removal of perfusion lag structure before ICA-FIX cleaning boosts reproducibility in fcMRI

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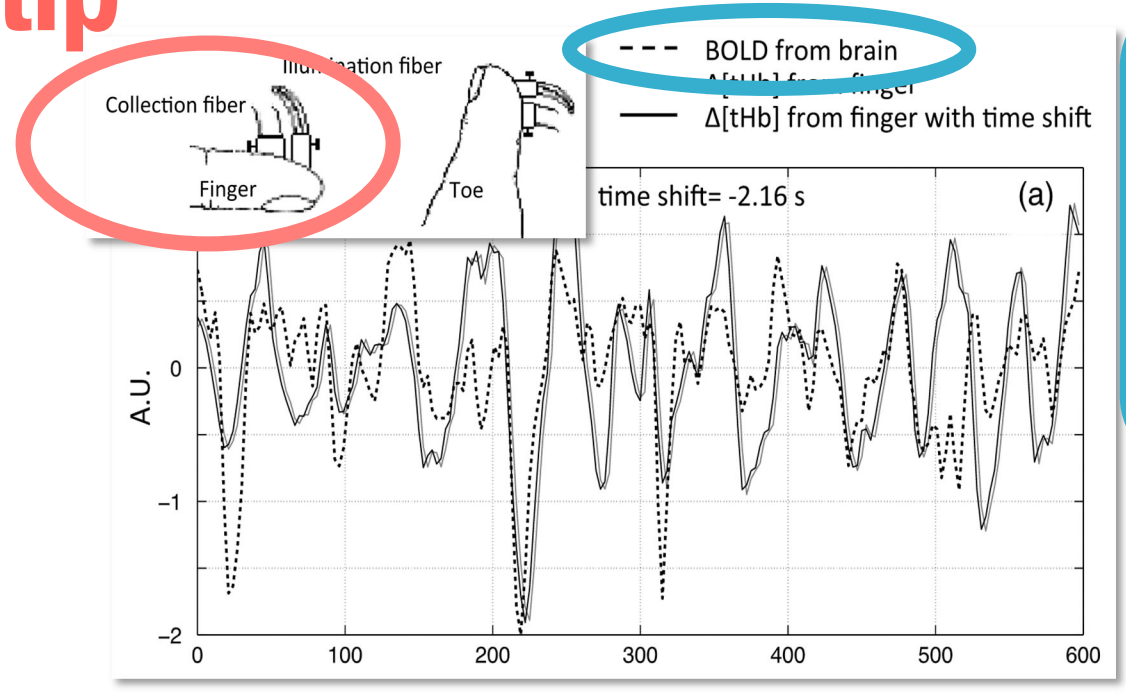
Bad news: fcMRI signal contains “slow noise”

NIRS signal from the fingertip

∝ fMRI global mean signal



sLFO

Spontaneous low-frequency oscillation

Systemic circulation

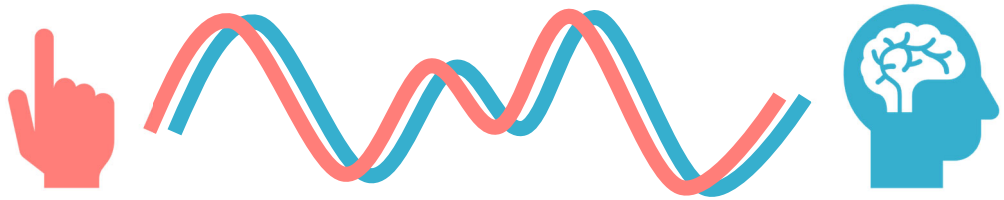
↓

Not from local neuro-vascular coupling

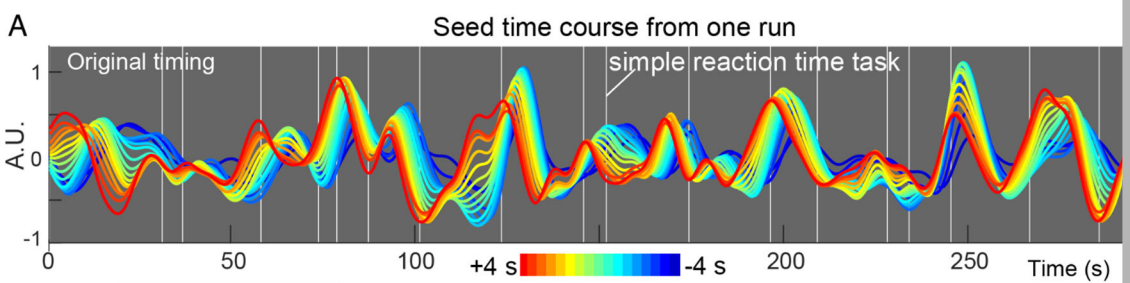
Tong, Hocke, Licata, Frederick. (2012) J Biomed Opt.

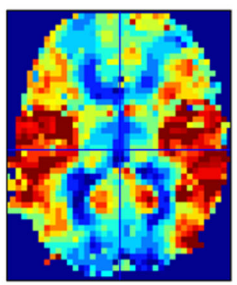
Good News: It is detectable!

Phase delay (lag) observed between fingertip and brain
→ How about *within* the brain?

