Human Cerebral Cortex Organization Estimated by Functional PET-FDG Metabolic Connectivity

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1 – Introduction

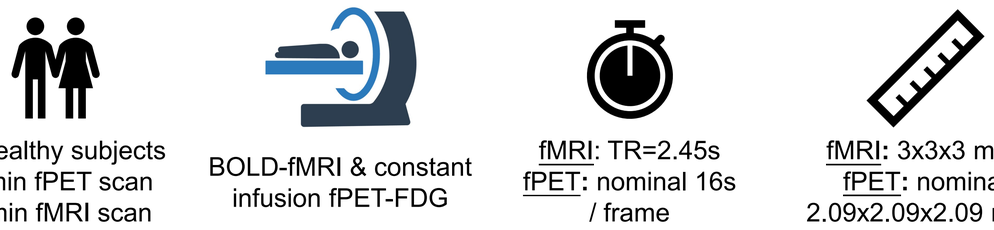
Functional connectivity (FC) derived from BOLD-fMRI has provided significant insights into human brain organization[1,2]. The recent introduction of constant-infusion functional [18F]PET (fPET)-FDG has enabled us to track dynamic changes in glucose metabolism over time[3,4], sparking growing interest in 'metabolic connectivity' (MC)[5,6]—the temporal synchrony of FDG-based metabolic dynamics between distant brain regions. In this study, we employed a connectivity gradient-based analysis scheme on a resting-state simultaneous fPET-fMRI dataset[7], aiming to characterize the detailed cortical organization of fPET-derived MC and understand its differences from fMRI-derived network structures.

2 – Major Findings

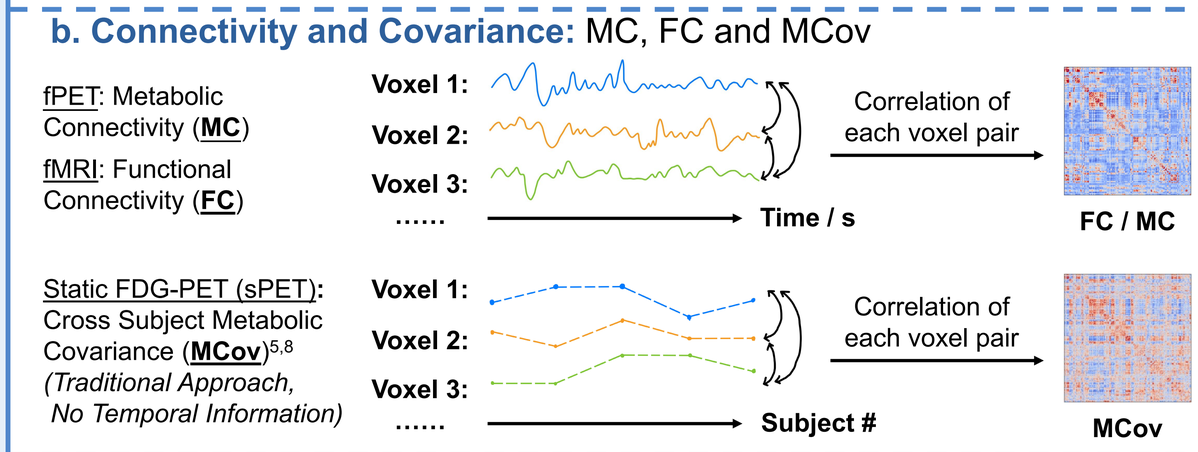
- The cortical organization estimated by MC exhibits robust spatial features that deviate from those of FC (***panel 4***)
- Low-frequency components (> 5 mins) dominate MC (***panel 5a***)
- Mechanisms such as imperfect baseline removal or consistent scanning experience across subjects may also result in apparent MC (***panel 5b***)

