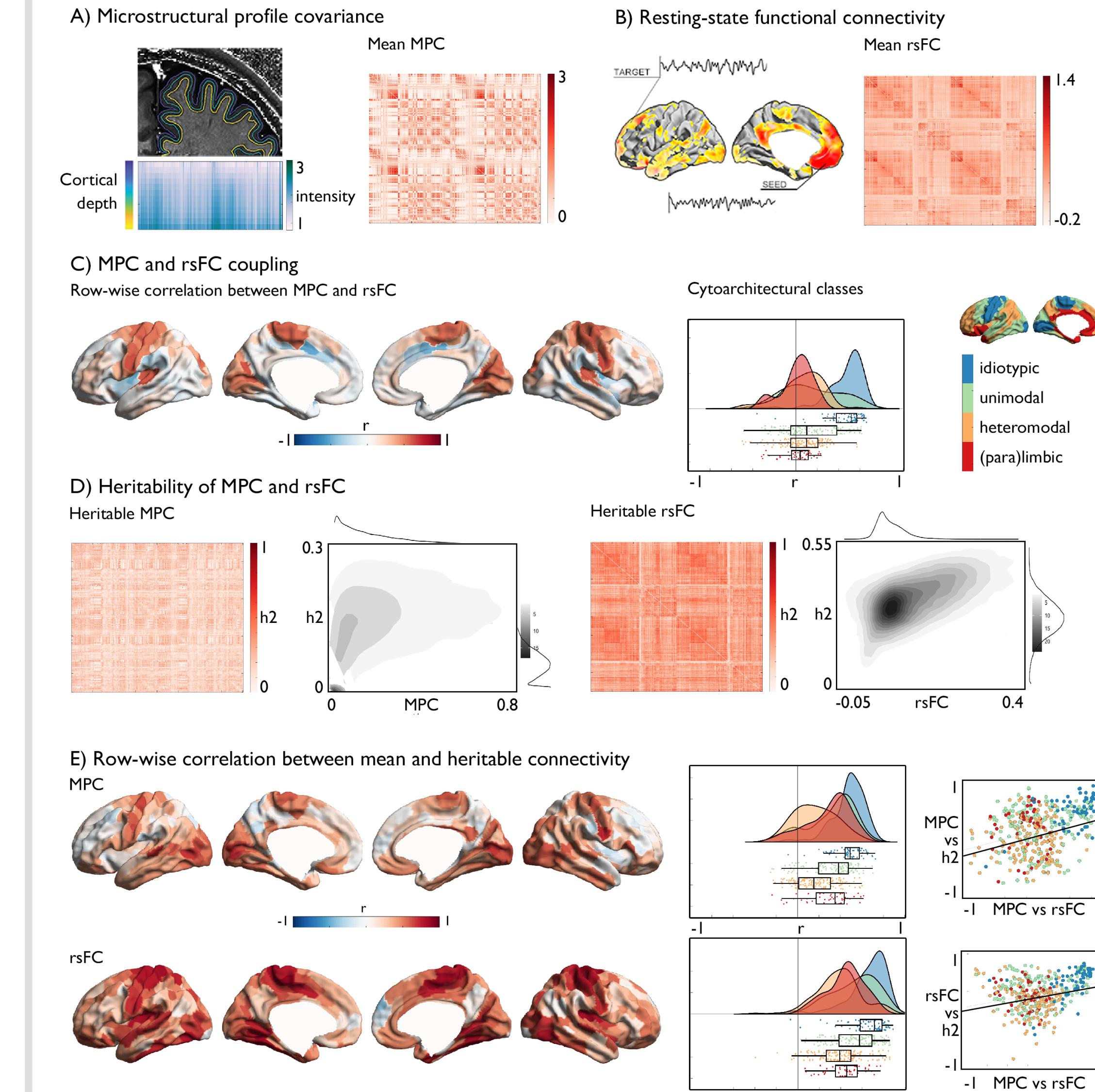


Fig 2. Microstructure-function coupling in macaques