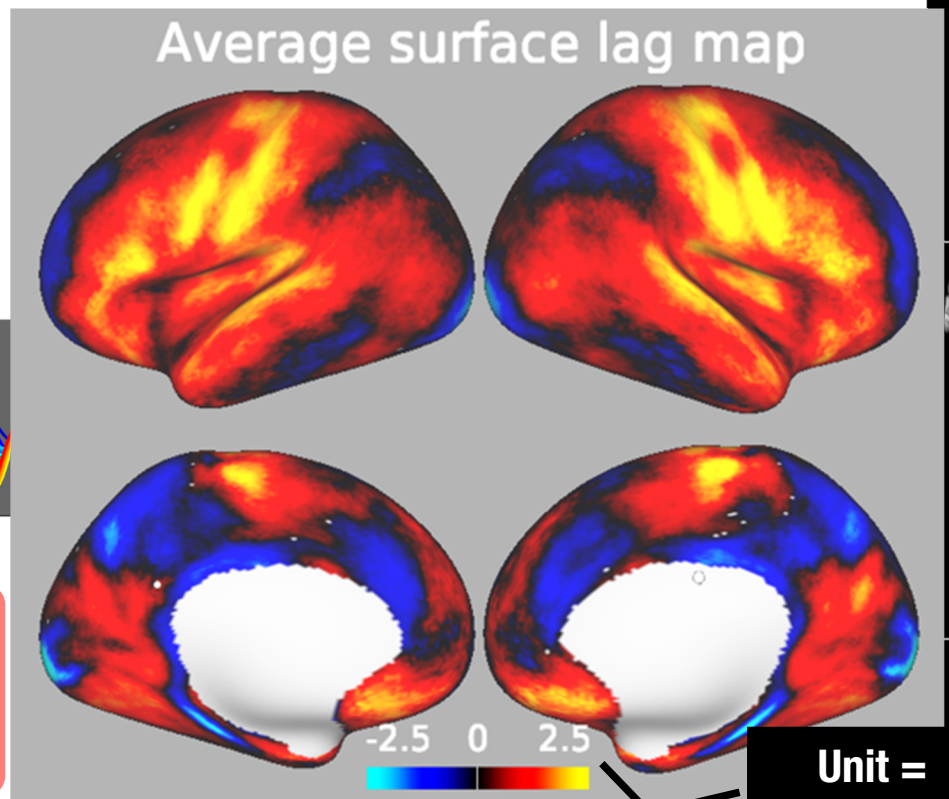


Tong & Frederick (2010) NeuroImage



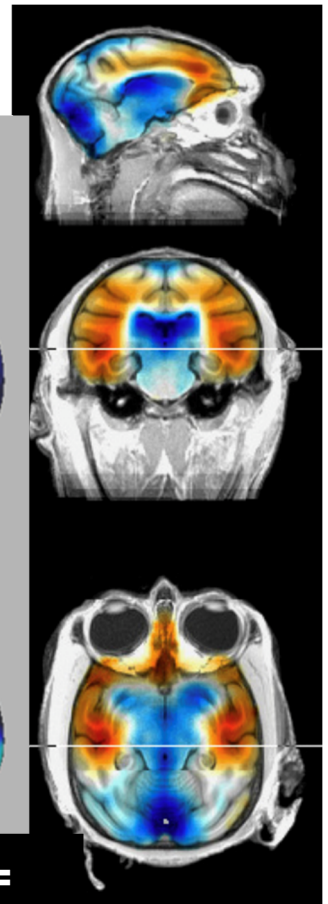


"Lag Mapping"
Relative perfusion timing



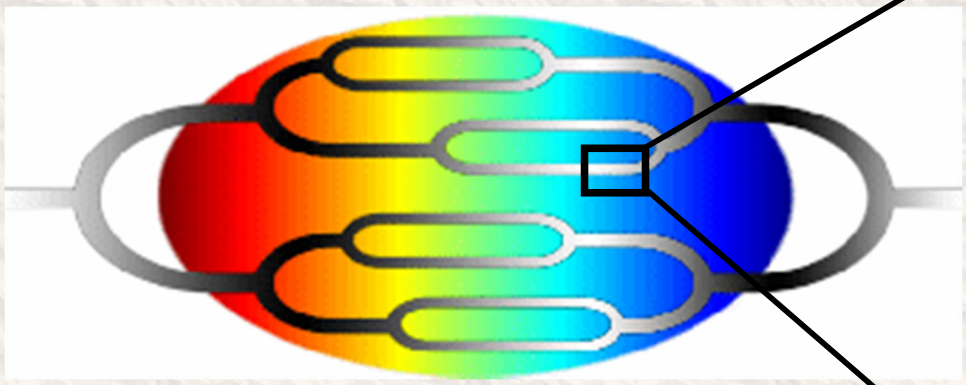
Unit = seconds

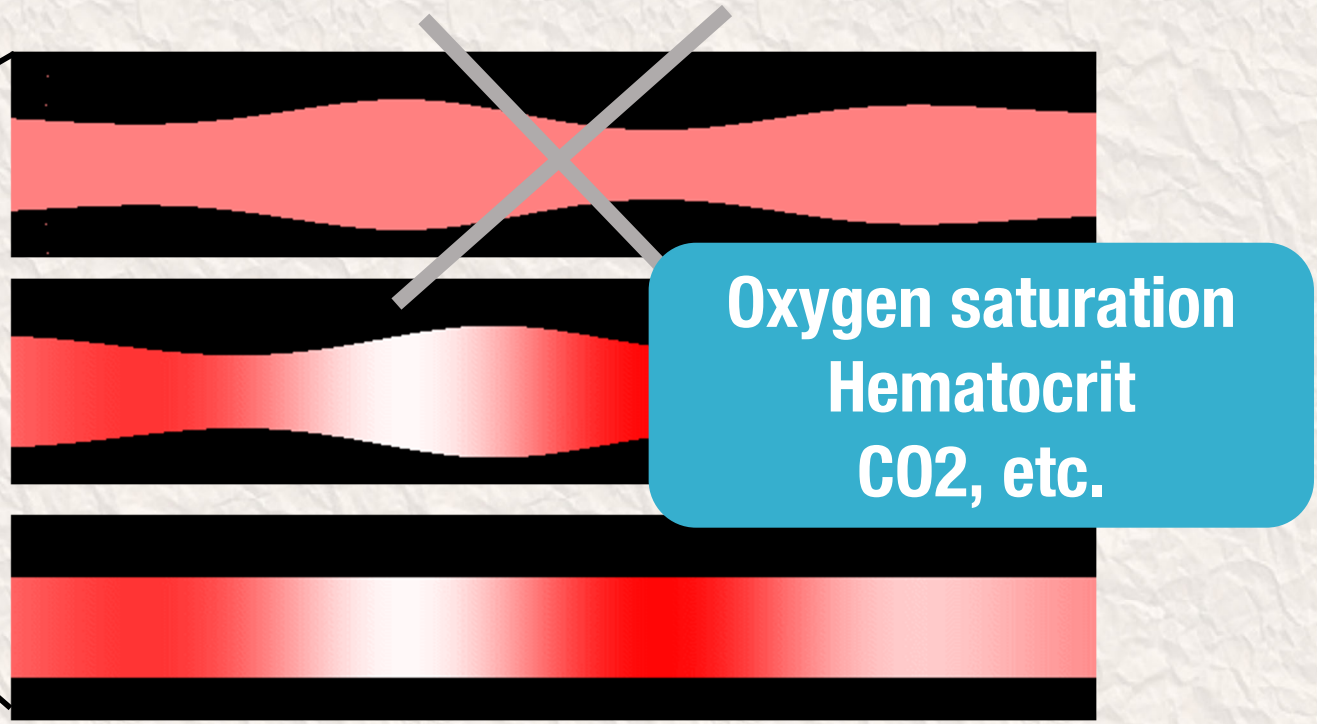
Aso, Hayashi HBM2020



sLFO = variation of deoxy-Hgb density

- Working hypothesis: sLFO is independent of vascular response or CBF change





Aso (2019) PLoS ONE

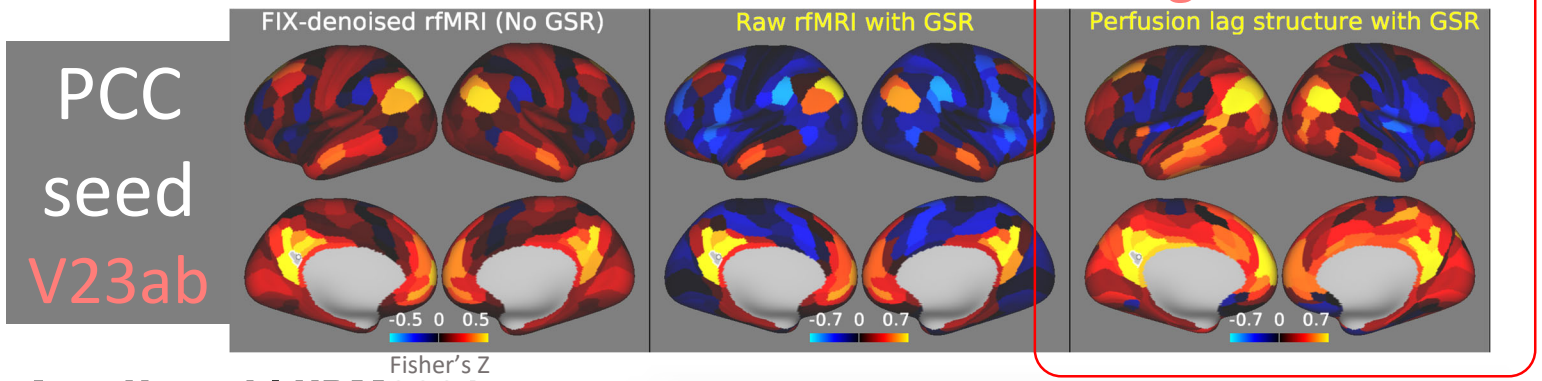
OK, so what's the problem?

- **The lag structure has its own correlation structure**

