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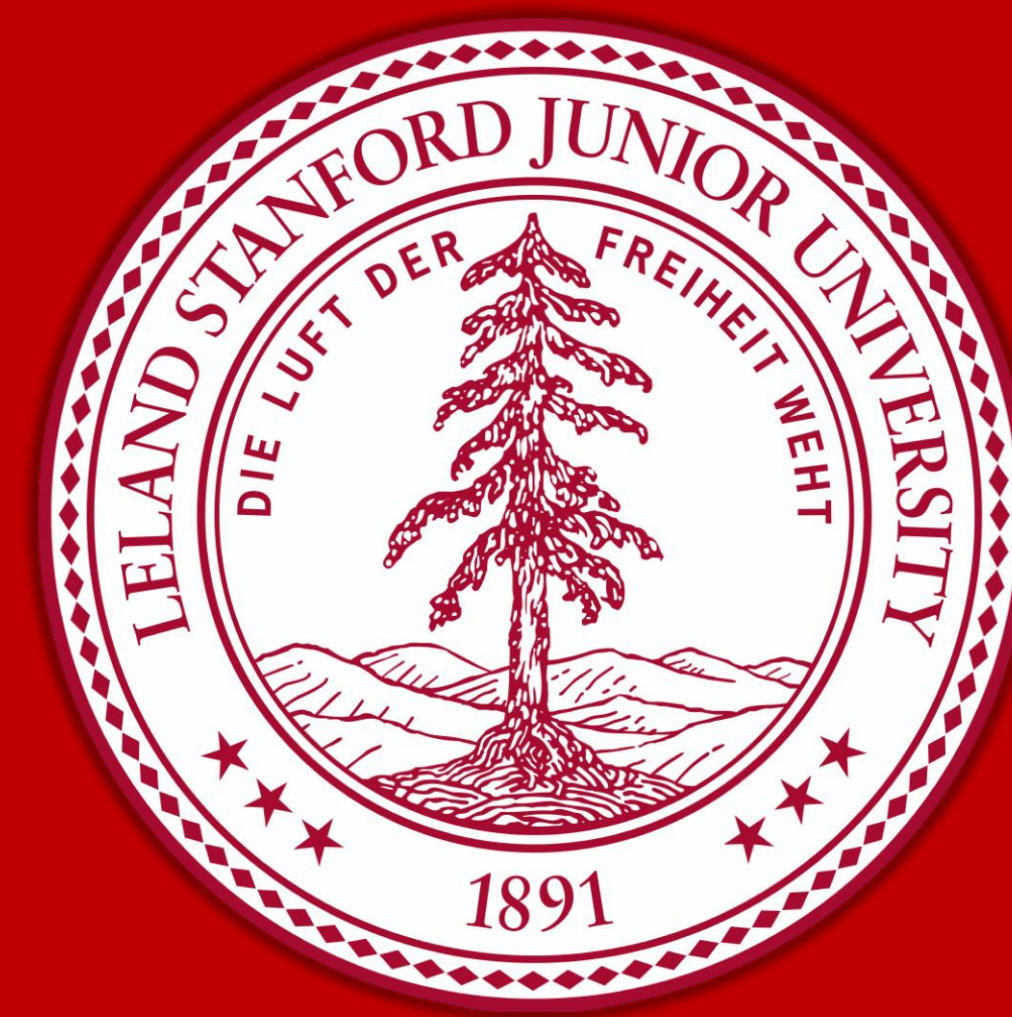
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Concordance between white-matter pathways and functional circuits linking the VWFA and IPS

