Science on Tap

The organization of human cerebral cortex estimated by functional PET-FDG: the promise and controversy of “metabolic connectivity”

23 Feb 2024, Penghui Du

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CANDY Lab

Penghui Du

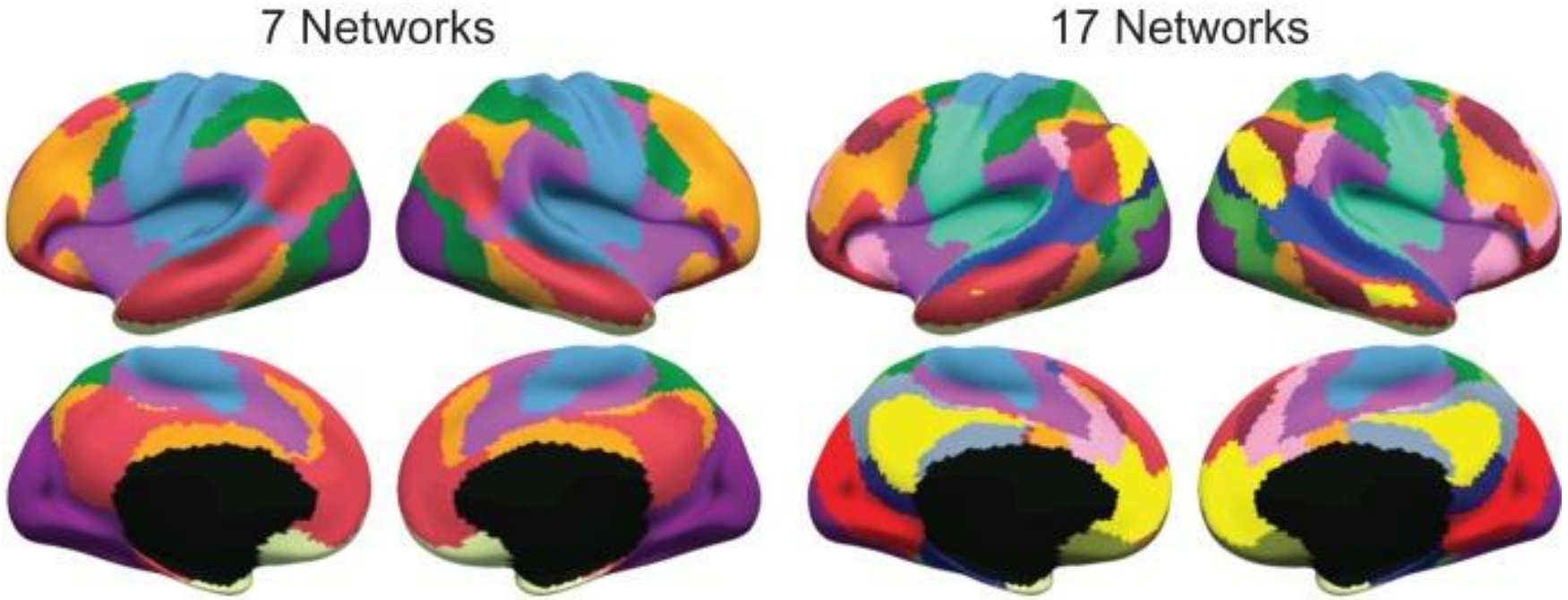
Content

- Background
- Methods & Results
  - **Promises:** Could fPET-FDG-based “Metabolic Connectivity” provide complementary insights into the local/global organization of the human brain?
  - **Controversies in interpretation:** Is “Metabolic Connectivity” primarily driven by instantaneous, short-term changes in glucose uptakes?
- Take Home Message

Functional MRI (fMRI) based functional connectivity has shed enormous insights into the functional organization of the cerebral cortex

Resting-state networks

- **Idea:** Voxels within the same network tend to have **synchronized fMRI dynamics**.
- **Method:** Clustering, Independent Component Analysis, Community Detection, etc.

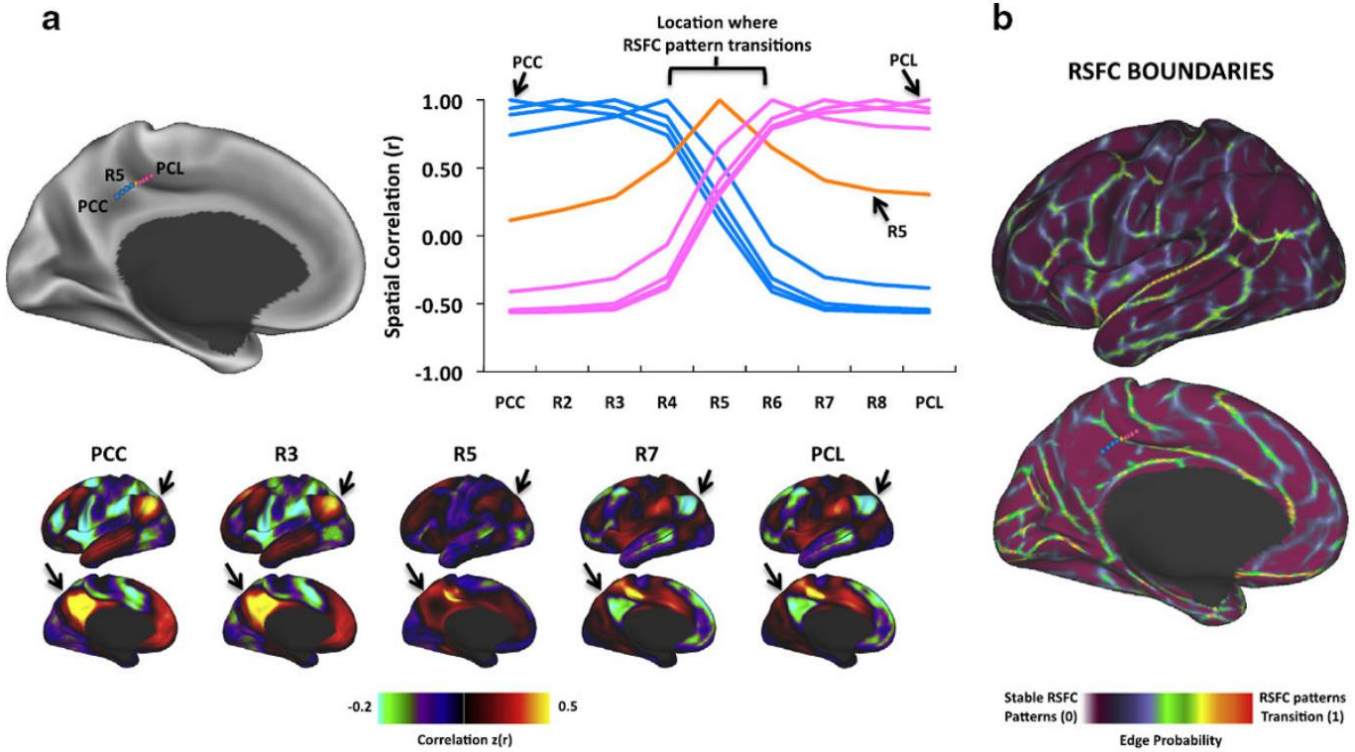


Yeo et al., J Neurophysiol. 2011

Functional parcel boundaries can be delineated by abrupt changes in the connectivity patterns

Boundary Mapping

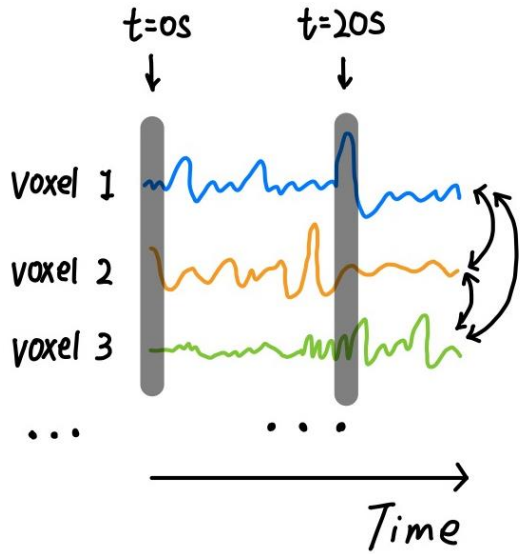
- **Idea:** Different brain regions have **different connectivity patterns**. There is a **sharp transition in connectivity** when crossing the boundaries separating different regions.
- **Method:** Calculate correlation of connectivity, then do edge-detection



Wig et al., Neuroimage, 2013

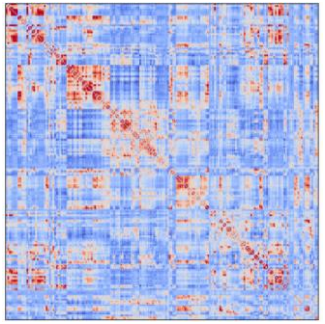
Emerging interests in mapping the cerebral architecture using metabolic information
"Metabolic networks" using static PET FDG: across-subject metabolic covariance

fMRI:



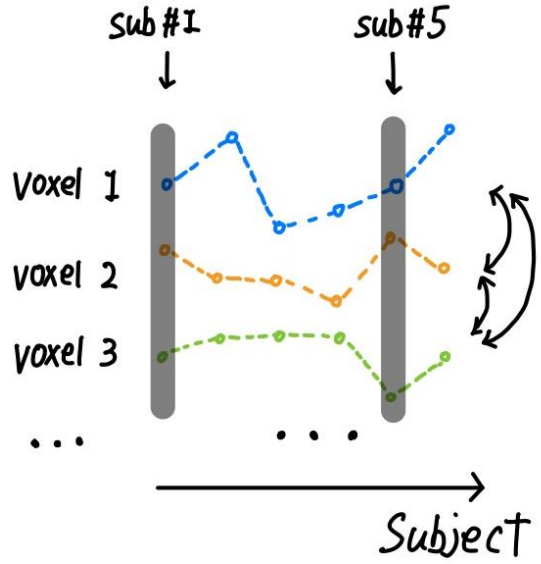
Calculate correlation of each voxel pair

Using BOLD time series



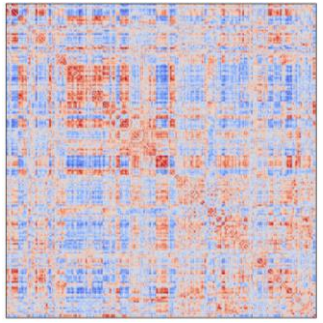
Functional Connectivity (FC)

Static PET-FDG:



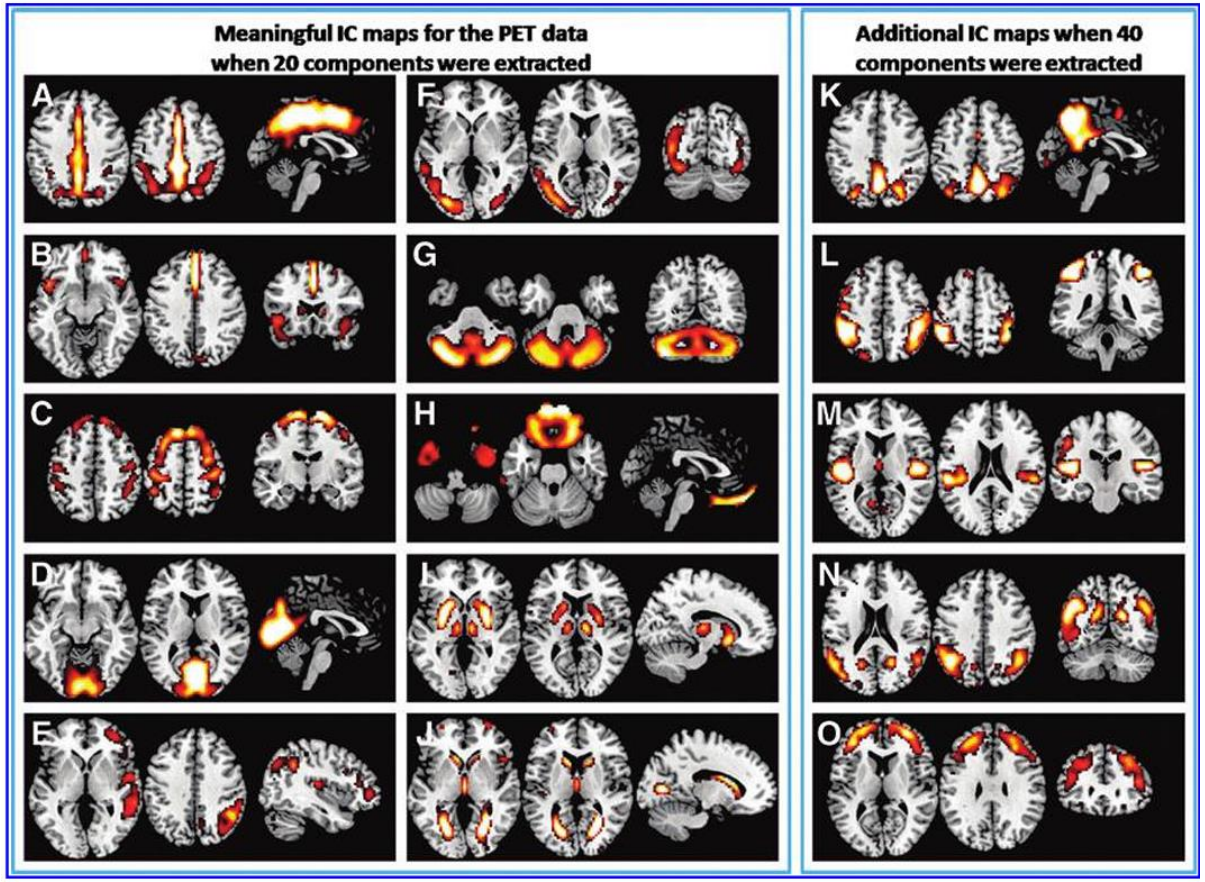
Calculate correlation of each voxel pair

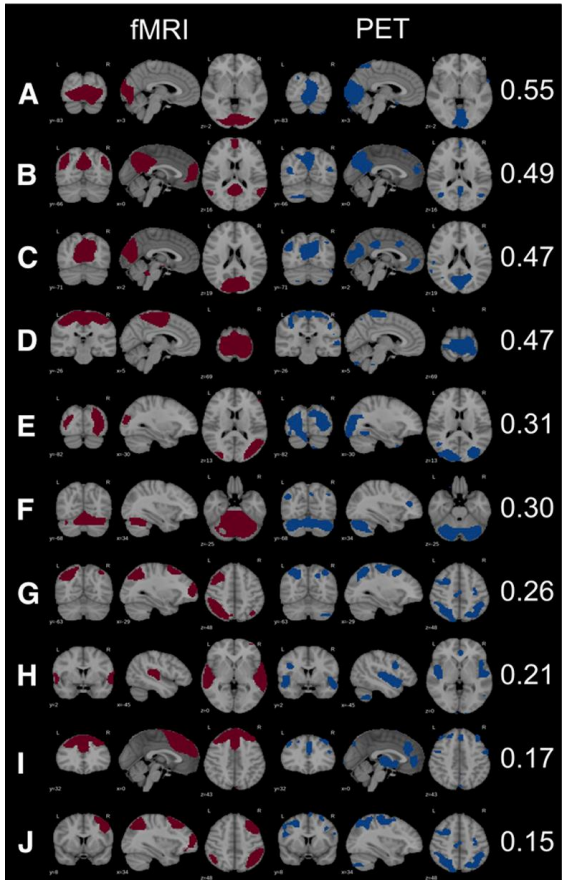
Treat subjects as time series



Cross-Subject Metabolic Covariance (MCov)

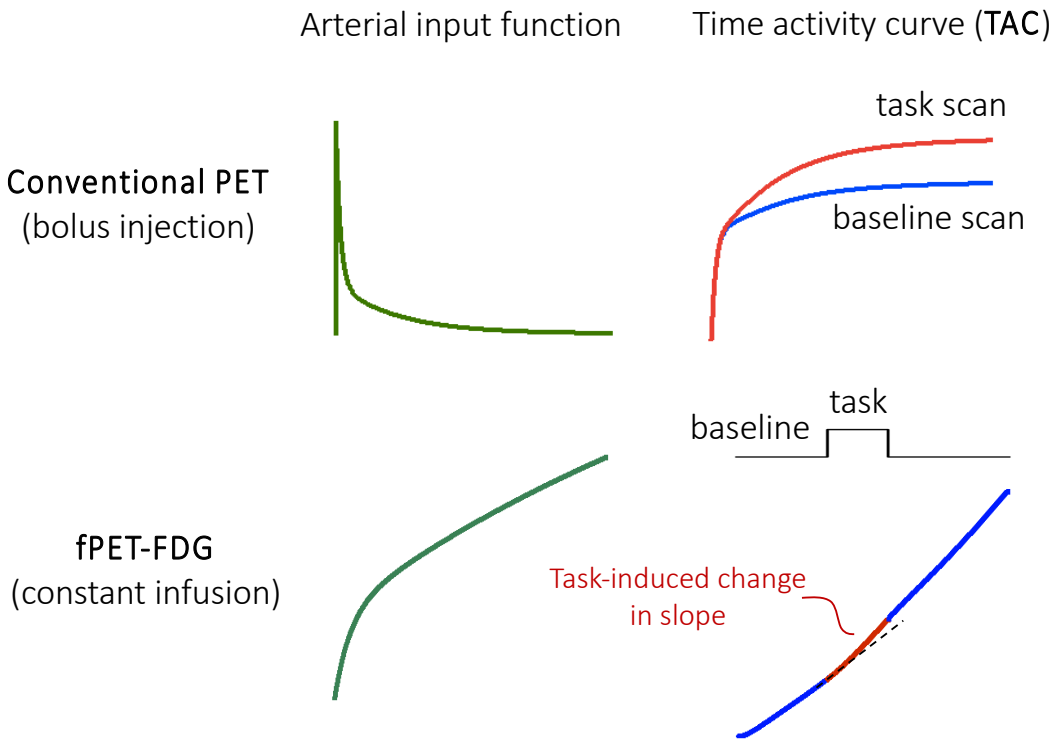
Exemplar “metabolic” networks identified by static PET-FDG based across-subject metabolic covariance