Chen (2020) NeuroImage; Tong (2015) FNS

Resting-state "physiological networks"

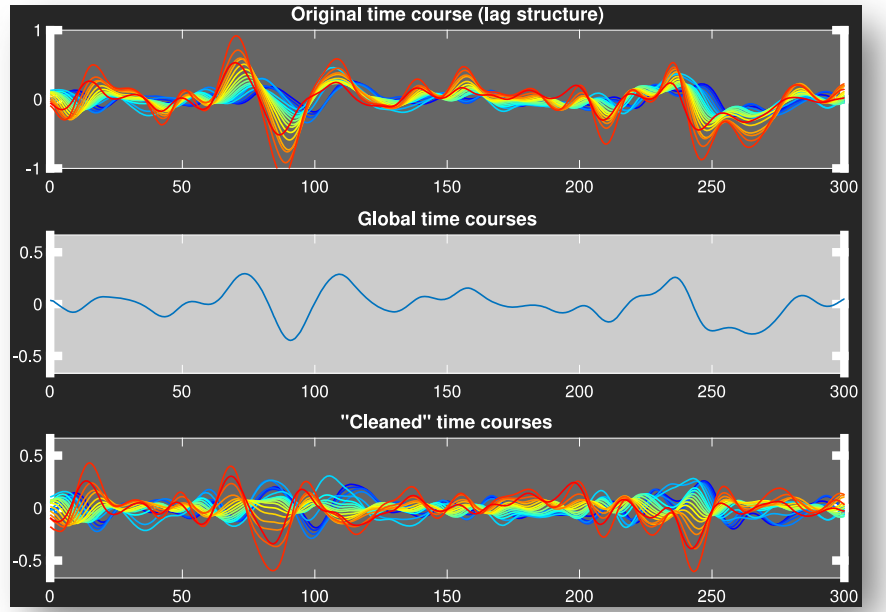
Jingyuan E. Chen[a,b,*], Laura D. Lewis[c], Catie Chang[d], Qiyuan Tian[a,b], Nina E. Fultz[a], Ned A. Ohringer[a], Bruce R. Rosen[a,b,e], Jonathan R. Polimeni[a,b,e]



Aso, Hayashi HBM2021

- **GSR doesn't do!!**
  - **The lag structure is a major part of global signal, but GSR leaves the correlation structure**
  - **Tailored regression of sLFO <u>for each voxel</u> is needed**