3 – Methods

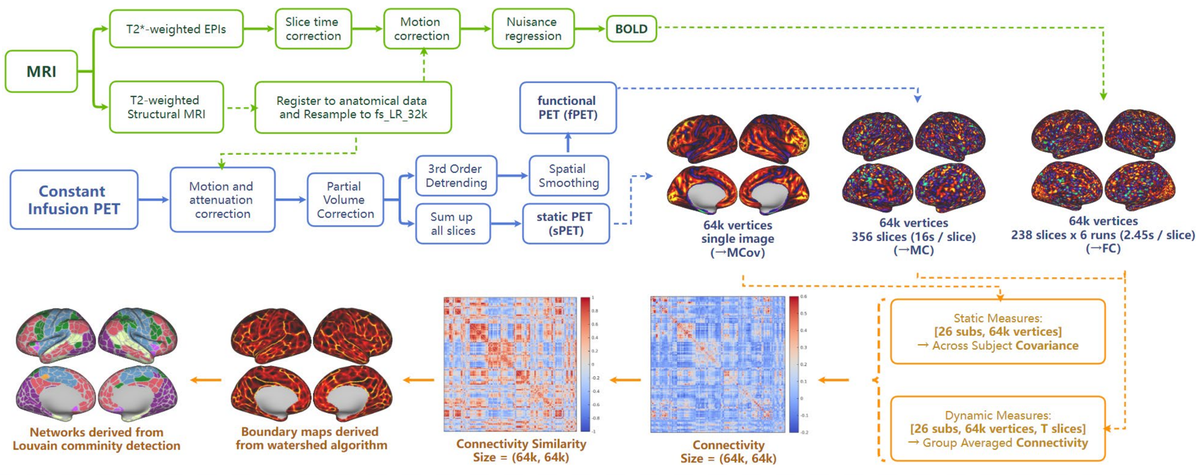
a. Dataset: Monash rsPET-MR Dataset[7]



b. Connectivity and Covariance: MC, FC and MCov

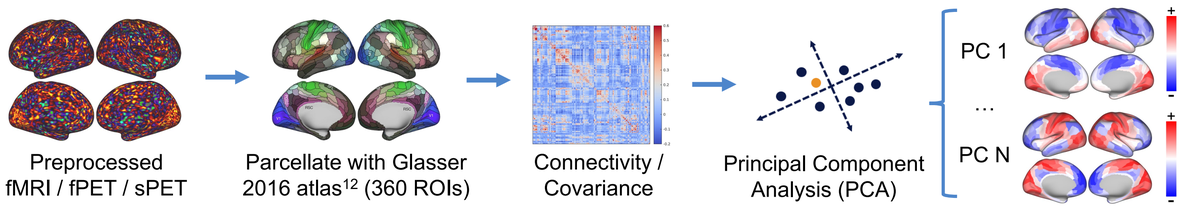


c. Preprocessing, Boundary Mapping[9], and Network Detection[2,10]

