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

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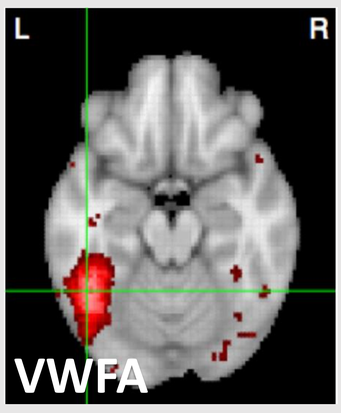
## Background

- The **visual word form area (VWFA)** is thought to be functionally specialized for words based on its preferential activation to written words[1].
- **However, recent studies have suggested that the VWFA shows stronger intrinsic functional connectivity with fronto-parietal attention systems along the dorsal-evetral axis than fronto-temporal language systems[2].**




- VWFA white matter pathways with fronto-parietal systems and their correspondence with functional connectivity remain poorly understood[4], 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.

## Specific aims of the current study

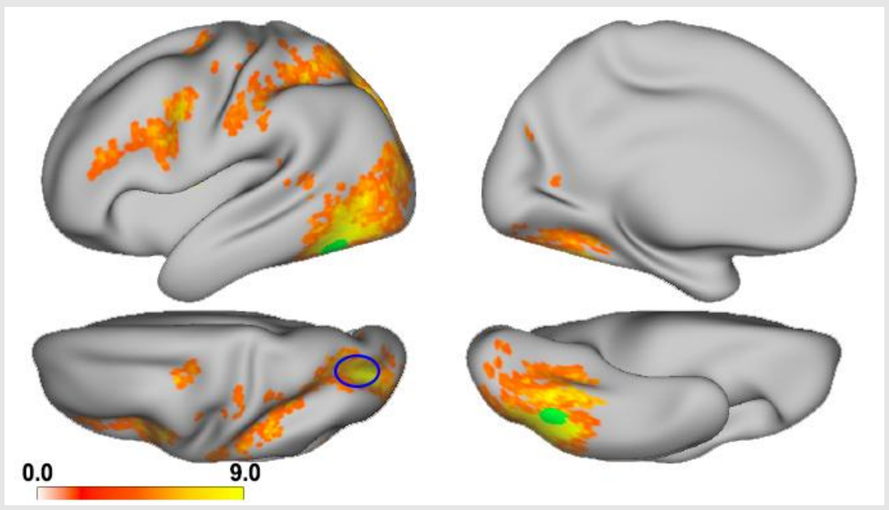
- **Delineate the structural and functional connectivity of VWFA** in a large HCP sample, focusing on the **contrast between fronto-temporal language regions vs. fronto-parietal attention networks, particularly, IPS**.
- Examine **the concordance of structural and functional connectivity of VWFA**.
-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

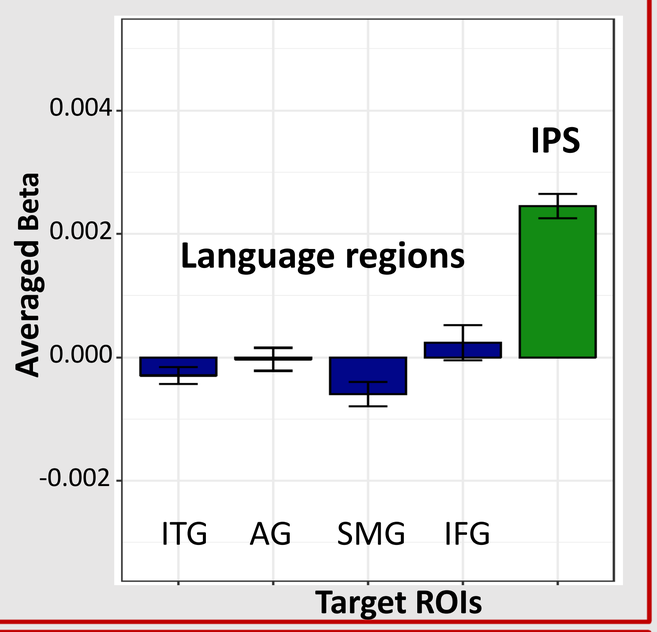
## Method

- **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 tractorgraphy:** 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-wise[6], and thresholded at $p < 0.0001$ (FDR corrected).
- **Concordance between functional and structural connectivity:** We fit, at the individual level, a regularized linear model[7], 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.

