Correlations between PET and Resting State fMRI of Default Network using Simultaneous PET/MR: Preliminary Results

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Background: Our long-term goal is to examine brain function and metabolism concurrently in autism using a combined PET/MR scanner and F-18-fluorodeoxyglucose (FDG) with a focus on circuits underlying social, emotional and cognitive processing. To demonstrate feasibility of simultaneous PET/MR imaging and analysis, we are conducting preliminary studies on healthy participants.

Methods: Six well characterized healthy participants (4 males; mean age 26.4±5.6 y) were enrolled to complete a whole-body simultaneous PET/MR scanning (Biograph mMR, Siemens). After injection of approx. 370 MBq FDG, we acquired dynamic scans 0-60 minutes post injection. Simultaneously, MR imaging, including anatomic T_1-MPRAGE (5'), T_2 spin echo (4'), two consecutive sessions of resting state echo planar imaging scans was performed. An 18-s 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 summed PET images (127 slices) of each subject. A total of 120 masks (regions of interest, ROIs), including left and right, for cortical (96) and subcortical regions (24) based on Harvard-Oxford Atlas were generated. Image preprocessing was then carried out using Mango and FSL and predetermined volumes of interest defined in a standard atlas. Briefly, the SUV maps were registered to the subject's T1 images that, in turn, were registered to the MNI152 2mm template. Initial ROI analyses focused on the posterior cingulate cortex (PCC) and anterior medial prefrontal cortex (aMPFC), the midline hubs of the default network. The ROIs were defined as spheres centered at published coordinates[1] with a 4 mm radius (MNI coordinates (PCC=-8,-56,26) and (aMPFC=-6,52,-2) (**Fig. 1**). Following standard preprocessing and 24 motion parameters regression, we analyzed R-fMRI data using two distinct pipelines to account for nuisance signal regressions: one used global signal regression (GSR),[2] the other used component-based noise correction (compCOR).[3] Seed based correlation analyses provided intrinsic functional connectivity (iFC) between the two ROIs. Correlation analyses between SUV (either normalized by subject's mean cortical SUV (SUV_{COR_norm}) or by white matter (SUV_{WM_norm}) in PCC and the iFC between aMPFC and PCC were performed. Further, for each subject we measured fractional amplitude of low frequency fluctuations (fALFF)[4] as the fraction between the sum of amplitudes of the band ranging from 0.009 to 0.1 Hz and the entire frequency range detectable in a given signal. Subject-level voxel-wise fALFF maps were standardized into subject-level Z-score maps (i.e., by subtracting the mean voxel-wise fALFF obtained for the entire brain, and then dividing by the standard deviation). Across the 6 subjects we then identified two large clusters – one posterior (yellow) and one anterior (orange) – that exhibited greater amplitude of fluctuations than average (fALFF Z score > 2.3), and one cluster showing significantly lower fALFF than average (blue cluster, Z < -2.3) - this comprised white matter and CSF (**Fig. 2**). Correlations between fALFF, SUV_{WM_norm} and SUV_{COR_norm} in these three clusters were explored.

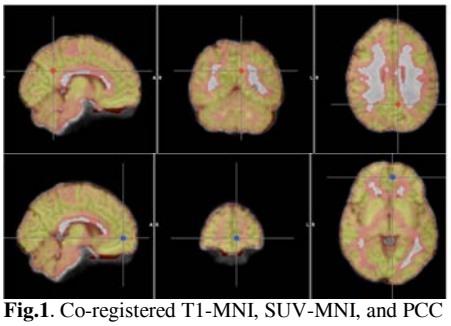

Fig.1. Co-registered T1-MNI, SUV-MNI, and PCC mask (red, top) and aMPFC mask (blue, bottom).

Results: FDG-SUV for PCC and aMPFC (R^2=0.74) were highly correlated. Regardless of the pipeline used to analyze R-fMRI data, iFC between aMPFC and PCC significantly correlated with PCC_FDG(SUV) (**Fig. 3**). Additionally, **Table 1** shows the values of fALFF, SUV_{WM_norm} and SUV_{COR_norm}, and their correlations for the three clusters in the 6 healthy participants. We found significant correlations between both SUV_{WM_norm} and SUV_{COR_norm} with fALFF in the frontal fALFF-positive mask (Positive_Mask_2: p=0.02). Negative correlations were also substantial, albeit non-significant, between SUVs and fLAFF values in the negative (blue) mask.

Conclusions: Our data demonstrate the feasibility of correlating FDG glucose metabolism and resting-state fMRI data acquired simultaneously via combined PET/MR. We demonstrated that PCC-based iFC with the anterior node of the default network is positively related to glucose consumption which in turn is related to fluctuations in the BOLD signal specific to gray matter regions. The fMRI signals are indirect measures of neuronal activity, thus, the ability to simultaneously interrogate metabolism (and eventually neurochemistry) and fMRI indices of brain function in the same temporal and spatial frames of reference will provide greater insights into whole brain network organization.

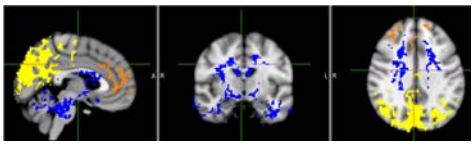

Fig. 2. Three fALFF defined clusters: posterior (yellow frontal (orange) had Z score >2.3; blue cluster, Z<-2.3.

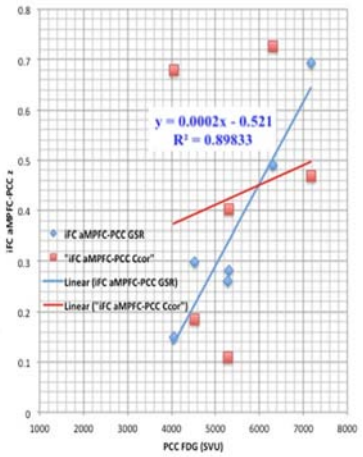

Fig. 3. Correlation of PCC_FDG(SUV) with iFC_aMPFC_PCC_GSR

References

1. Andrews-Hanna et al., J Neurophysiol 104:322–335, 2010; 2) Fox el al., J Neurophysiol_101:3270-83, 2009; 3) Behzadi et al., Neuroimage 37:90-101, 2007; 4) Zou et al., Neuroimage 49:1432–1445, 2010.

Table 1. fALFF and SUV values and their correlations in 6 healthy participants for three fALFF defined masks

	Positive_Mask_1 (yellow)			*Positive_Mask_2 (orange)*			*Negative_Mask_1 (blue)*		
	fALFF	SUV_{WM_norm}	SUV_{COR_norm}	*fALFF*	SUV_{WM_norm}	SUV_{COR_norm}	*fALFF*	SUV_{WM_norm}	SUV_{COR_norm}
HC01	0.745	1.469	1.282	1.150	1.430	1.247	-0.910	1.018	0.888
HC02	0.798	1.868	1.690	1.000	1.248	1.129	-0.674	0.836	0.756
HC03	0.574	1.494	1.336	1.130	1.409	1.259	-0.820	0.889	0.794
HC04	0.481	1.452	1.264	1.085	1.408	1.225	-0.813	1.010	0.879
HC05	0.665	1.552	1.402	1.224	1.434	1.295	-0.899	0.881	0.796
HC06	0.855	1.433	1.226	1.188	1.433	1.226	-0.916	0.980	0.838
Correlation r (P value)		0.324 (0.531)	0.26 (0.618)		**0.874** (**0.023**)	**0.882** (**0.02**)		-0.604 (0.205)	-0.593 (0.215)