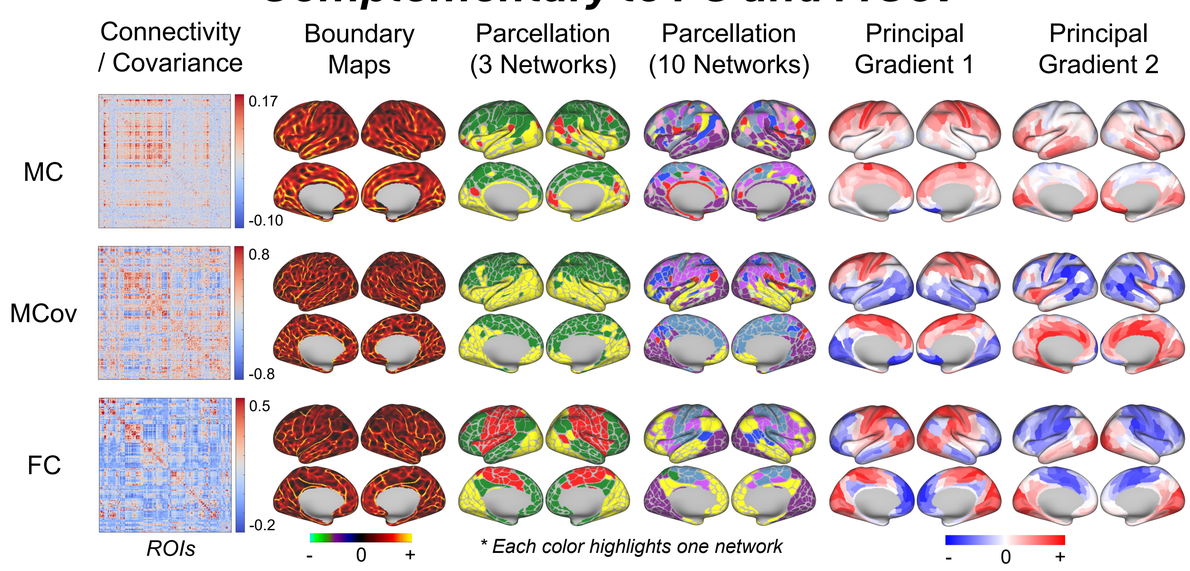


d. Principal Gradients of Connectivity[11]

A concise representation of connectivity, able to capture its major spatial patterns.



4 – Cortical Organization Revealed by MC Complementary to FC and MCov



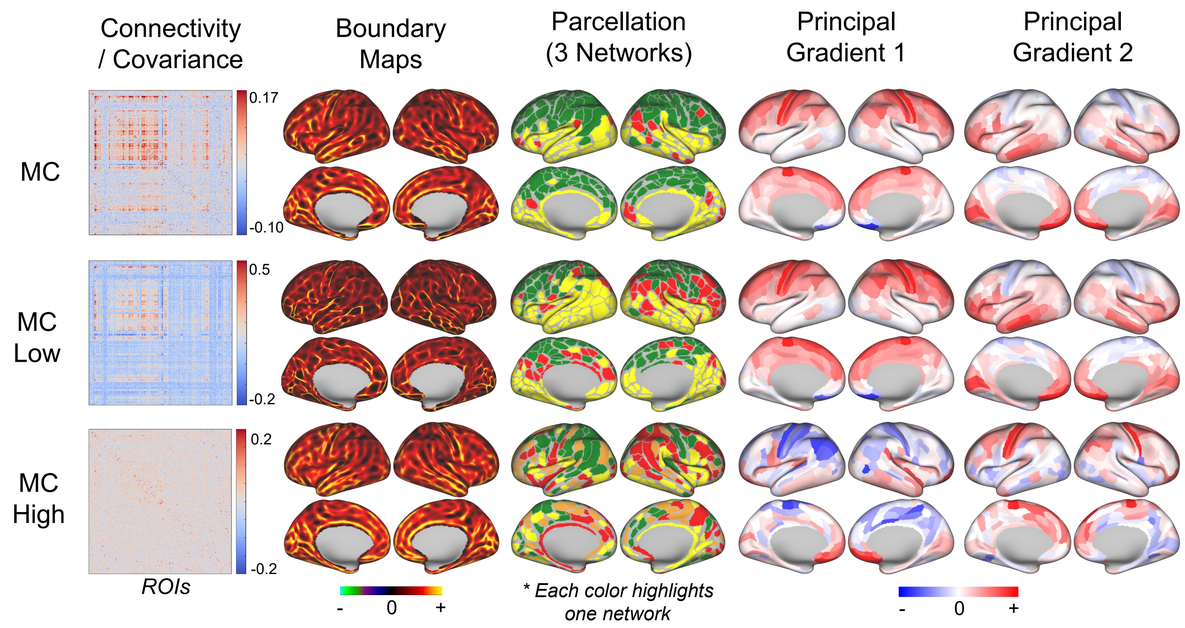
As shown in 3-net parcellation and further validated by principal gradients:

- MC is characterized by a prominent **fronto-parietal** component and an **inferior temporal-occipital** component
- Results of MC show **moderate similarity with MCov** and **deviate from FC**, in line with previous studies[5,8].