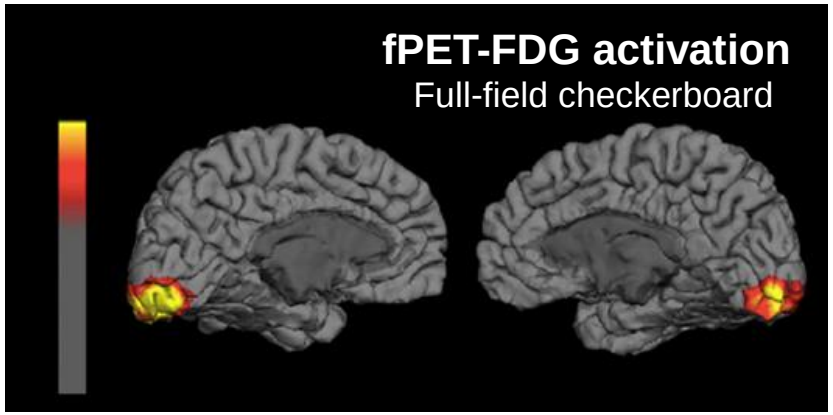


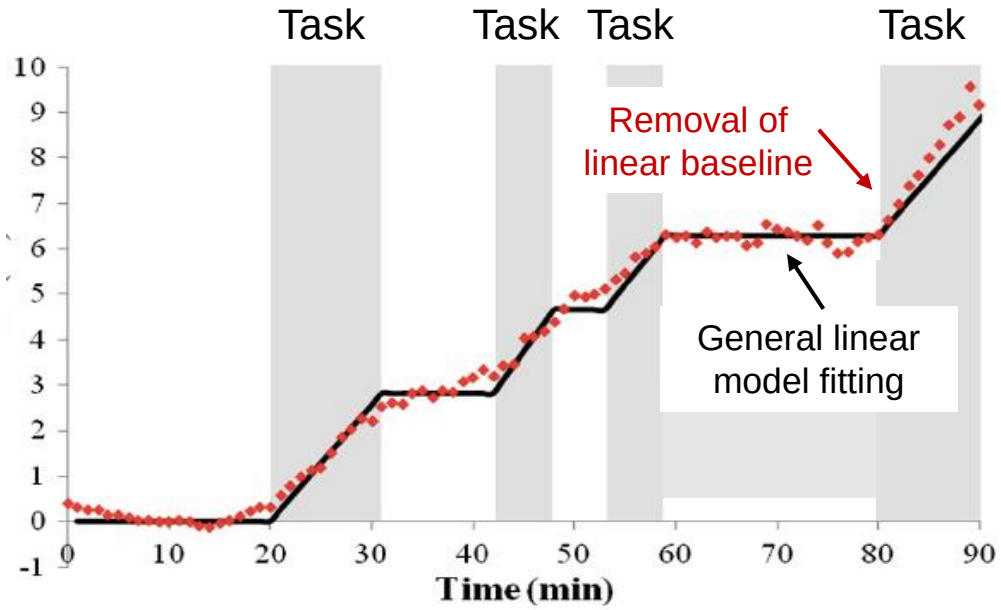


Di et al., Brain Connect. 2012; Savio et al., J Nucl Med. 2017.

Functional PET-FDG (fPET): Mapping dynamic, functional changes in brain metabolism in a manner akin to fMRI

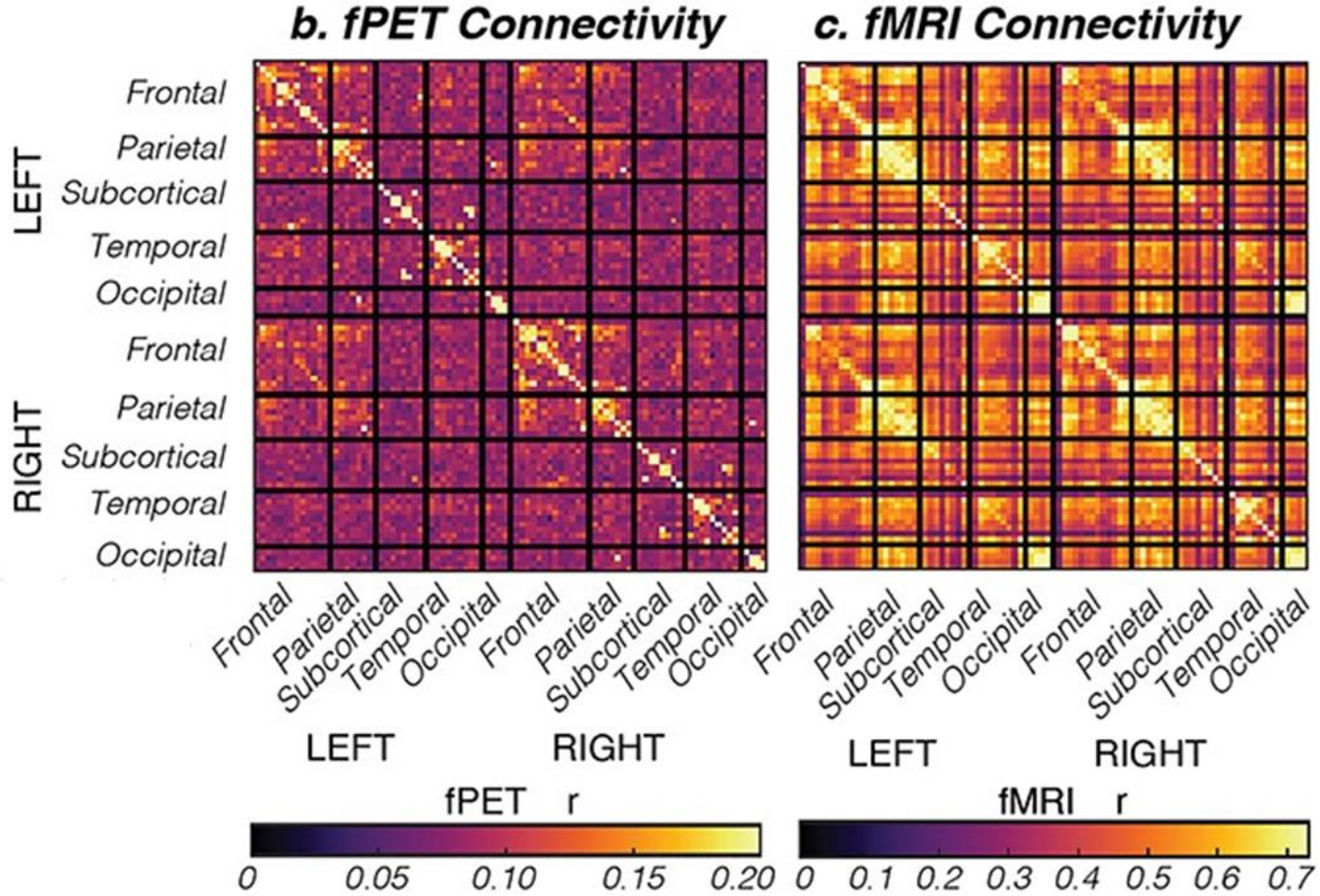


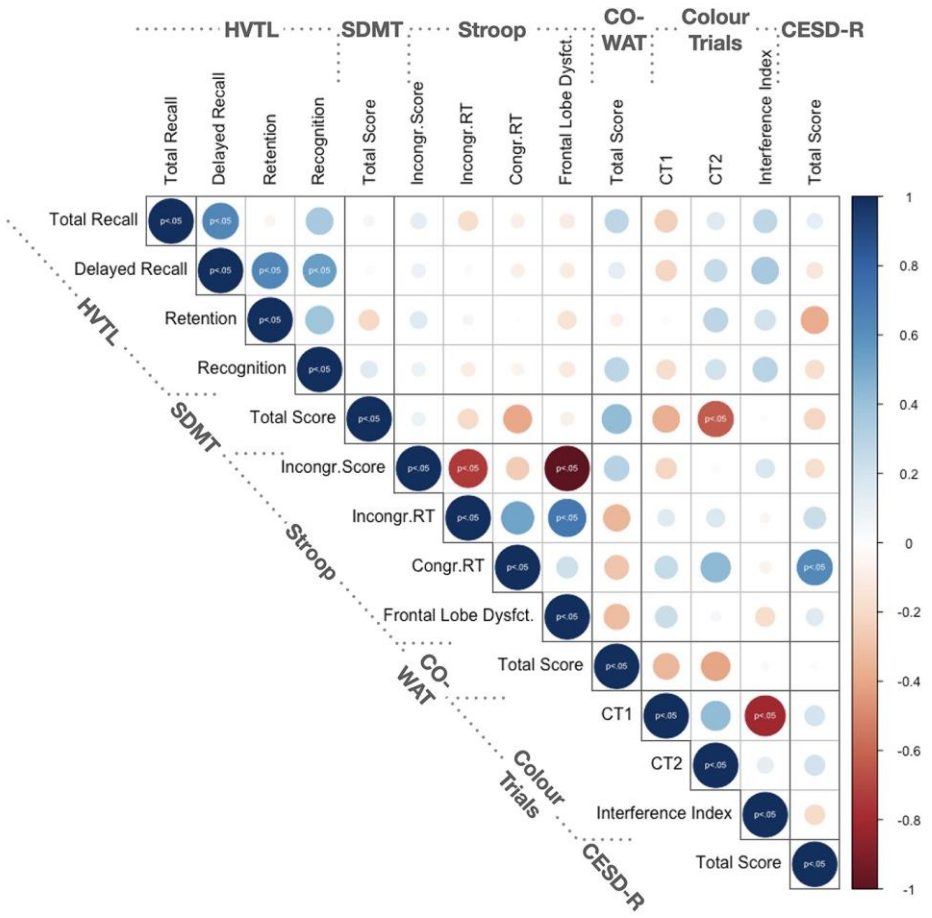




Villien et al., NeuroImage, 2014; see also Hahn et al., J Nucl Med. 2016, Rischka et al., NI, 2018