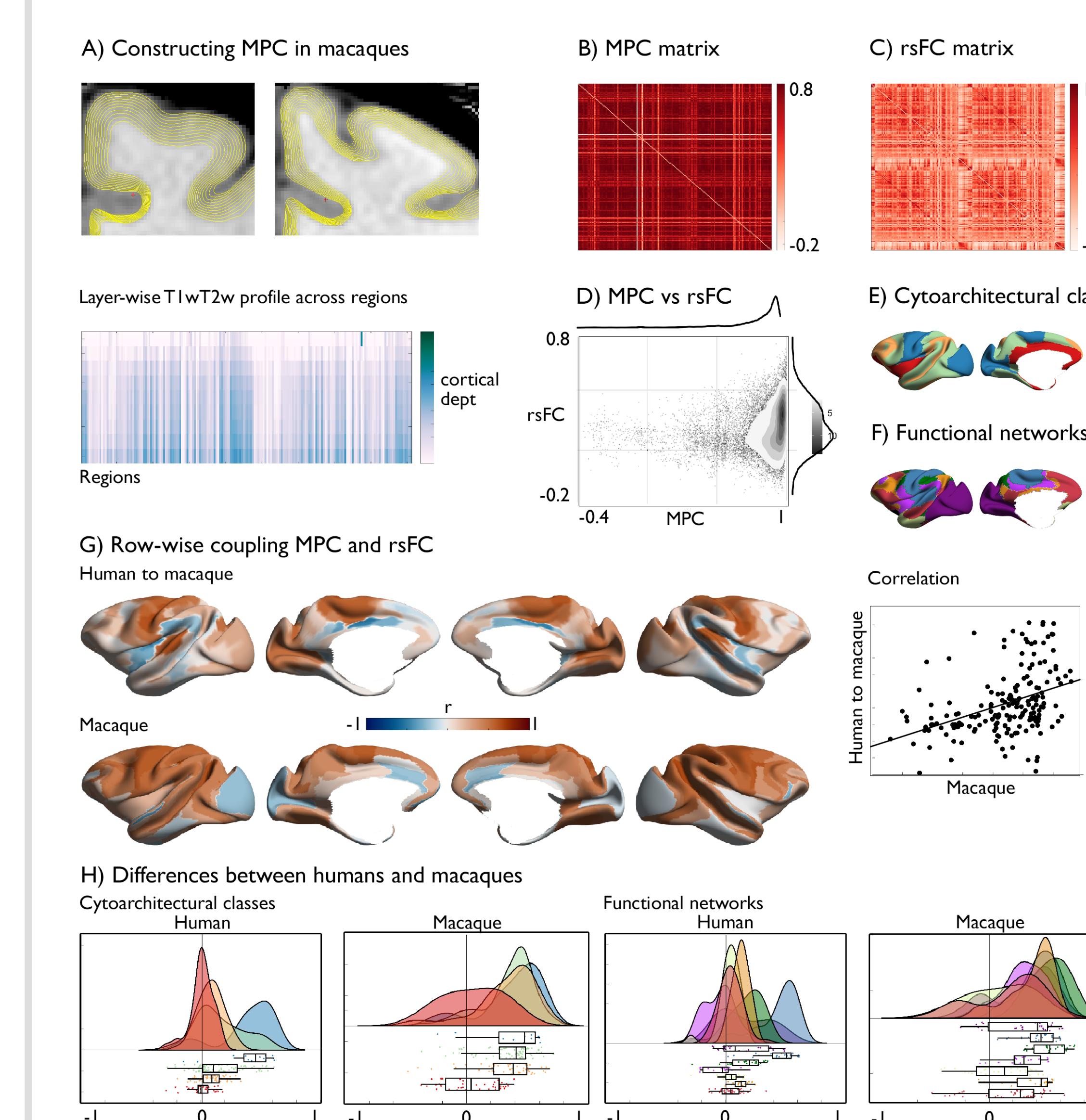


Fig. 3 Difference in organizational gradients of MPC and rsFC in humans and macaques