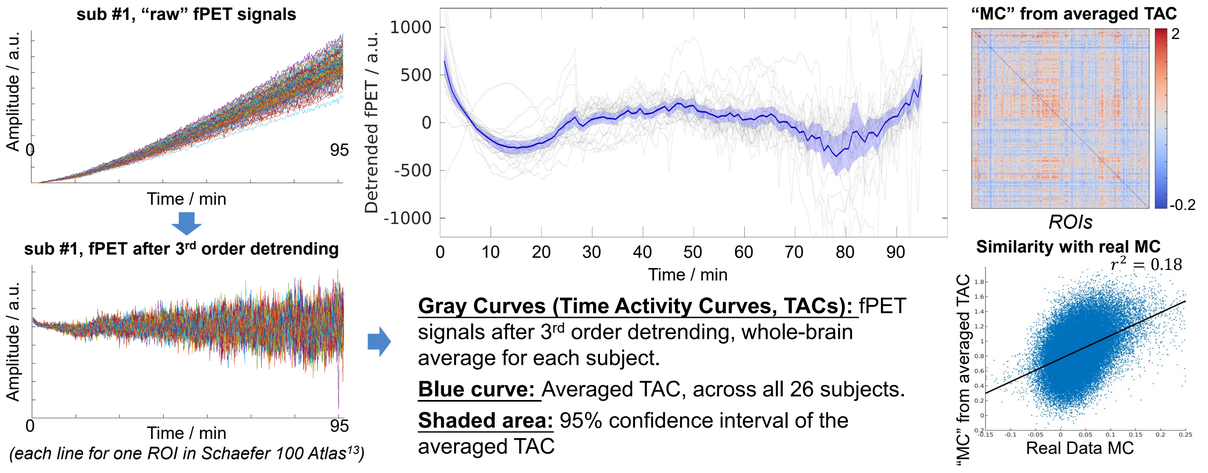
Owing to the low sensitivity of fPET, the results of MC are **noisier than those of MCov and FC** (smaller connectivity correlation scales, more fragmental 10-net parcellation).

5 – Is MC Primarily Driven by Short-Term Changes in Glucose Uptake?

a. Low frequency component (>5min) dominates MC



b. Subjects share similar ultra-slow fPET signal trend after detrending



Gray Curves (Time Activity Curves, TACs): fPET signals after 3rd order detrending, whole-brain average for each subject.

Blue curve: Averaged TAC, across all 26 subjects.

Shaded area: 95% confidence interval of the averaged TAC

(each line for one ROI in Schaefer 100 Atlas[13])

c. Other mechanisms, in addition to instantaneous changes in glucose metabolism, could also give rise to apparent MC?

1. Tracer Kinetics[14]? (Imperfect Baseline Removal[15])

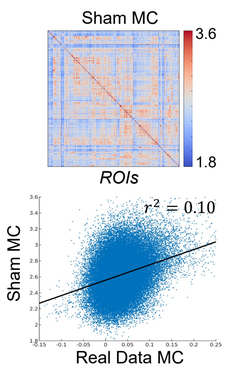
Sham Dataset (No Functional Changes Over Time)

Resting-state fPET data → ROI-wise fitting

Irreversible 2-tissue compartment model (assuming constant K_1, k_2, k_3 throughout the scan)

C_P ⇄ (K_1, k_2) C_1 → (k_3) C_2

sham fPET data → **Sham Data MC**



2. Shared Scanning Experiences Across Subjects?

Sub #1 ... Sub #N

Similar Scanning Instruction?
Scanning Noise?
Similar Task Design?
...

References and Acknowledgements

[1] Biswal et al., 1995; [2] Yeo et al., 2011; [3] Villien et al., 2014; [4] Hahn et al., 2016; [5] Jamadar et al., 2021; [6] Yakushev et al., 2017; [7] Jamadar et al., 2020; [8] Di et al., 2012; [9] Gordon et al., 2016; [10] Blondel et al., 2008; [11] Margulies et al., 2016; [12] Glasser et al., 2016; [13] Schaefer et al., 2018; [14] Volpi et al., 2023; [15] Coursey et al., 2023.

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