Erdoğan, 2016 "Dynamic GSR", Aso 2019



• The lag structure has its own “connectivity”, or correlations

- Tong (2015) FNS, Chen (2020) NeuroImage

Aso, Hayashi HBM2021

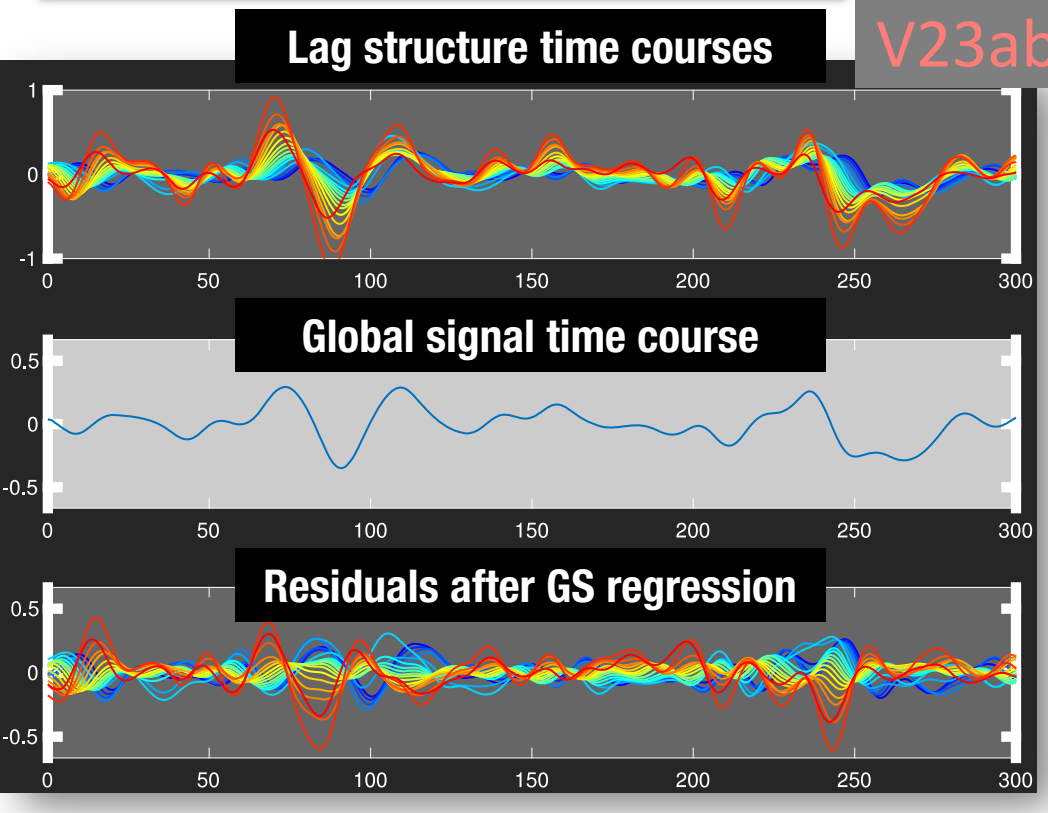
Can apparent resting state connectivity arise from systemic fluctuations?

Yunjie Tong[1,2], Lia M. Hocke[1,3], Xiaoying Fan[1,2], Amy C. Janes[1,2] and Blaise deB Frederick[1,2]*

[1] McLean Imaging Center, McLean Hospital, Belmont, MA, USA, [2] Department of Psychiatry, Harvard University Medical School, Boston, MA, USA, [3] Department of Biomedical Engineering, Tufts University, Medford, MA, USA

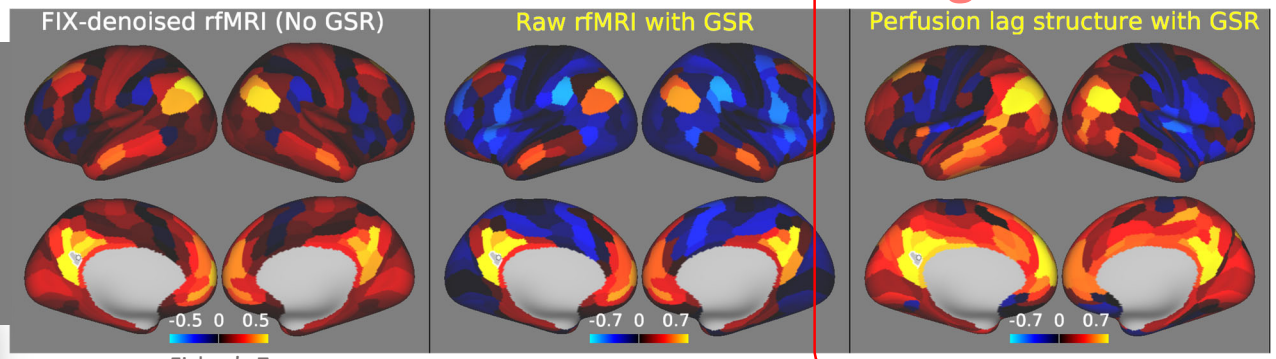
Resting-state “physiological networks”

Jingyuan E. Chen[a,b,*], Laura D. Lewis[c], Catie Chang[d], Qiyuan Tian[a,b], Nina E. Fultz[a], Ned A. Ohringer[a], Bruce R. Rosen[a,b,e], Jonathan R. Polimeni[a,b,e]



PCC seed V23ab

FIX-cleaned data | Raw data | Lag structure



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- The lag structure is a major part of global signal, but GSR leaves the correlation structure
- Tailored regression of sLFO <u>for each voxel</u> is needed

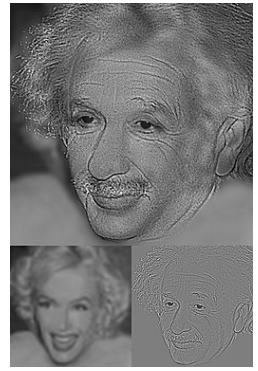
Erdoğan (2016) FNS *“Dynamic GSR”*, Aso (2019) PLoS One

