Concurrent CBF/CMRGlc Changes during Visual Stimulation: A Combined fMRI-PET Study

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Introduction Functional brain imaging has contributed to a greater understanding of regional brain function at rest, during normal sensorimotor and cognitive function, and in disease states. Most functional neuroimaging methods are sensitive to CBF, glucose metabolism, or a complex interaction between blood flow, blood volume, and oxygen utilization (BOLD). In pathological conditions, resting alterations in regional CBF and metabolism have contributed to clinical diagnosis and management. While a tight coupling between regional neural activity and changes in blood flow and metabolism has long been recognized *(1-3)*, the exact mechanism for this coupling remains uncertain. Here we report the development and initial validation of a novel method for concurrent, measurement of CBF and glucose utilization by combining the arterial spin labeling (ASL) perfusion fMRI (4) and fluorodeoxyglocose (FDG)-PET. The preserved sensitivity of perfusion fMRI at low task frequencies (4,5) is compatible with the temporal resolution of FDG-PET.

Methods Five healthy subjects were scanned during 8Hz checkerboard visual stimulation and rest. The scanning protocol began with BOLD fMRI using a blocked paradigm with 1 min blocks of visual stimulation alternating with 1 min of fixation. Subsequently, ASL perfusion MRI was measured during 10 min of fixation as the baseline. Finally, a 10 min ASL perfusion MRI scan was carried out during visual stimulation. At the beginning of this acquisition, the subject was injected with FDG. Once the 10 minute scan was completed, subjects were removed from the MRI scanner and moved to the PET scanner to measure regional FDG accumulation. A resting PET scan was carried out on a separate day using a similar stimulation protocol but outside the MRI scanner. For each subject, CBF and PET images were generated for the visual stimulation and the baseline, along with a BOLD activation map. SPM group analysis was performed on these images to reveal the activation induced by the visual stimuli. The concurrent measured PET and CBF images during visual stimulation were compared after global activity normalization. Percentage signal increases of CMRglc, CBF and BOLD and distances between the activation centroids in the primary visual cortex were calculate to estimate the concordance of activations across three modalities. PET data were corrected for the 10 min activation, comprising only about 50% of FDG uptake (6).

Subject	Signal increases (%)			Centroid distances (mm)		
	CMRglc	CBF	BOLD	CMRglc-CBF	CBF-BOLD	CMRglc BOLD
S1	47.4	9.1	0.3	9.57	4.62	13.19
S2	-2.1	45.8	0.8	11.75	2.04	10.33
S3	26.7	17.0	1.7	2.29	4.17	2.67
S4	29.9	41.4	1.0	14.80	1.85	13.41
S5	20.3	28.3	1.1	13.76	2.70	11.56
Mean (SD)	24.4 (17.9)	28.3 (15.6)	1.0 (0.5)	10.43 (4.97)	3.08 (1.25)	10.23 (4..41)

Table.1 Concordance across the stimuli induced CMRglc, CB and BOLD activations in the primary visual cortex.

Results Fig.1 shows the concurrently measured CBF and CMRGlc images during visual stimulation. Normalized CMRGlc was well matched to CBF, but within visual cortex relative CBF was slightly stronger than CMRGlc in some regions. This may attributable to the suboptimal 10 min activation protocol for PET. Compared to rest, all three modalities showed significantly stimuli induced activations in visual cortex (Fig.2). The percentage signal increases in the primary visual cortex and the distances between the activation centroids showed excellent concordance (Table 1).

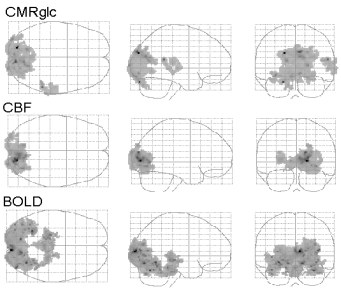

Fig.2 SPM{t} maps of CMRglc, CBF and BOLD.

Conclusions These results demonstrate the feasibility of obtaining concurrent CBF and CMRGlc by combining fMRI-PET. This method will be useful for a broad range of studies investigating the magnitude and spatial distribution of the coupling between regional CBF and regional glucose utilization in a variety of conditions including functional activation, pharmacological modulation, or pathological states. Future studies will be needed to determine the optimum duration for combined fMRI-PET studies of task activation. Arterial blood samples were not acquired for this study, but could easily be performed aside the fMRI scanner and could then be generated to obtain absolute quantification of the cerebral glucose metabolism.

References

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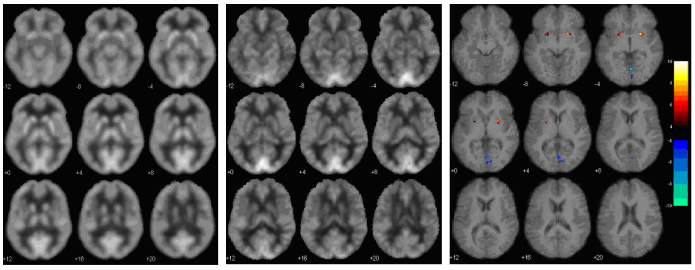

Fig.1. Group results comparing the concurrently measured CMRglc and CBF images during visual stimulation, left: CMRglc; middle: CBF; right: CMRglc vs. CBF.