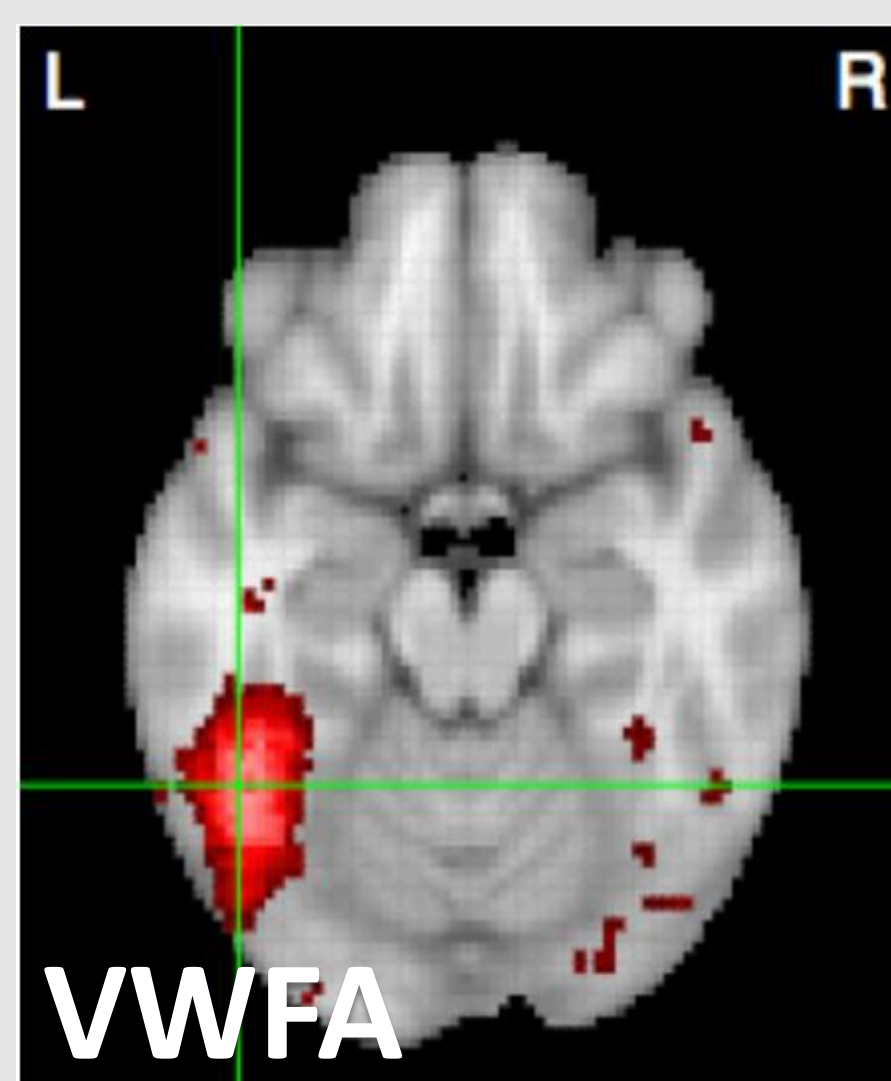


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Background

- The **visual word form area (VWFA)** is thought to be functionally specialized for words based on its preferential activation to written words¹.
- However, recent studies have suggested that the VWFA shows stronger intrinsic functional connectivity with fronto-parietal attention systems along the dorsal-ventral axis than fronto-temporal language systems².**
- VWFA white matter pathways with fronto-parietal systems and their correspondence with functional connectivity remain poorly understood⁴, limiting our understanding of its core cognitive functions.
- According to the “connectivity constraints” account^{4,5}, the origin and function of VWFA depends on its connectivity fingerprints. For example, if it is specialized in processing word stimuli, it should show stronger structure-function correspondence with the language systems, more than with the attention systems.