Method: Let's get rid of it

HCP test-retest dataset N=40

https://github.com/RIKEN-BCIL/HCPstyle-BOLDLagMappingAndCleaning

"De-perfusioning"
affects only slow components



ICA-FIX

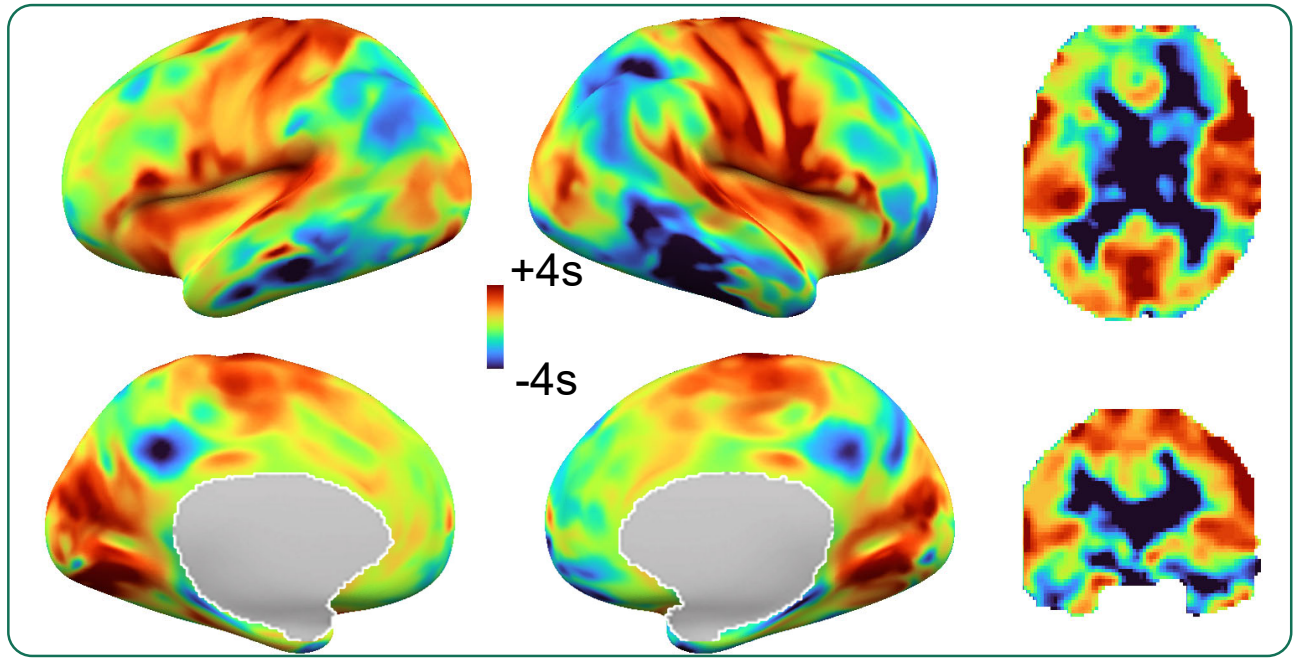
ICA-FIX

Compare Day-1 and Day-2

Subject #599671

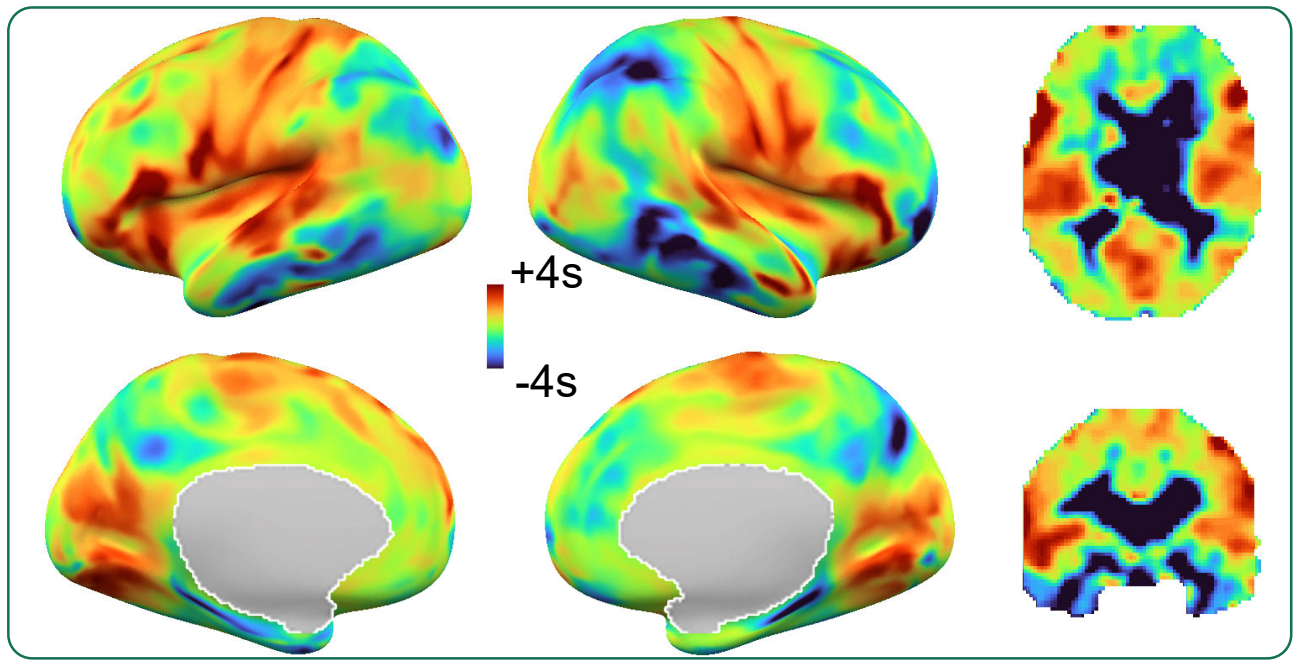
Lag map

day-1



Lag map

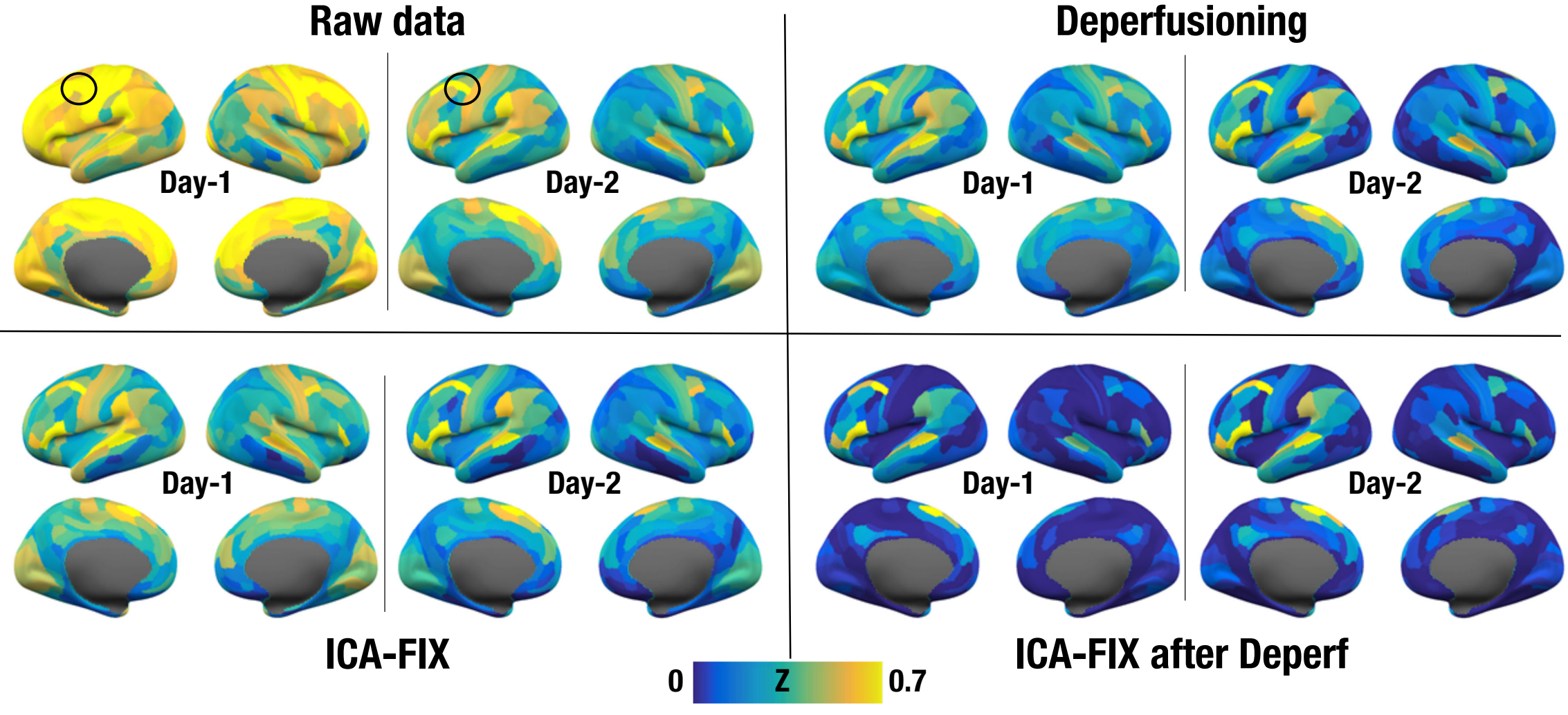
day-2

