Preliminary Multi-Modal Image Analysis in Epilepsy using Simultaneous PET/MR

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Background: Surgery for treatment-resistant epilepsy can be effective, but the decision to operate depends on a careful assessment of the risk-benefit profile for each patient. A combined PET/MR scanner with simultaneous acquisition permits simultaneous imaging of physiologic & pathophysiologic processes and provides both anatomical & functional information on the same subject at the same time. It allows direct correlations of PET data with MR-detected patterns of neural synchrony in both grey and white matters; e.g. resting-state fMRI (RS-fMRI), diffusional kurtosis imaging, and MRS. This multi-modal analysis will facilitate the identification of an optimal biomarker.

To date, the majority of the connectivity analyses of brain organization conducted have been based on fMRI time series. The fMRI signals are indirect measures of neuronal activity; thus, the ability to simultaneously interrogate metabolism and fMRI indices of brain function in the same temporal and spatial frames of reference will provide greater insights into whole brain network organization. To demonstrate this feasibility, we initiated a comparative study in neurotypical controls (NC) and epilepsy patients (Epi) using F-18-fluorodeoxyglucose (FDG). We report here quantitative data analysis to correlate glucose metabolism with RS-fMRI in Epi compared to NC.

Methods: Six NC and 11 Epi patients (avg. age 26 and 36, respectively) were imaged on a whole-body simultaneous PET/MR scanner (Biograph mMR, Siemens). After injection of approx. 370 MBq FDG, dynamic brain PET scans were acquired for ~90 min. Simultaneously, MR imaging, including T1, T2, RS-fMRI, field map and other sequences, were performed. Dixon sequence was acquired to obtain a μ-map for attenuation correction (AC) of PET data. Standard uptake values (SUV) were mapped via MATLAB on a summed PET image (127 slices) of each subject. Comparative analyses were conducted in the MNI space, with initial regions of interest (ROIs) analyses focused on the posterior cingulate cortex (PCC) and anterior medial prefrontal cortex (aMPFC), part of the default network. The ROIs were defined as 4 mm spheres centered at MNI coordinates (-8,-56,26) for PCC and (-6,52,-2) for aMPFC.[1] Amplitude of low-frequency fluctuation (ALFF) and fractional ALFF (fAlff) values[2] were derived from the RS-fMRI data for all subjects based on the same volume and coordinates. Correlation analysis between SUV and ALFF, and fALFF were performed. Twelve additional ROIs, corresponding to 6 brain networks (**Fig. 1**, **Table 1**), were defined using previously described coordinates.[3] Mean SUV values normalized by either subject's mean cortical SUV (SUV_{COR_norm}) or by white matter (SUV_{WM_norm}) were obtained for each ROI and employed both in between-group comparisons and in SUV/ALFF/fALLF correlational analyses.

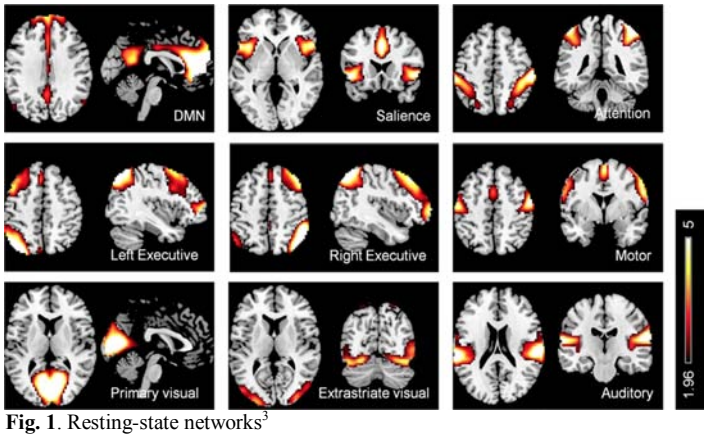

Fig. 1. Resting-state networks[3]

Table 1. Comparative SUV values (SUV_{COR_norm} and SUV_{WM_norm}) at 7 networks in neurotypical controls vs. epilepsy patients

Network	ROI label	SUV_{WM_norm}		P value	SUV_{COR_norm}		P value
		NC	Pt		NC	Pt	
Default	MPFC	1.57	1.67	0.228	1.39	1.48	0.132
	PCC	1.57	1.68	0.315	1.38	1.49	0.366
L Executive	LSFG	1.45	1.5	0.546	1.28	1.33	0.421
	LIPL_Ex	1.53	1.52	0.482	1.35	1.35	0.763
R Executive	RSFG	1.43	1.37	0.366	1.27	1.22	0.546
	RIPL_Ex	1.82	1.56	0.482	1.61	1.56	0.763
Salience	LIFG	1.56	1.43	0.228	1.38	1.26	0.269
	RIFG	1.34	1.42	0.132	1.18	1.26	0.228
Attention	LIPL_Att	1.38	1.46	0.056	1.22	1.3	0.228
	RIPL_Att	1.42	1.5	0.056	1.25	1.33	0.228
Sensorimotor	LSMC	1.34	1.49	0.191	1.19	1.32	0.159
	RSMC	1.36	1.27	0.688	1.2	1.13	0.763
Extrastriate	LMOG	1.42	1.33	0.421	1.25	1.18	0.315
	RMOG	1.02	1.07	0.191	0.9	0.94	0.012

Results: Significant between-group differences in SUV_{COR_norm} values were observed in the Right Extrastriate network ($p=0.012$); borderline significantly different SUV_{WM_norm} values were noted in the Left and Right Attention network ROI (**Table 1**). The correlations between the two ROIs in each of the 7 networks for all subjects were calculated and transformed into Fisher's **z**-score. One-sample **t**-tests were conducted on the subjects' Fisher's **z**-scores of NC correlations against the corresponding **z**-score of Epi correlations. The results showed borderline significant between-group difference in correlations for sensorimotor network ($p=0.07$). ALFF values at PCC in 13 subjects (6 NC, 7 Epi) were significantly correlated with SUV_{WM_norm} at Left ($p=0.05$) and Right Attention Network ROIs ($p=0.022$).

Conclusions: To our knowledge, quantitative data analysis correlating glucose metabolism with RS-fMRI at 7 networks in epilepsy has never been studied. In this pilot study, we compared the group difference in the glucose metabolism at the 7 networks generally considered to be functionally connected. Since the ALFF reflects the BOLD fluctuations over a period of time that has the same temporal scale as the PET data, we also examined the group difference in the correlations of PET-SUV and fMRI-ALFF values at 7 networks. Our preliminary results demonstrated the feasibility of this approach and support our hypothesis that multi-modal analysis will facilitate the identification of an optimal biomarker.

References

1. Andrews-Hanna et al., J Neurophysiol 104:322–335, 2010; 2) Zou et al., J Neurosci Methods 172:137–141, 2008; 3) Di and Biswal, Brain Connectivity 2:275-283, 2012; 3) Di and Biswal, Brain Struct Funct, 2013.