Method

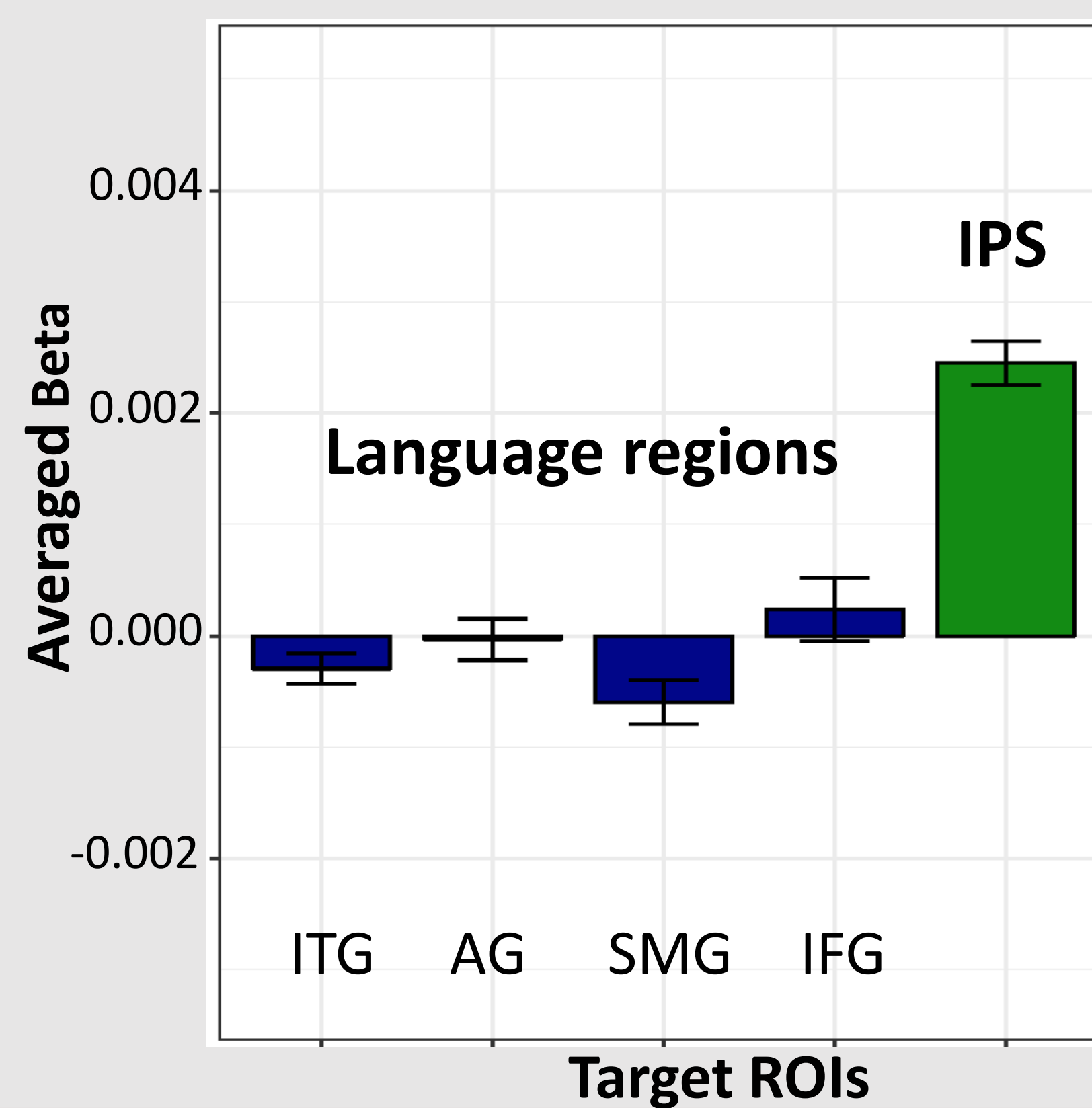
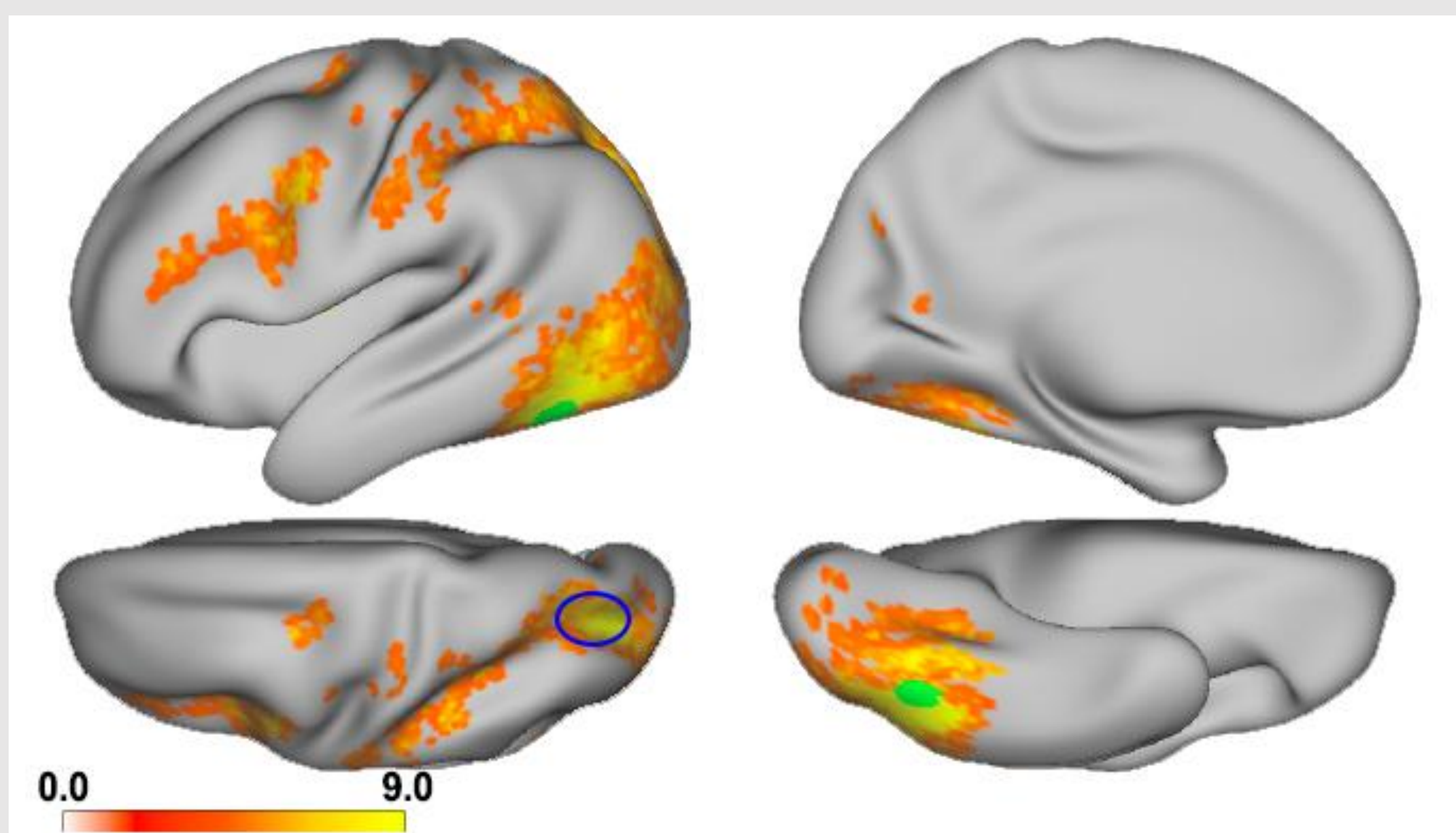
- Dataset:** High-quality resting-state fMRI (rfMRI) and diffusion MRI data in 85 participants (age range: 31–35 years old; 46 Females) from the HCP.
- Functional ROIs:** All ROIs were defined as a 6mm-radius geodesic disc centering on the MNI coordinate. **The VWFA** (-45, -57, -12); **Language-related regions:** Left IFG (-53, 27, 16), SMG (-49, -57, 28), AG (-56, -43, 31), and ITG (-61, -33, -15); **Parietal attentional regions:** IPS (-25, -62, 51).
- Resting-state functional connectivity:** Surface-based resting-state functional connectivity (rsFC) for each grayordinate vertex was computed from the FIX-denoised grayordinate-space rfMRI data. For each cortical vertex, the correlation between its time course and the average VWFA time course was computed, and the Fisher *r*-to-*z* transformation was applied. The group-average rsFC map was thresholded at $p < .05$ (FDR corrected).
- Structural connectivity with probabilistic tractography:** For each surface vertex in the grey-white matter interface, we computed the cortico-cortical connectivity through probabilistic tractography seeding 5,000 streamlines per vertex. We averaged the connectivity profiles for all VWFA vertices, computed the group-wise⁶, and thresholded at $p < 0.0001$ (FDR corrected).
- Concordance between functional and structural connectivity:** We fit, at the individual level, a regularized linear model⁷, to predict the functional connectivity matrix from the structural connectivity matrix. Then, we conducted a *t*-test for significance at the group level. Finally, we analyzed which vertices' structural connectivity predicted resting-state connectivity by rejecting vertices with a 0 weight on the linear model parameter at $p < 0.0001$ (FDR corrected).
- Behavioral measures:** **Language-related measures:** word reading and vocabulary; **Attention-related measures:** Flanker task from NIHToolbox.