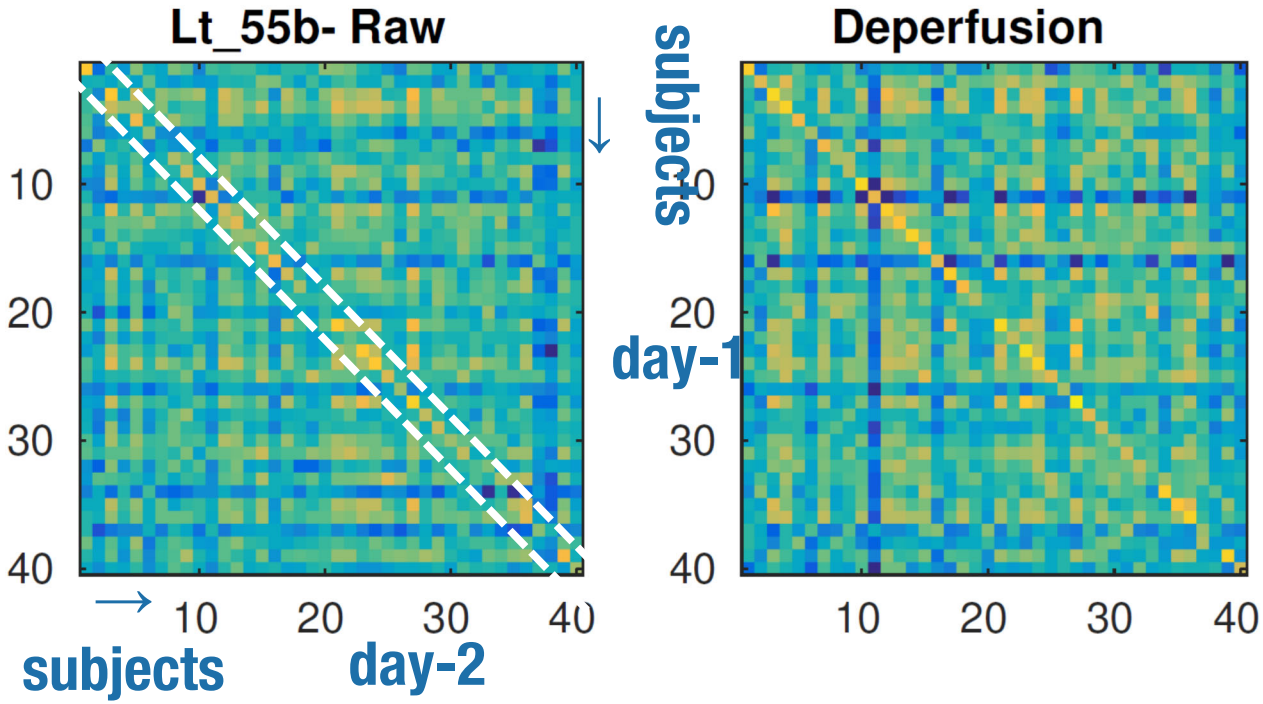


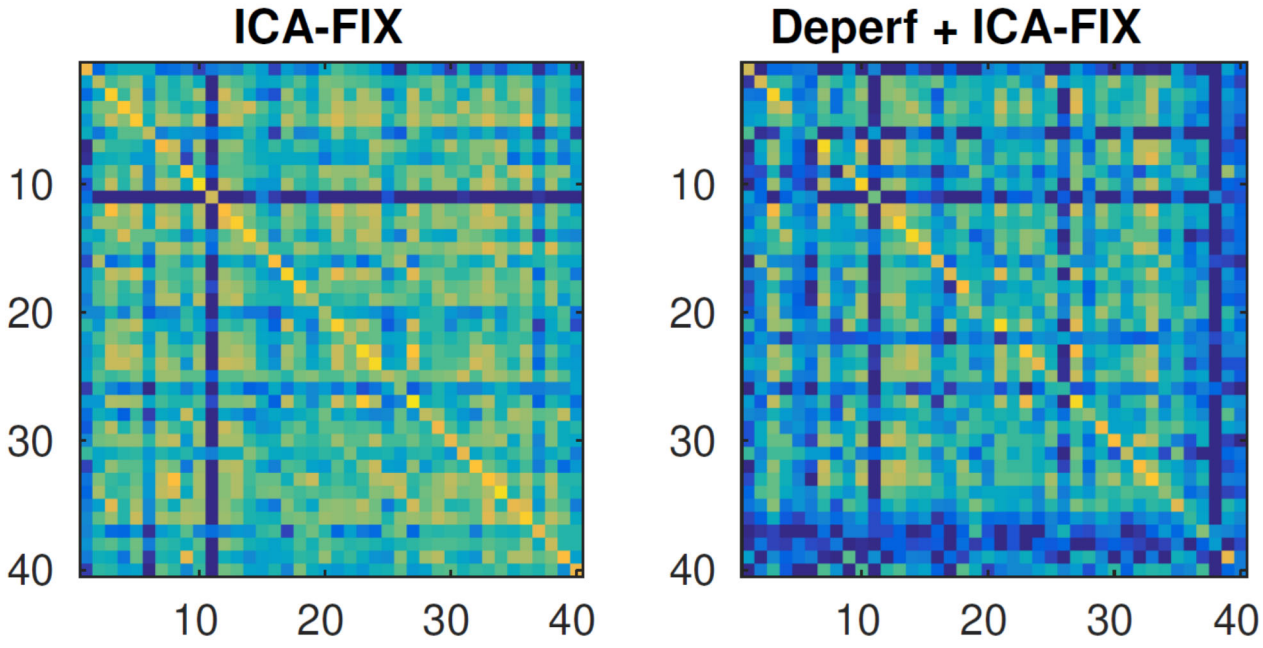
What was removed by deperfusioning: Consistent across visits, because it's predominantly vascular anatomy