“Metabolic Connectivity” (MC) derived from the intra-subject temporal synchrony of fPET-based metabolic dynamics





Jamadar et al., Cereb Cortex. 2021; Voigt et al., Cereb Cortex. 2023

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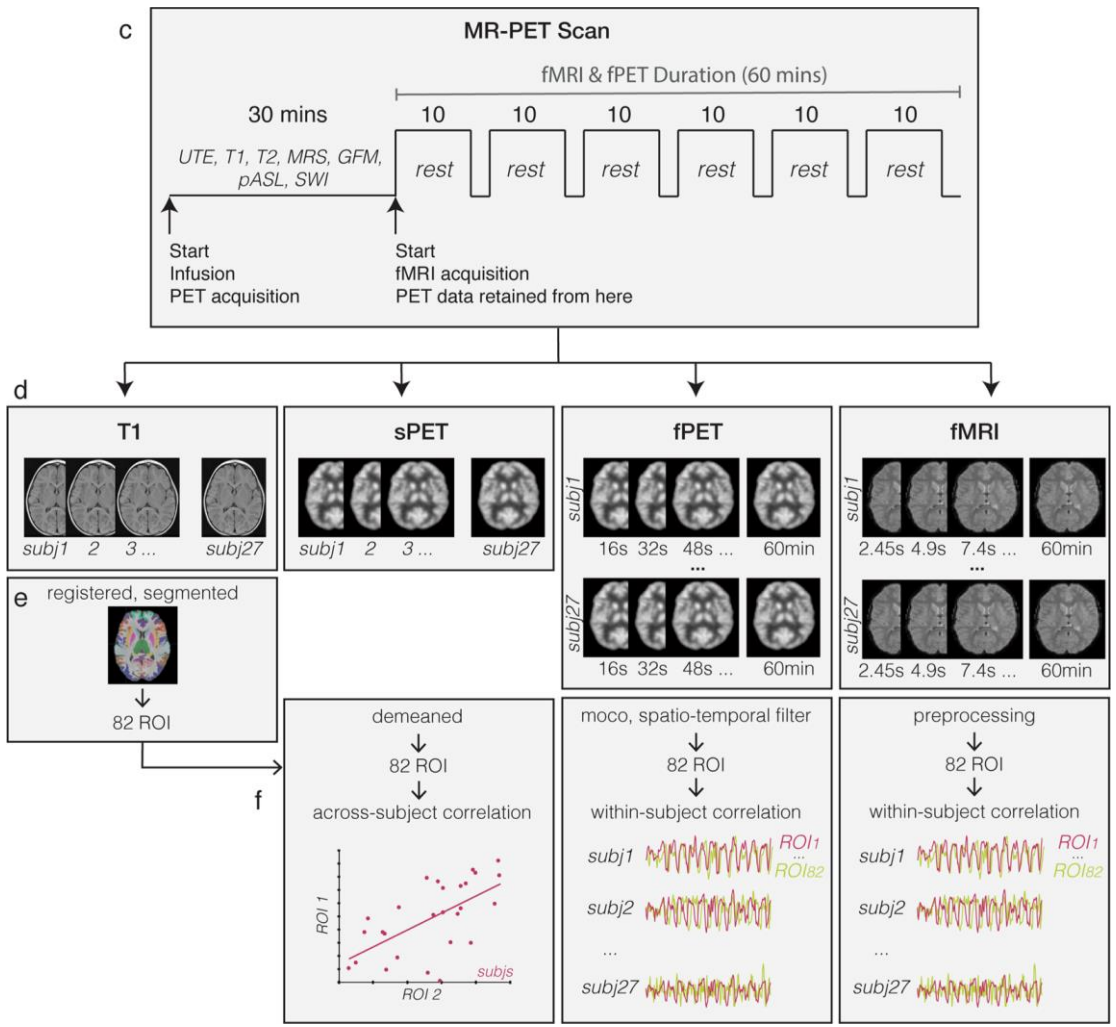
Monash resting-state PET-MR Dataset

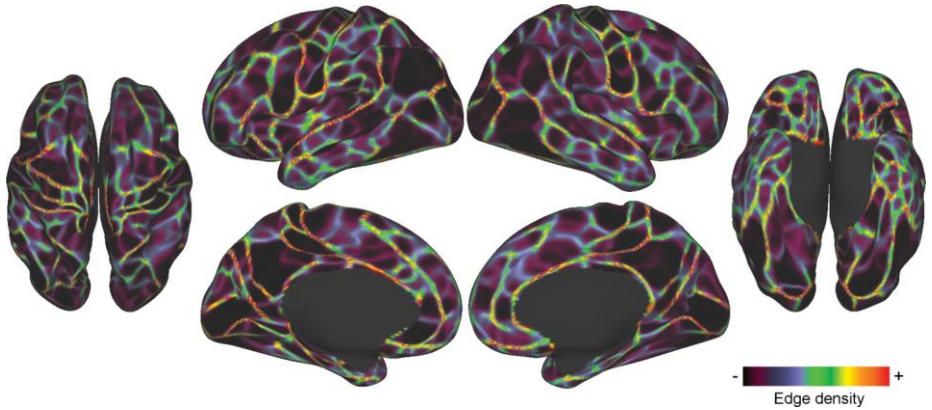
- Publicly available
- 26 Healthy Young Subjects
- fMRI: (60 min)
  - TR = 2450ms
  - Voxel size: 3x3x3 mm^3
- fPET: (90 min)
  - Reconstructed nominal resolution:

    16 s/frame, 2.09x2.09x2.09 mm^3

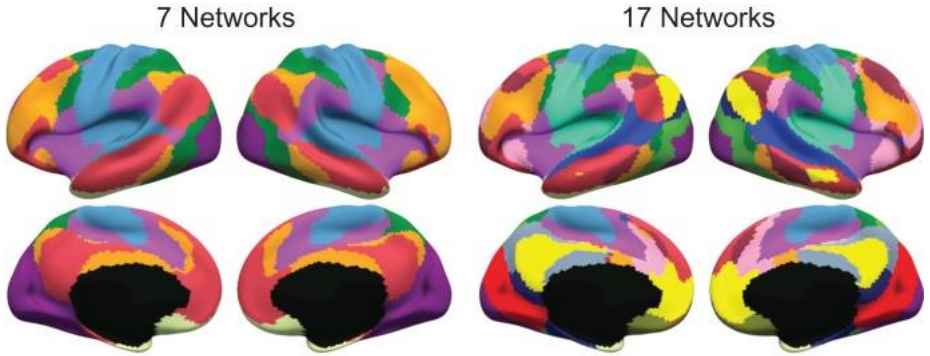


Jamadar et al., Sci Data. 2020

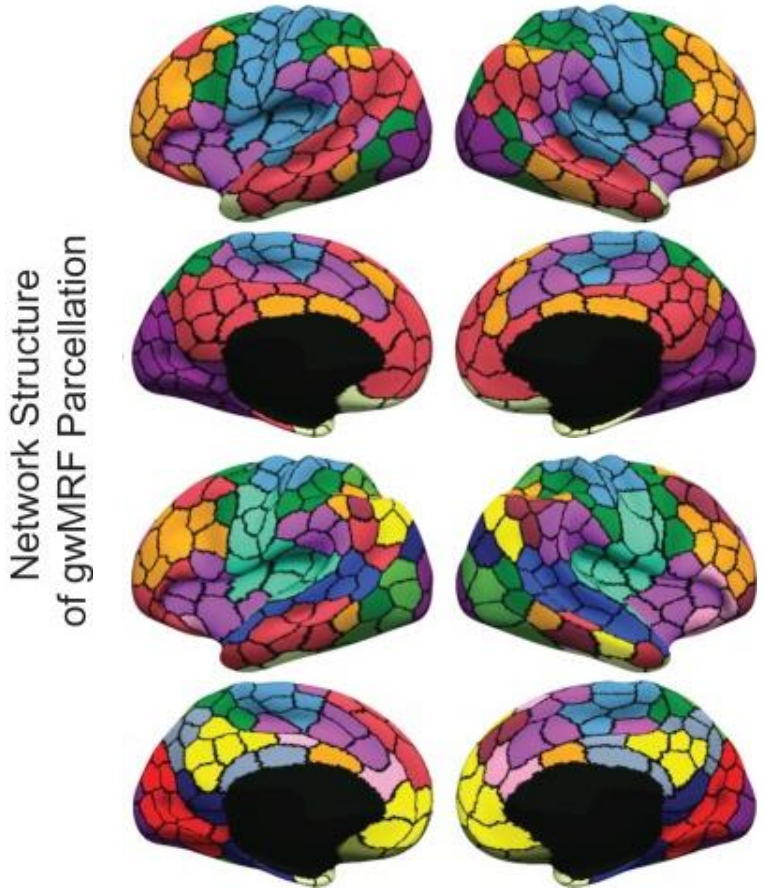
Local-Global approaches for brain parcellation