Specific aims of the current study

- Delineate the structural and functional connectivity of VWFA** in a large HCP sample, focusing on the **contrast between fronto-temporal language regions vs. fronto-parietal attention networks, particularly, IPS.**
- Examine the **concordance of structural and functional connectivity of VWFA.**
- Investigate the **brain-behavioral relationships** of the functional and structural circuits of VWFA with respects to **language and attentional skills.**

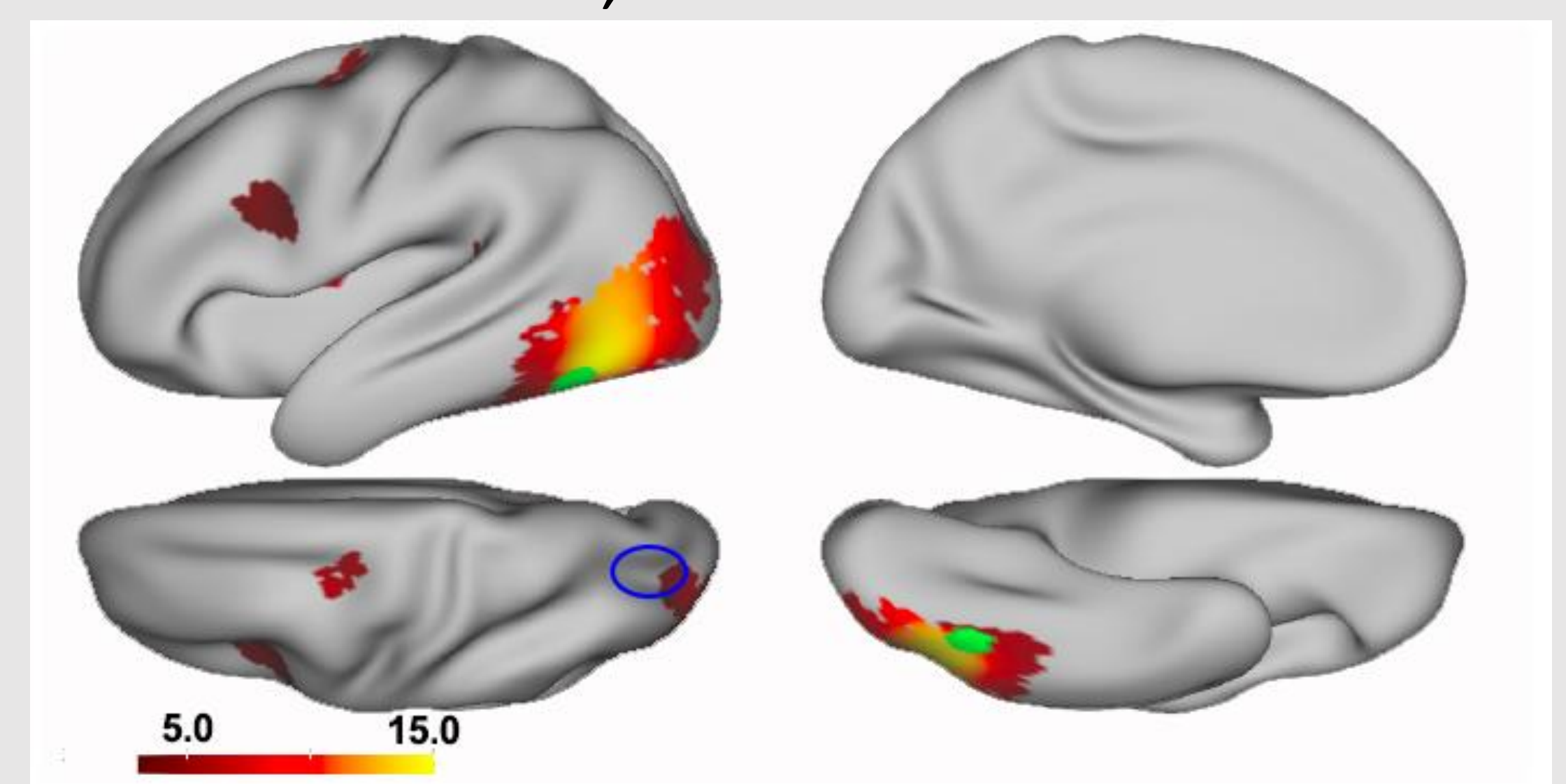
Resting-state Functional connectivity associated with VWFA and IPS

The VWFA showed significant functional connectivity locally with VTOC, as well as distal regions such as IPS, dlPFC and pMTG/STG. VWFA connectivity was stronger with IPS than with language-related regions.