Subject #599671, Superior Language Network/Area 55b seed

Glasser (2016) Nature



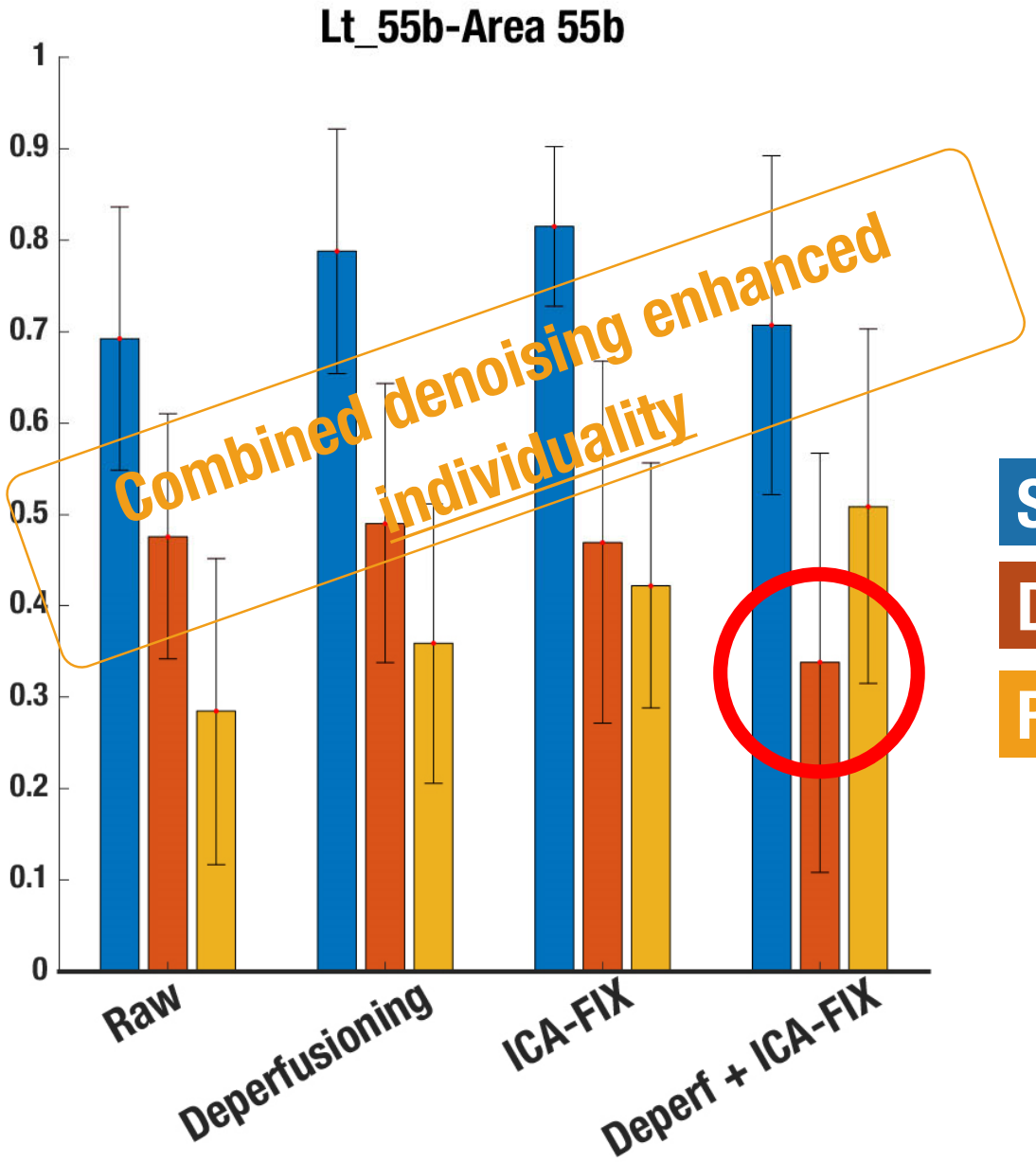




Network similarity as a reproducibility measure

- Every combination b/w day-1 and 2 (Spearman's rho)
- Diagonal elements are within-subject, i.e., reproducibility

Denoising makes them stand out by diminished between-subject similarity!



Individuality:

relative within-subject reproducibility

Same subject

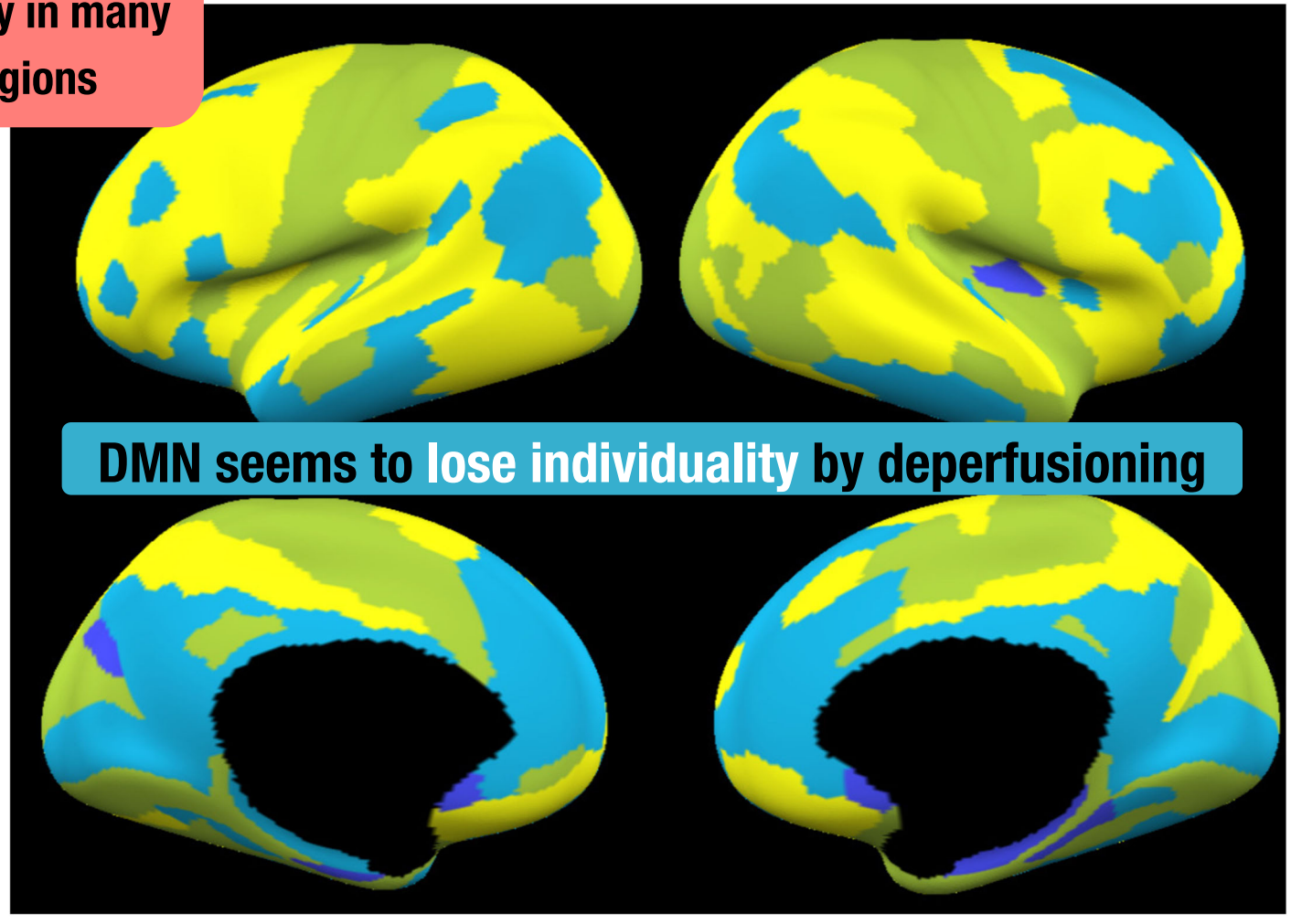
Different subject

Relative reproducibility (ratio)

How about the other seeds?

Best denoising (for individuality) for each seed region

Combined method enhanced individuality in many seed regions



Dep+ICAFIX
Combined method

Deperfusioning

ICA-FIX

Raw

Summary

- Test-retest reproducibility of FC generally improved by the two denoising procedures, suggesting both approaches are basically valid.
- The deperfusioning+ICA-FIX combined method achieved highest relative reproducibility (=individuality) by suppressing between-subject similarity.
- Denoising effects were not uniform across networks, mirroring the previous works on physiology-driven spurious FC.
- The combined method is recommended.

"…low reproducibility does not necessarily imply low accuracy"
(Harrison 2015 NeuroImage)