Create parcels using boundary maps



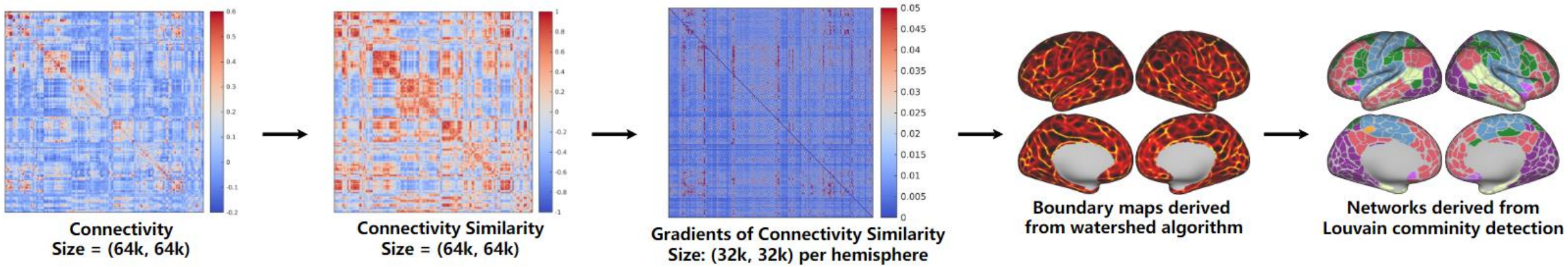
Assign each parcel **to a network**
(clustering, community detection)



Yeo et al., J Neurophysiol. 2011; Gordon et al., Cereb Cortex. 2016; Schaefer et al., Cereb Cortex. 2018.

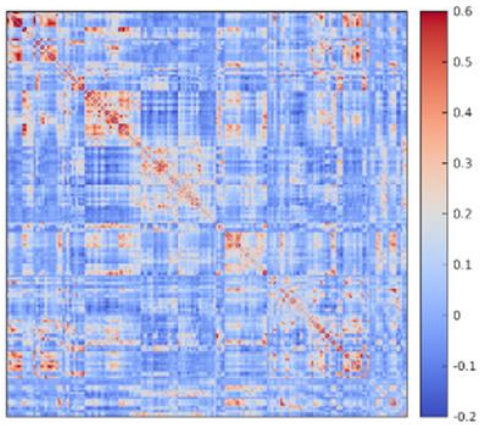
Scheme of Analysis

Connectivity, Boundaries and Networks:



Du et al., In Prep

Scheme of Analysis



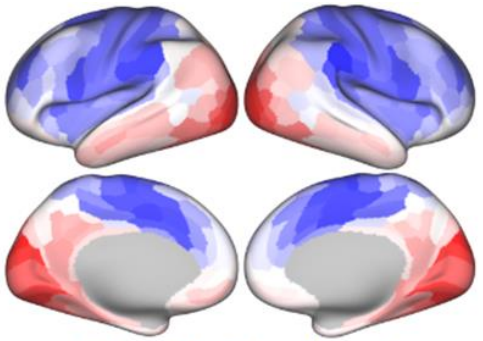
Connectivity
(using Glasser 2016 Atlas)
Size = (360, 360)

Principal Component Analysis:

Get N dominant connectivity patterns that explains the largest percent of variance

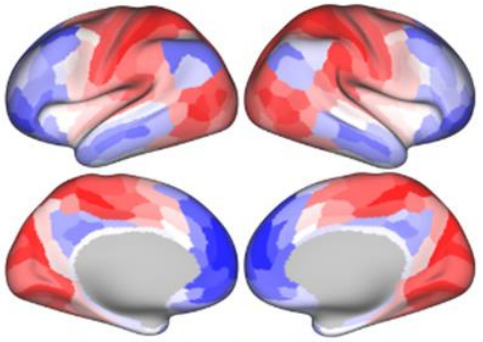
Size = (360, N)

Principal Gradients of Connectivity:



Principle Gradient 1

• • •



Principle Gradient N

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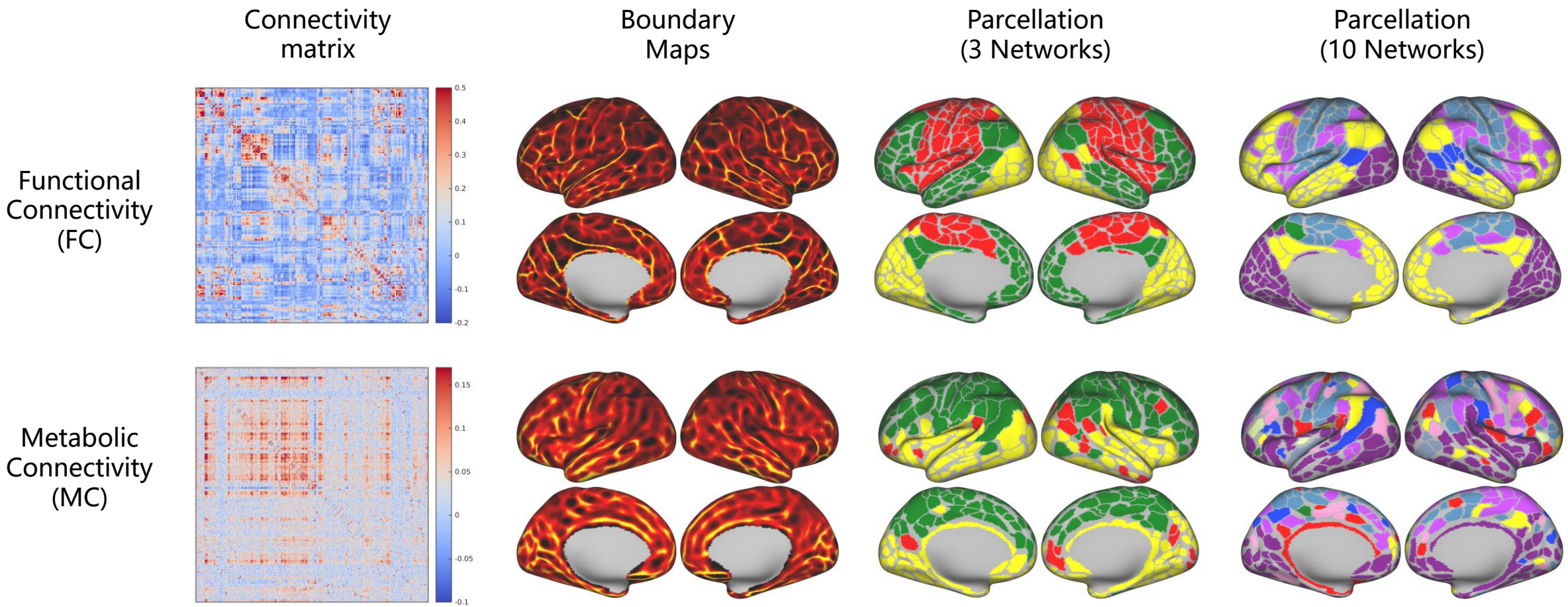
fPET-based MC results in robust network patterns and cortical parcellations that deviate from those derived from fMRI-based FC