## Resting-state Functional connectivity associated with VWFA and IPS

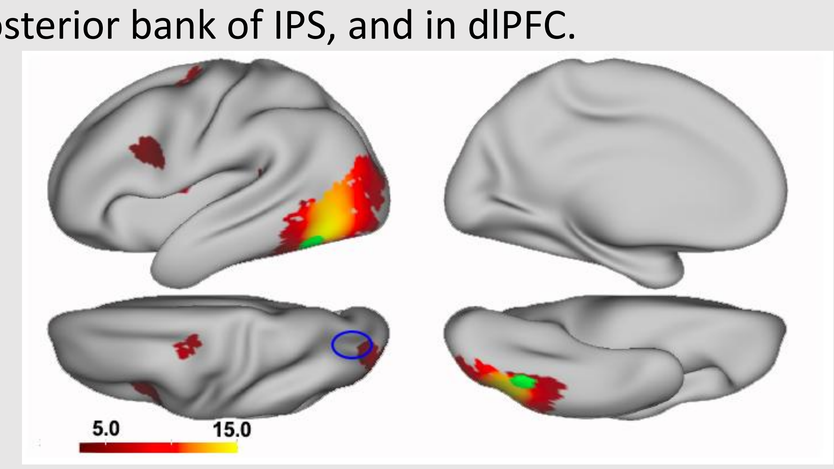
The VWFA showed significant functional connectivity locally with VTOC, as well as distal regions such as IPS, dlPFC and pMTG/STG. VWFA connectivity was stronger with IPS than with language-related regions.



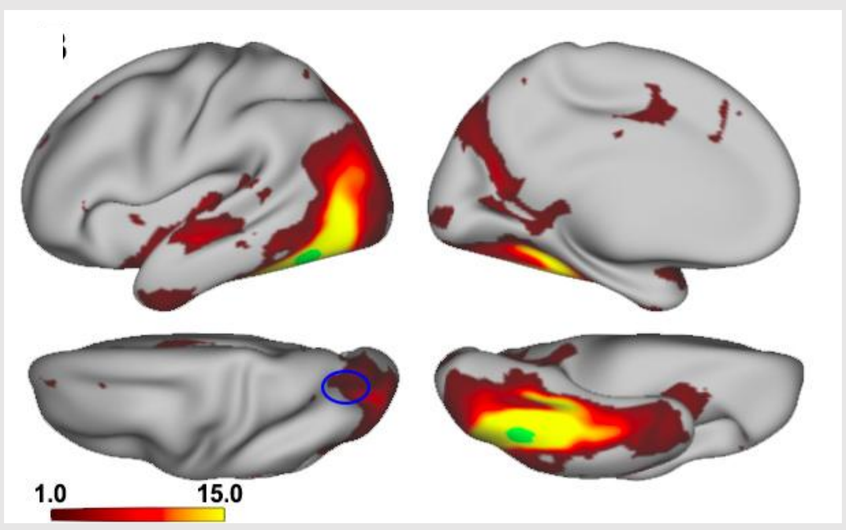

## Structural connectivity predicting the functional connectivity of VWFA with IPS

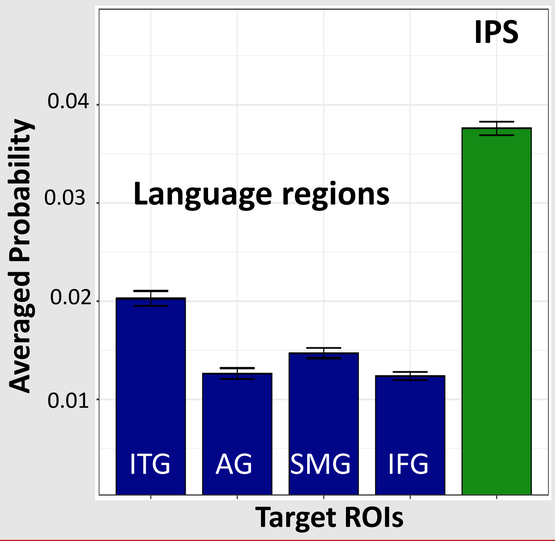
White matter tract probability significantly predicted rsFC of the VWFA ($r^2 = 0.186$, $SD = 0.081$), $t = 21.18$, $p < .001$). They converged most strongly in local VTOC circuits, but also extended to the posterior bank of IPS, and in dlPFC.




## Structural connectivity associated with VWFA and IPS

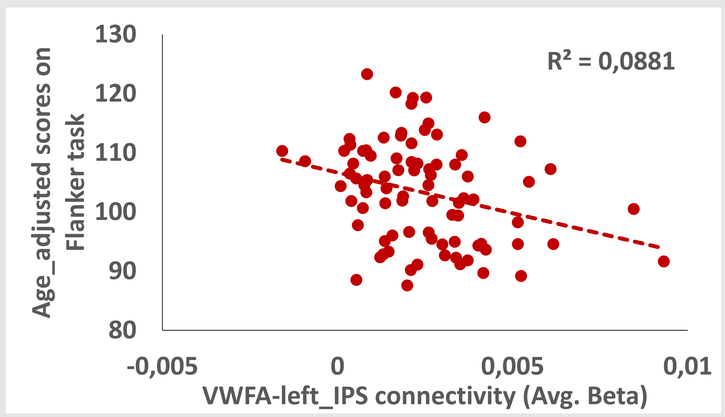
The VWFA showed significant structural connectivity locally within VTOC, as well as distal regions such as IPS, ATL, STS/STG, and cuneus. VWFA connectivity was weaker with langauge regions compared to that with IPS.




## 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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