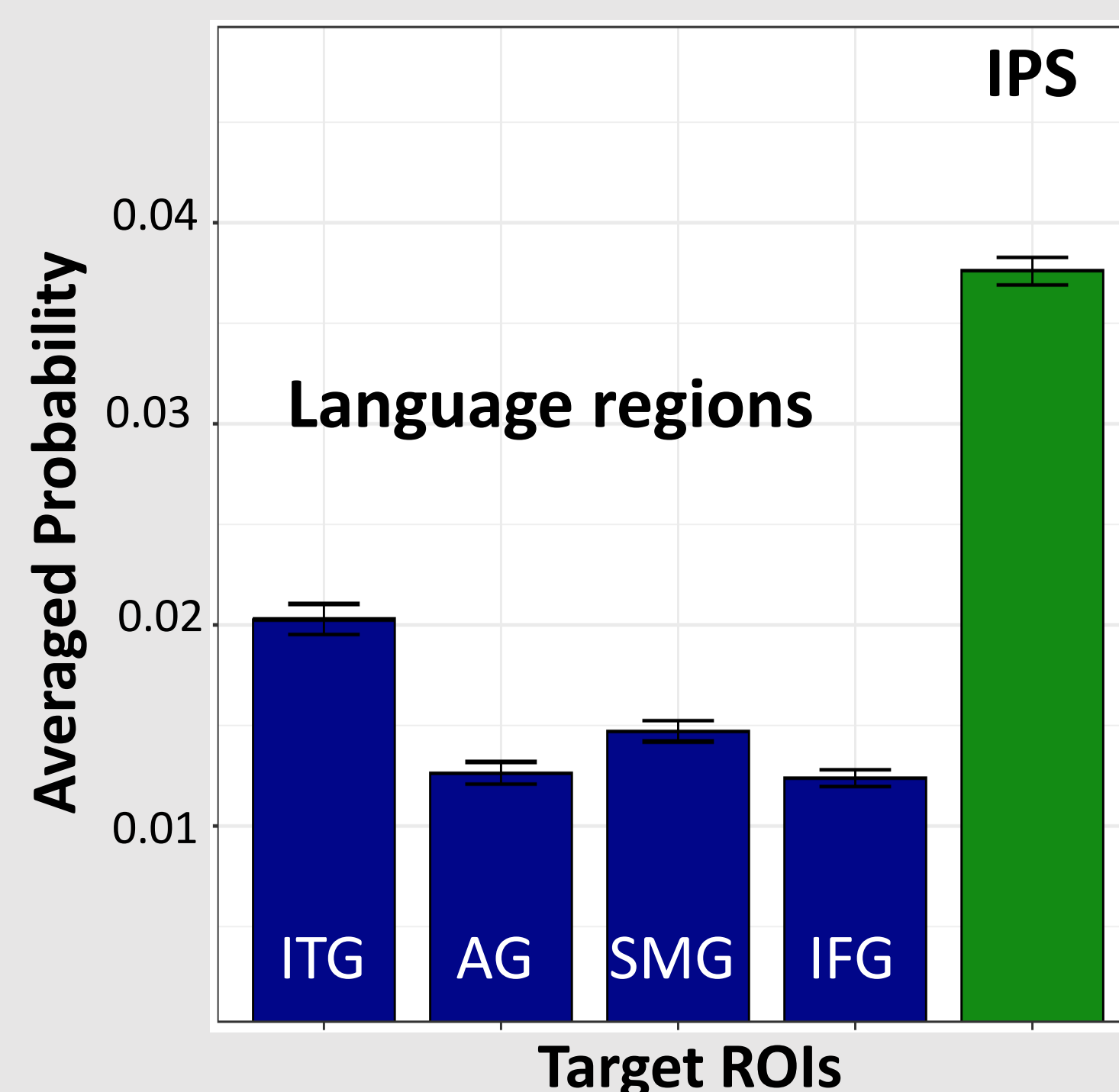
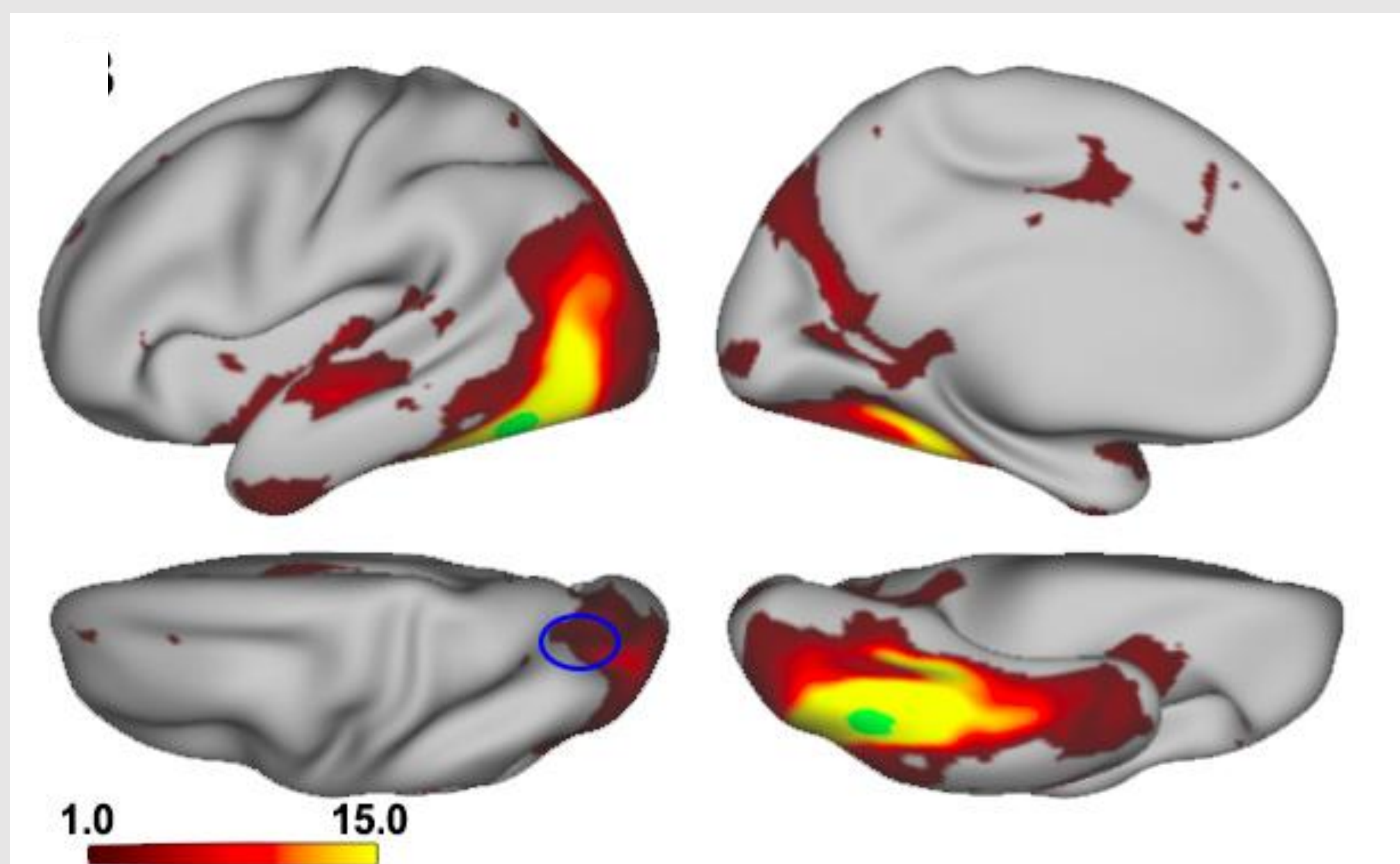
Structural connectivity predicting the functional connectivity of VWFA with IPS