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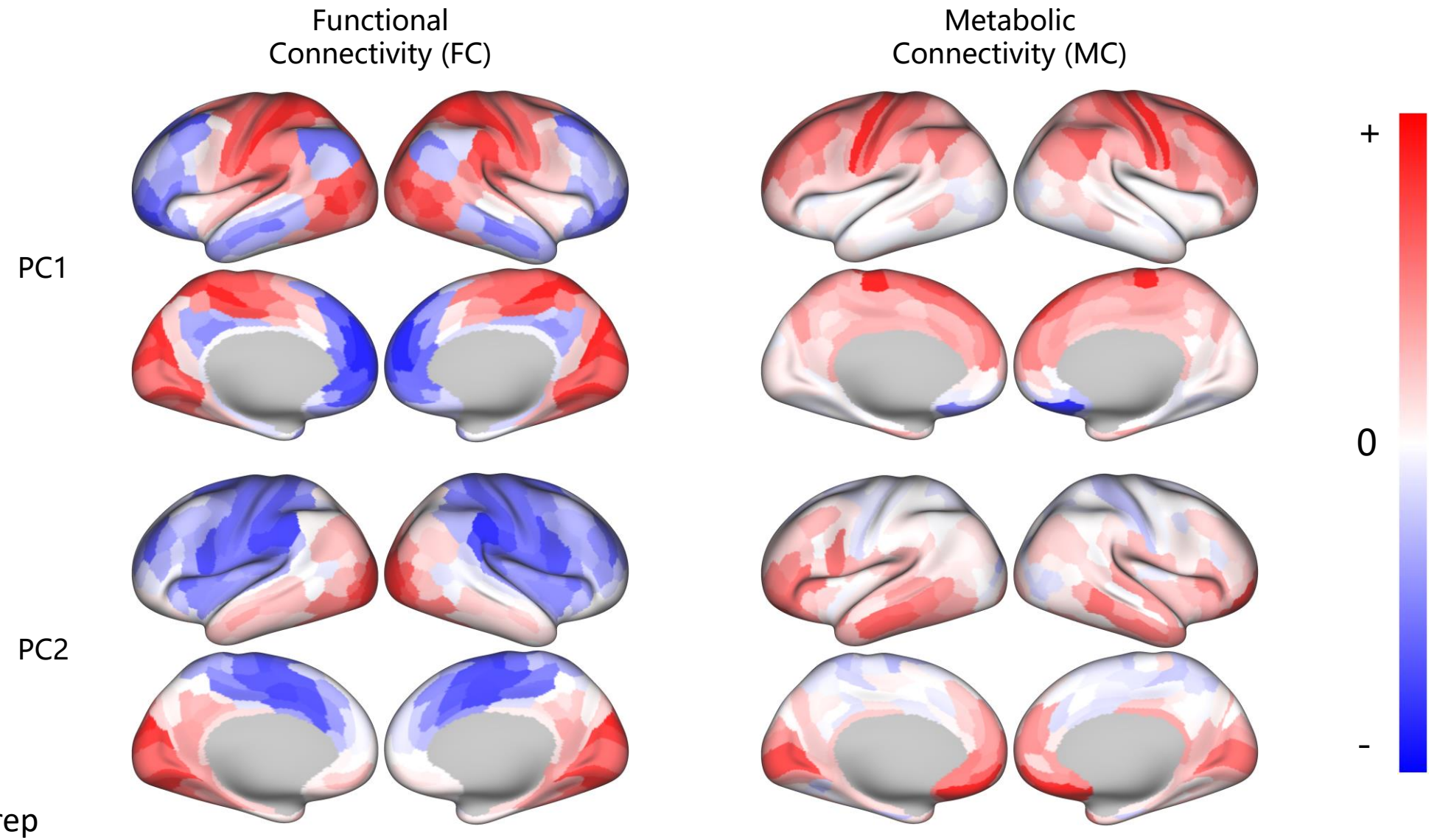
Principal Gradients of connectivity



Du et al., In Prep

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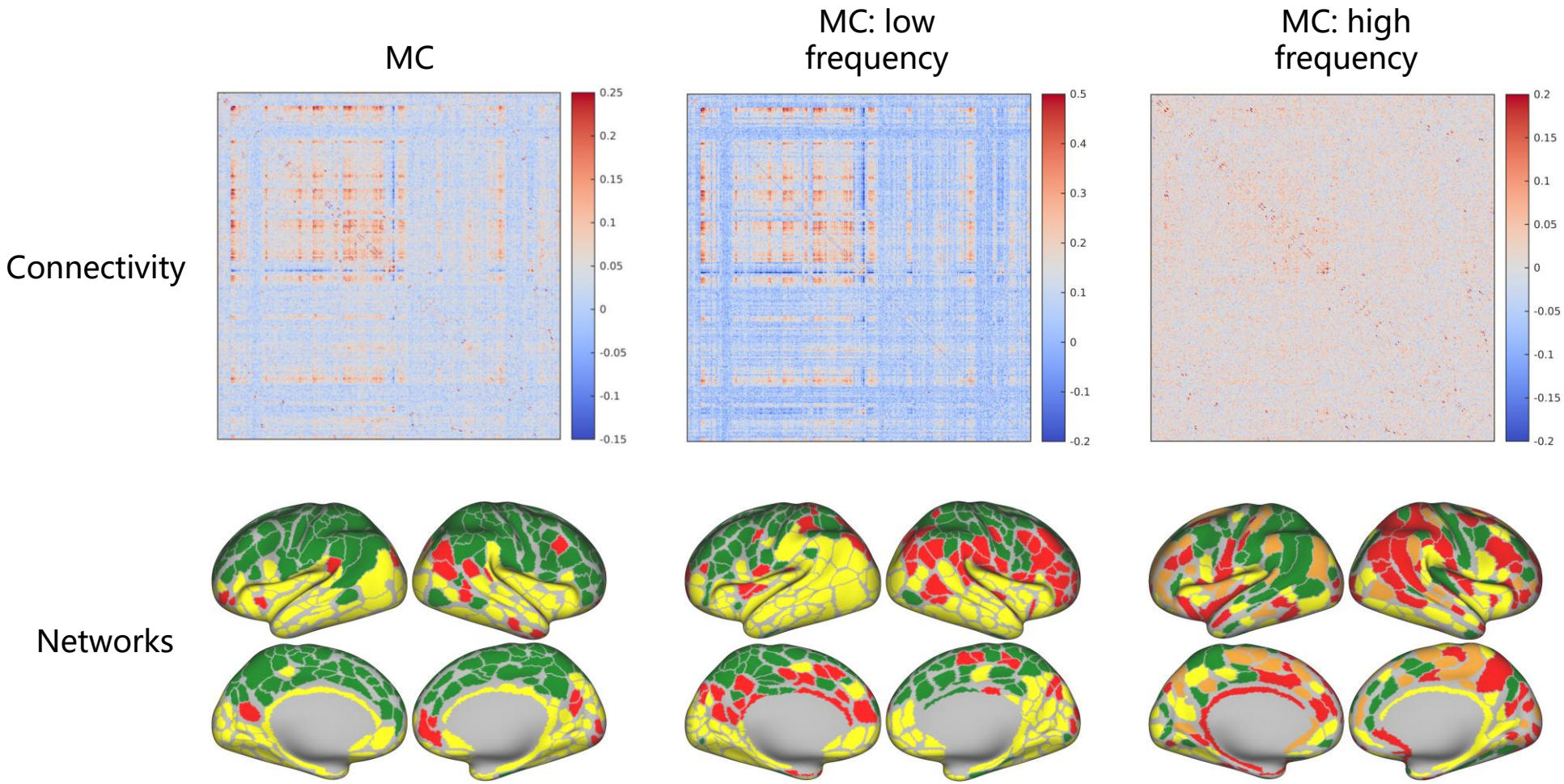
Low frequency component (>5min) dominates MC



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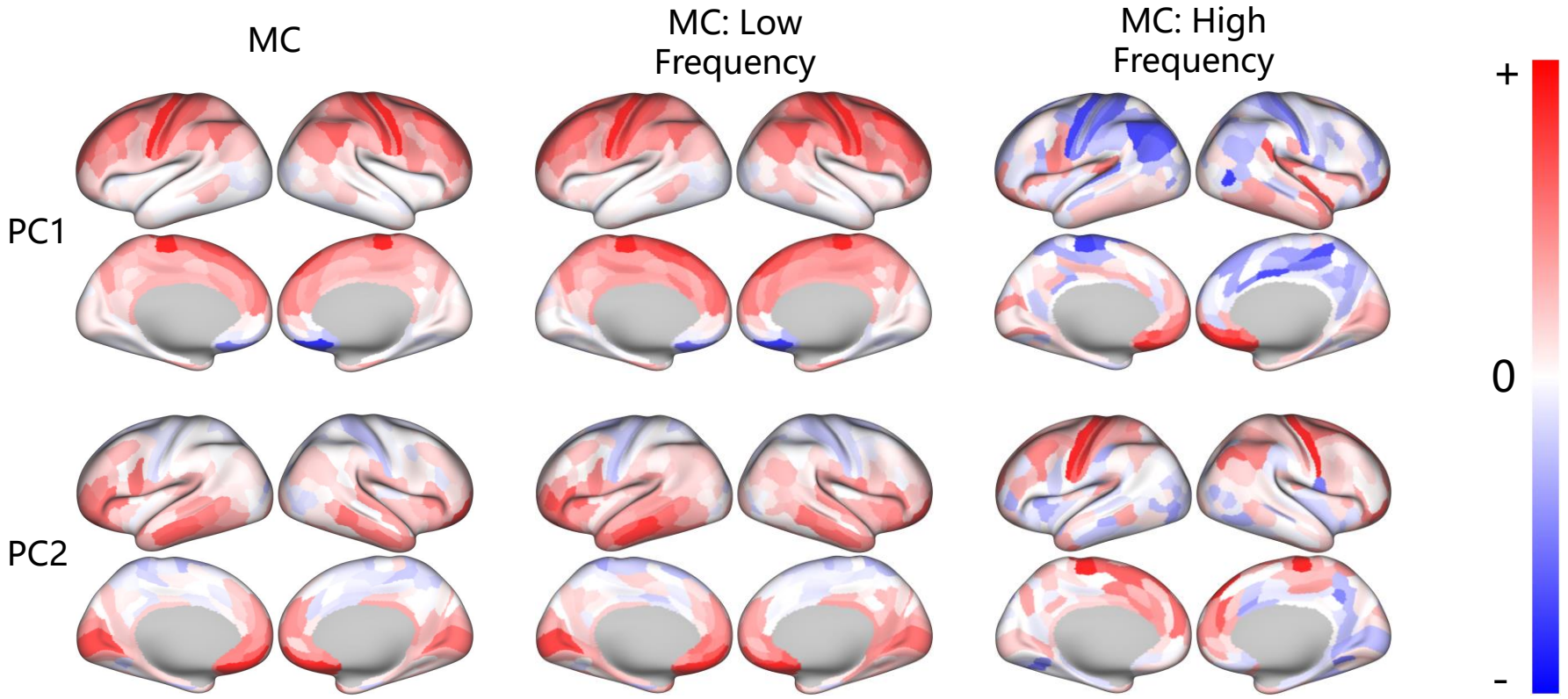