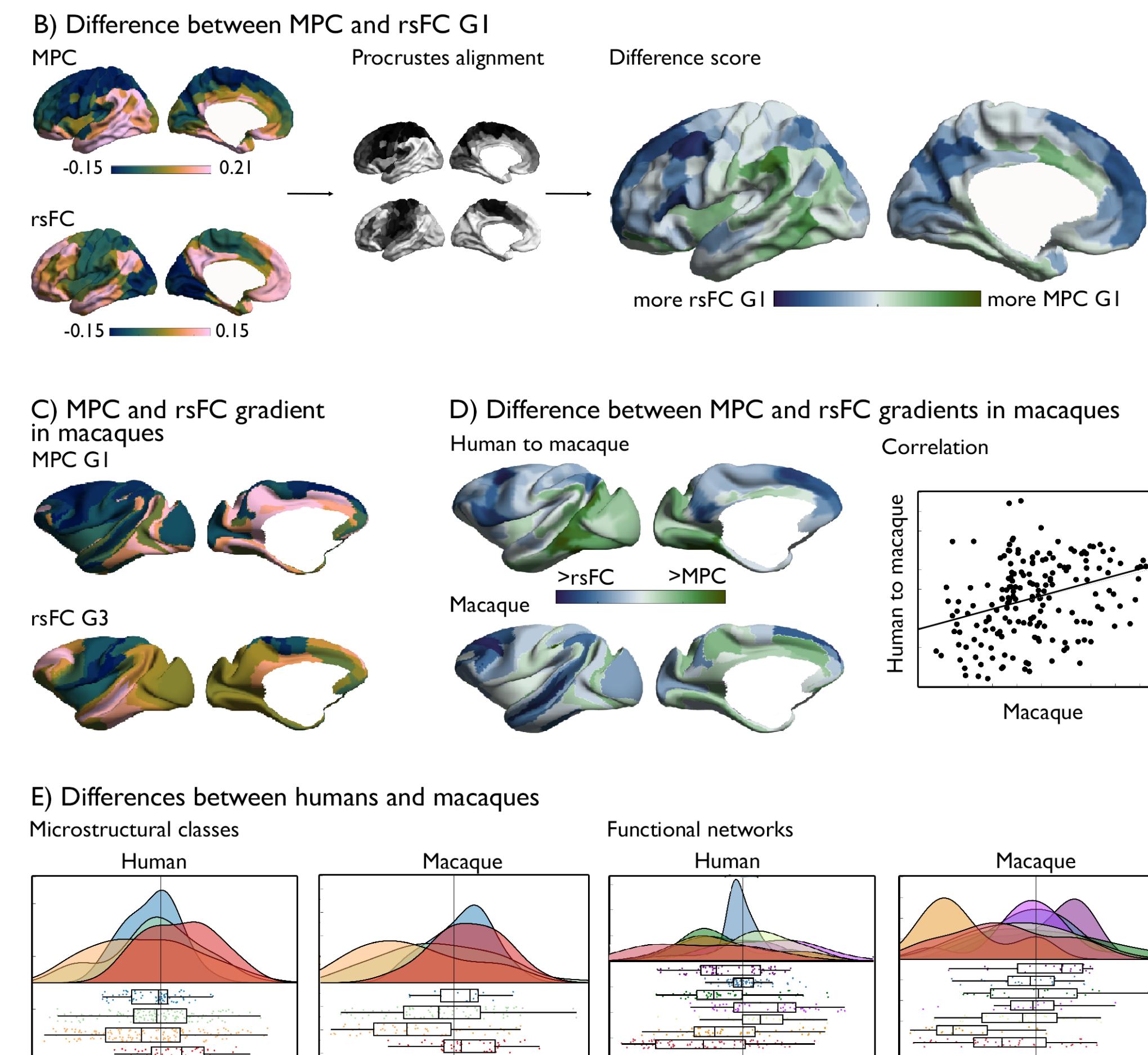
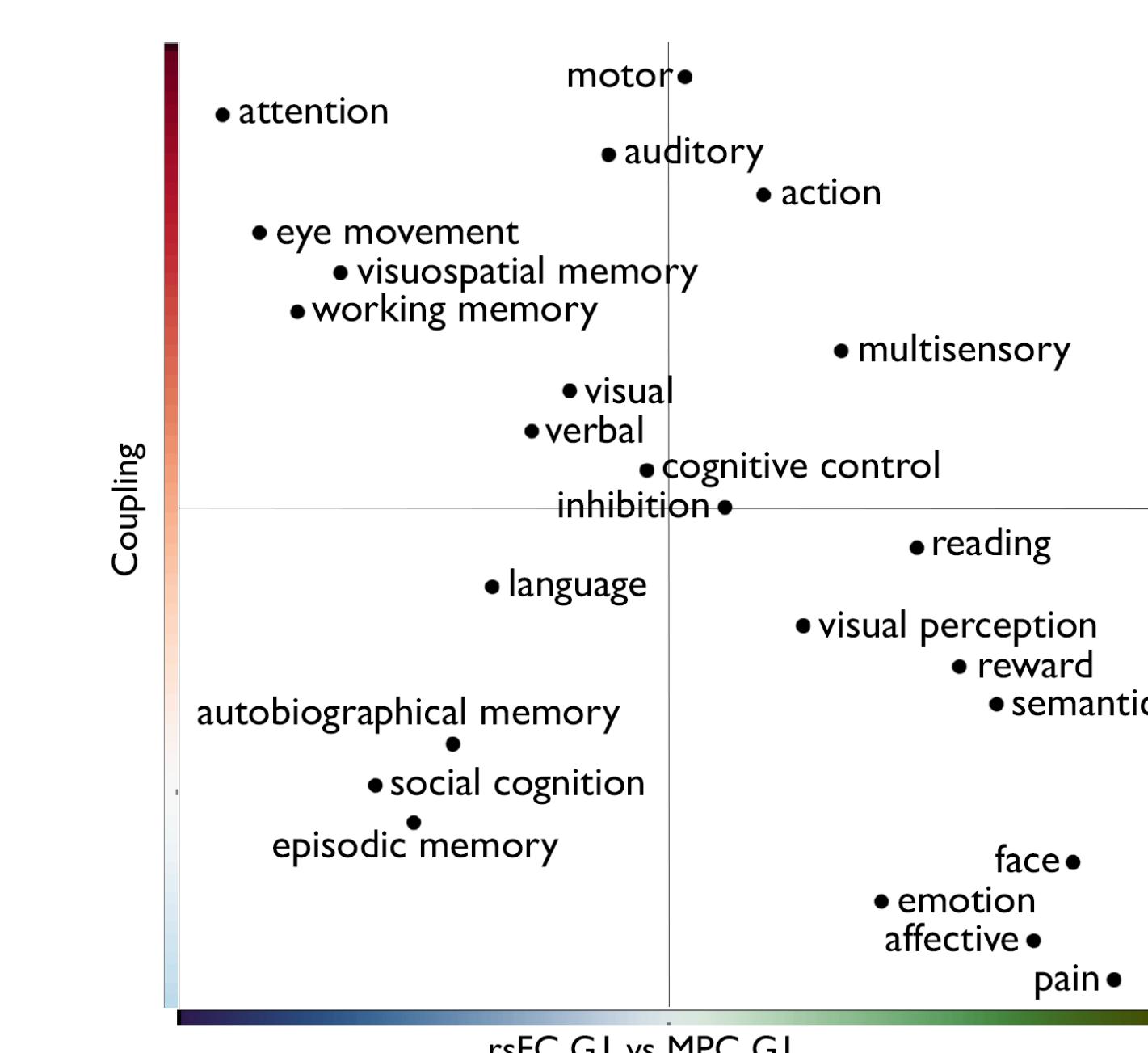
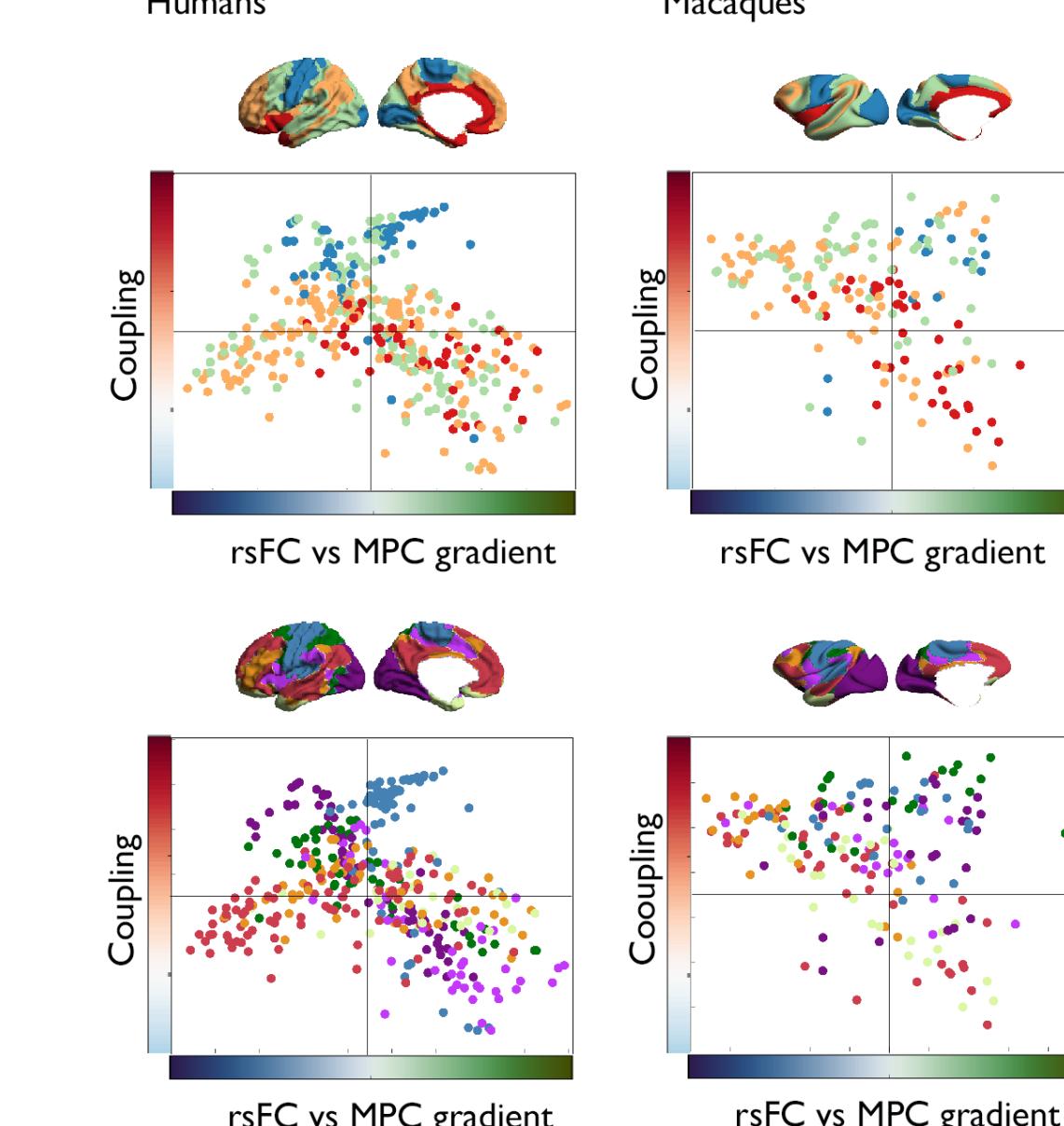


Fig 4. Behavioral and cognitive quadrants of structure-function coupling



Summary

To identify uniqueness of human structure-function coupling and decoupling, our study established that microstructural profiles and intrinsic functional connectivity are indeed less correlated as a function of cortical hierarchy, i.e. primary regions show most correlation and paralimbic regions least correlation between cortical structure and function.

Genetic correspondence, examined using twin design human neuroimaging, of both structural and functional connectivity profiles was least in heteromodal regions, relative to the rest of the cortex.

Furthermore, heteromodal but not paralimbic regions showed markedly less coupling between cortical structure and function in humans relative to macaques.

Last, we observed a differentiable topological organization of transmodal cortex in structure and function, again dissociating heteromodal and paralimbic regions, which was heritable and comparable between humans and macaques.

Together, our observations suggest that particularly heteromodal regions are uniquely decoupled in humans. This decoupling may reflect evolutionary adaptations giving rise to unique human cognitive capacities such as social cognition and autobiographic memory.

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Bonus: Genetic decoding