White matter tract probability significantly predicted rsFC of the VWFA ($r^2 = 0.186$, $SD = 0.081$), $t = 21.18$, $p < .001$). They converged most strongly in local VTOC circuits, but also extended to the posterior bank of IPS, and in dlPFC.



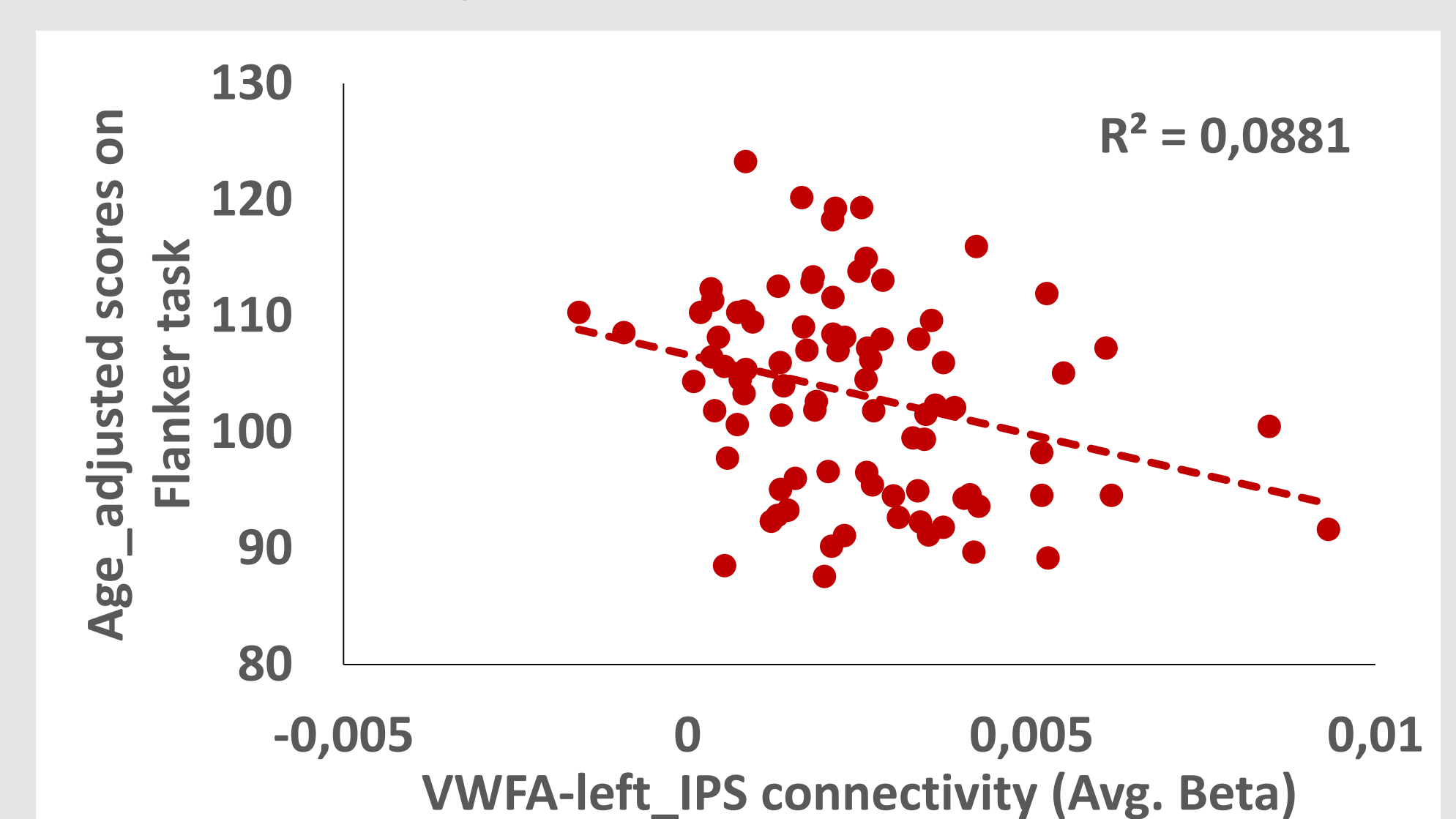
Structural connectivity associated with VWFA and IPS

The VWFA showed significant structural connectivity locally within VTOC, as well as distal regions such as IPS, ATL, STS/STG, and cuneus. VWFA connectivity was weaker with language regions compared to that with IPS.



Functional connectivity of VWFA with IPS associates with attentional/control skills

We found that VWFA-IPS rs-functional connectivity was associated with the performance on the Flanker task, but no association of any other behavioral measures with any other VWFA circuits.



CONCLUSION

- Structural** connectivity of VWFA was stronger with the IPS than language-related regions
- VWFA Functional** connectivity was stronger with the IPS than language-related regions
- VWFA-IPS functional connectivity predicted attention but not word reading skills.**
- Our findings support the view that the **VWFA plays a broader role in cognition than word reading**. Interaction of the VWFA with the IPS may support **visuospatial attention required for processing letter and number strings distributed in space.**

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