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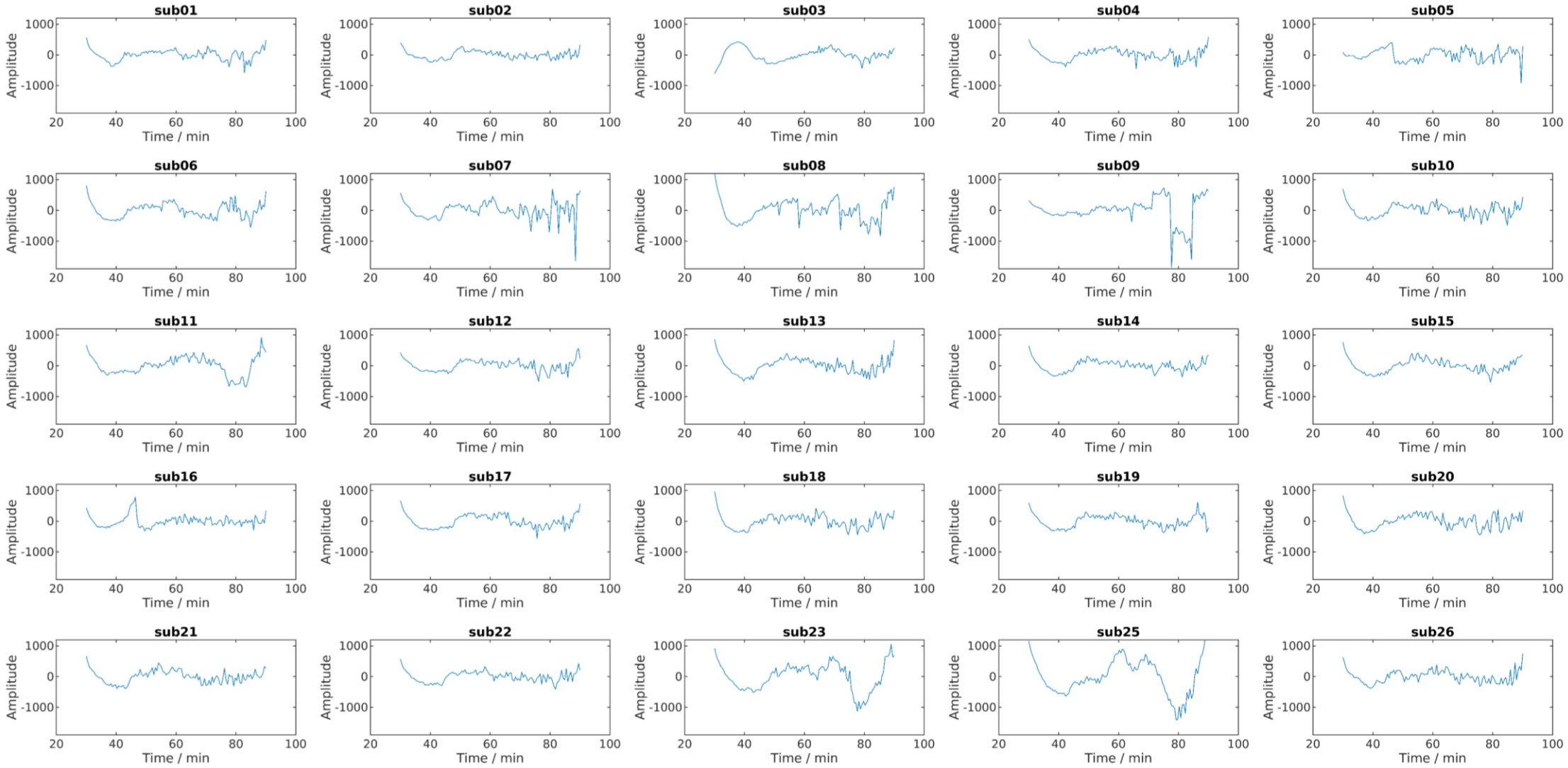
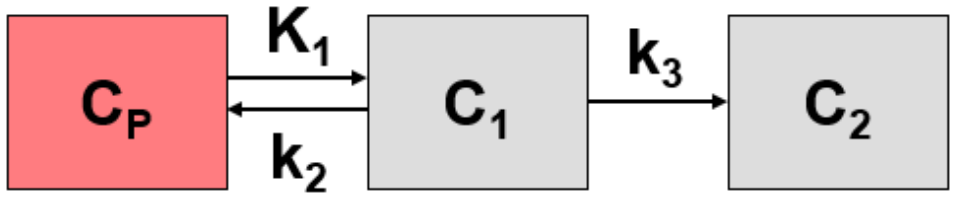
Alternative, non-metabolic mechanism underlying “metabolic connectivity?”



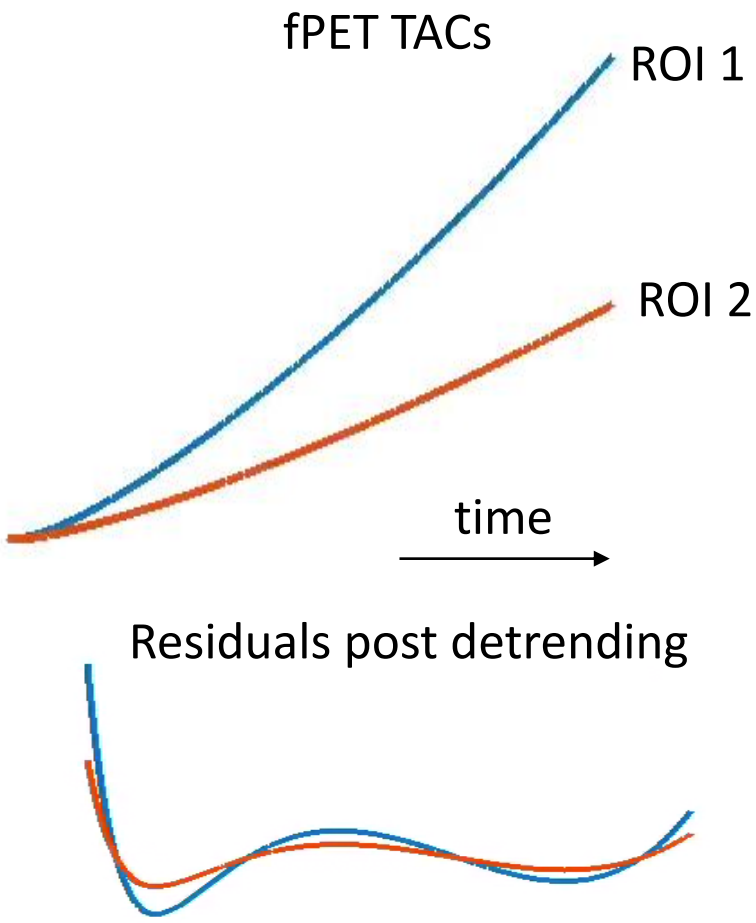
fPET time activity curves, after 3rd order detrending

Besides metabolism changes, low-frequency fluctuations of fPET time-activity curves (TACs) also reflect the accumulating effect of FDG

