Contribution ID: **33** Type: **Poster**

Novel insights into brain metabolism and functional coupling in healthy connectomes and their mismatch in pathology

Tuesday 10 September 2024 17:30 (45 minutes)

Glucose stands as the primary fuel source driving the energy-demanding process of neuronal activity. Glucose metabolism can be explored in vivo in human by [18F]FDG-PET. DCM-based effective connectivity (EC) provides a linear mechanistic view of brain dynamics by conceiving it as a mixture of dissipative and solenoidal flow speaking to the concept of kinetic energy (Benozzo et al. 2023). This study aims to explore the association between kinetic energy and glucose metabolism by comparing EC-derived functional flow patterns with [18F]FDG-PET measurements in healthy controls (HCs), finally investigating the disruption of this coupling in gliomas.

RsfMRI data of 42 HCs are described in (Volpi et al. 2022), while rsfMRI data of 43 patients are in (Silvestri et al. 2022). EC matrices, estimated through sparse DCM (Prando et al. 2020), are decomposed into PCov (partial covariance of the neuronal states) and S (differential cross-covariance, temporal directionality of neural activation) as in (Benozzo et al. 2023). From dynamic PET data (60-min), individual Metabolic Connectivity (MC) matrices, expressing the relationships between the metabolic states of different brain regions, are estimated according to (Volpi et al. 2022). Standardized Uptake Value Ratio (SUVR) is derived from static PET.

Partial Least Square Correlation is applied to HC pairs: PCov-MC, S-MC (upper triangular matrices), SUVR-PCov and SUVR-S (nodal strengths for PCov/S, ROI values for SUVR). Generalizability of multivariate correlations were 7-fold cross-validated. For each generalizable effective-metabolic pair, the corresponding regression line was identified, defining a normality band at the 90-percentile of the HC distances from the line. Finally, patients'metabolic and effective variables are projected onto the maximizing-covariance latent space identified in HCs. A tumor frequency map was obtained by combining tumor masks as weighted by the corresponding distance from the HC regression line (out-of-range patients only).

Cross-validation reveals good generalizability for PCov-MC and SUVR-S associations (r>0.76). The scatterplots between metabolic and effective scores for HCs and patient projections are in Fig. B. In both pairs, some patients notably diverge from the expected metabolic-effective coupling independently of tumor volume. As shown in Fig. C, SUVR-S pair is mostly altered for temporo-parietal tumors, while PCov-MC is mainly disrupted in patients with frontal lesions.

A dual metabolic-effective association emerges: one at local level (higher glucose uptake is related to sink nodes, i.e. nodes receiving inputs from the network) and one at network level (metabolic connectivity is related to undirected BOLD-signals covariance). Furthermore, our study unveils how these two distinct decoupling can differentiate patients based on the lesion location (and not its volume)—local disruption observed only for temporo-parietal lesions and network alterations for frontal lesions—providing novel insights into the physiopathology and the metabolic-kinetic link of glioma. While (Maleki Balajoo et al. 2022) already explored distinguishing pathologies (Alzheimer and Mild Cognitive Impairment) based on metabolism-function coupling, our study is a pioneer in gliomas and the introduction of EC measures allows both to link metabolism to the concept of kinetic energy, but also to decouple neuronal activity from the adverse effects of hemodynamic convolution, proposing metabolic-effective coupling as a new biomarker.

Primary authors: VALLINI, Giulia (Department of Information Engineering, University of Padova); Dr

BARON, Giorgia (Department of Information Engineering, University of Padova); Dr SILVESTRI, Erica (Department of Information Engineering, University of Padova); Dr VOLPI, Tommaso (Department of Radiology and Biomedical Imaging, Yale University,); Dr VLASSENKO, Andrei G. (Neuroimaging Laboratories at the Mallinckrodt Institute of Radiology, Washington University School of Medicine,); Dr GOYAL, Manu S. (Neuroimaging Laboratories at the Mallinckrodt Institute of Radiology, Washington University School of Medicine,); Dr CECCHIN, Diego (Department of Medicine, Unit of Nuclear Medicine, University of Padova,); CORBETTA, Maurizio (University of Padua); Prof. BERTOLDO, Alessandra (Department of Information Engineering, University of Padova,)

Presenter: VALLINI, Giulia (Department of Information Engineering, University of Padova)

Session Classification: Poster Session