Irreversible 2-tissue compartment model

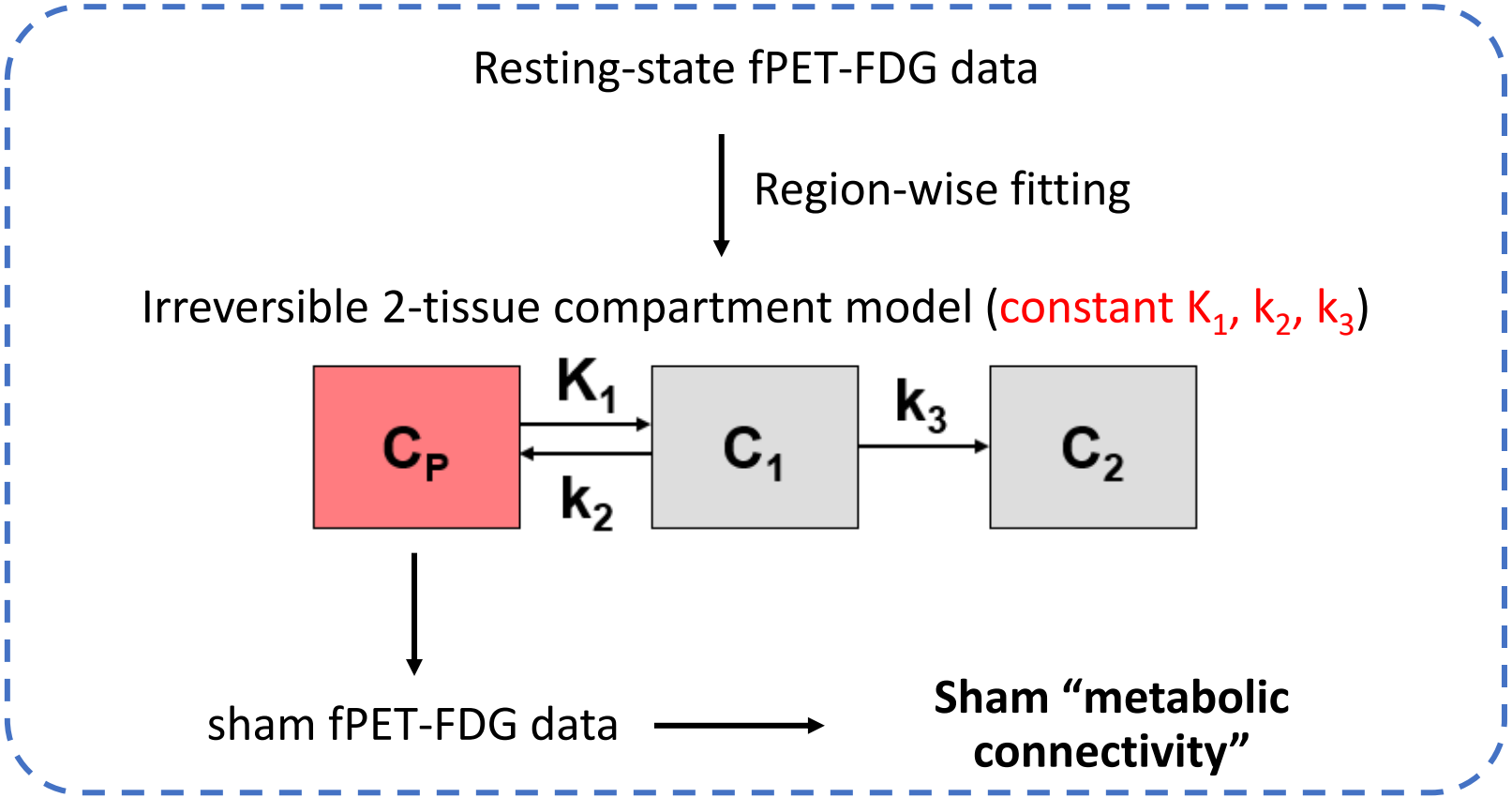


Rate constants vary across brain regions, resulting in spatially-varying TACs



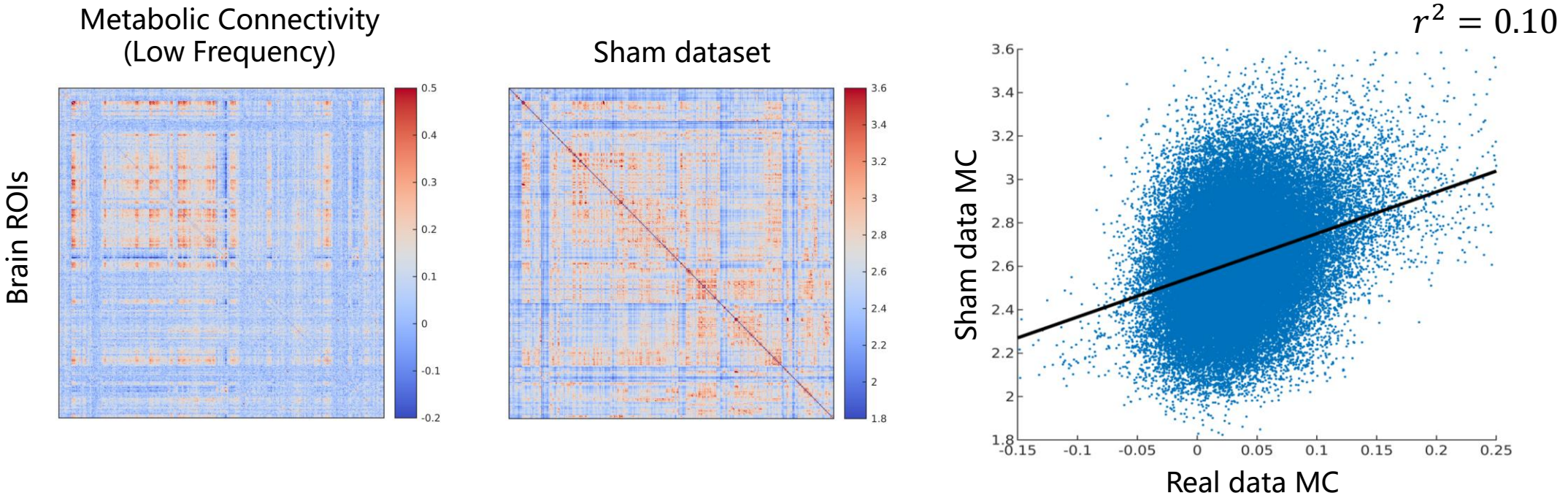
Testing the influence of accumulating FDG kinetics on “metabolic connectivity”

Sham dataset: no functional changes in metabolism over time



by Sean Coursey

Accumulating FDG kinetics may contribute partly to characterized "metabolic connectivity"



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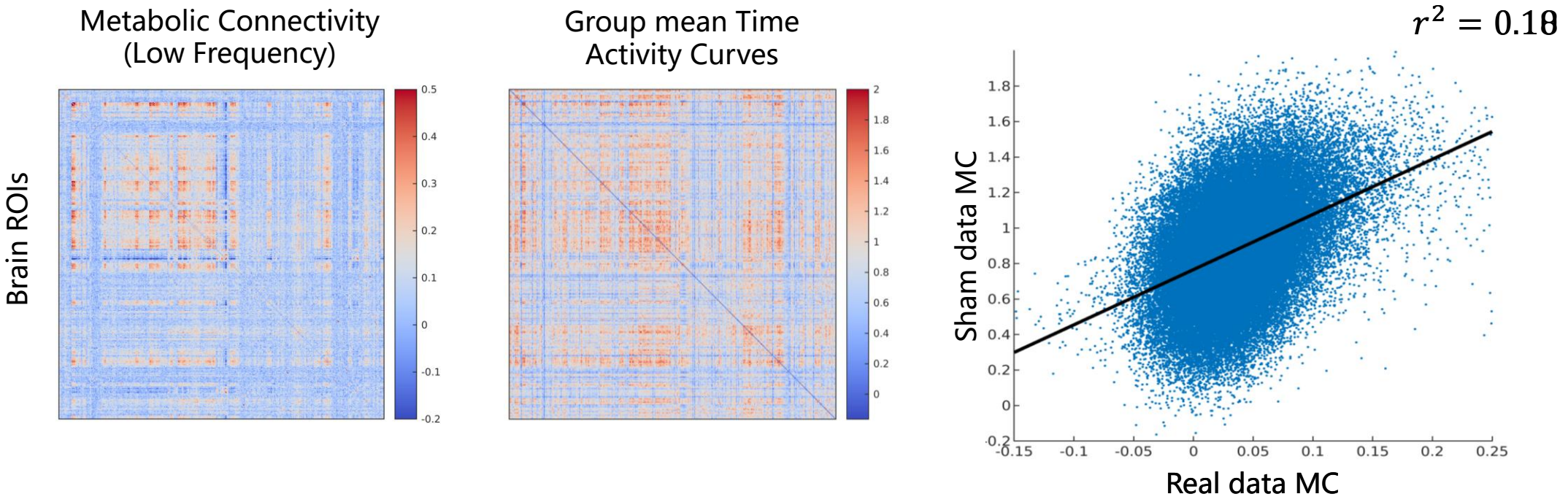
Resting state “metabolic connectivity” may also be partly caused by similar scanning experiences



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  - **Challenges:** Is “Metabolic Connectivity” really driven by synchronized neuronal activities? What are other potential mechanisms and potential caveats?
- Take Home Message

Take Home Message

- fPET “Metabolic Connectivity” shows robust spatial features distinct from FC, which could potentially provide complementary insights into the cortical organization.
- The interpretation of “Metabolic Connectivity” is challenging—not necessarily driven by rapid spontaneous changes in glucose metabolism, because:
  - Low-frequency component (>5min) is main contributor to fPET “Metabolic Connectivity”.
  - At low frequencies, apparent fPET dynamics may arise from alternative mechanisms, such as tracer kinetics (imperfect baseline removal) and slower-state changes coupled to scanning experiences.
- Promising but needs further investigation!

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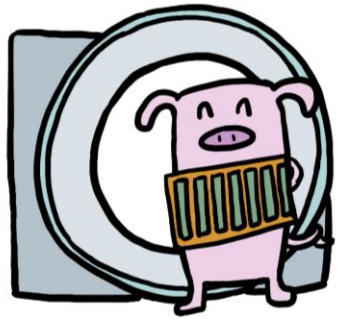

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