Dynamic fPET/fMRI of the human visual system

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Target audience: Neuroscientists, clinicians, physicists

Purpose:

Brain mapping of task-associated changes in hemodynamics and metabolism with positron emission tomography (PET) has been accomplished in the past by subtracting scans acquired during two distinct static states [1,2]. Here we show that PET can provide truly dynamic information on cerebral energy metabolism using concepts common to functional magnetic resonance imaging (fMRI). Using the widely available radiotracer, 2-[^{18}F]-fluoro-deoxyglucose (FDG), we show that quantitative glucose utilization changes during multiple visual stimuli can be determined from neuroimaging data acquired during FDG constant infusion in a single imaging experiment. Moreover, this functional PET (fPET-FDG) method can be accomplished simultaneously with fMRI (e.g. BOLD and ASL) and thus enables the first direct comparisons in time, space and magnitude of brain glucose utilization, hemodynamics and oxygen consumption.

Methods

Acquisition: The imaging studies were performed on a 3-T Tim MAGNETOM Trio MR scanner (Siemens) modified to support the BrainPET (Siemens), an MR-compatible brain PET scanner prototype. Five mCi of FDG was administered intravenously at a constant infusion rate of 0.01 ml/s for 90 min to 3 healthy subjects (1 female/2 males, mean age 32±2). The PET data were binned into 90 one-minute frames and reconstructed to 153 slices with a 5×5×5 mm^3 resolution.

MRI anatomical images consisted of a high-resolution MPRAGE and a dual ultra-short echo sequence to derive the PET attenuation map. BOLD imaging was acquired around the first full-field checkerboard paradigm (Fig. 1A). and consisted of a GRE EPI acquisition (TR/TE=3000/30 ms, voxel size = 3x3x3mm^3, 47 slices). Pseudo-continuous ASL imaging was acquired around the second full-field checkerboard (Fig 1A) (TR/TE$_1$/TE$_2$ = 4000/10/30ms, labeling duration = 1.6 s, post-label delay = 1 s, voxel size = 3.4x3.4x6 mm^3).

PET Processing: Pairwise subtraction of the 90 PET images was accomplished to generate a time series related to the derivative of radioactivity accumulating in each voxel (Fig 1C). Data were smoothed using a 12 mm Gaussian kernel. FSL was used to analyze the PET time series using a general linear model (GLM) consisting of 3 different explanatory variables (EV): full-field, hemi-field left, hemi-field right checkerboard stimulus. Percent signal change from the activated voxels (Fig.1 D, E, F) was derived from GLM analysis.

MRI Processing: ASL and BOLD were processed using the FSL software. MR data were motion corrected with FSL using MCFLIRT, smoothed with a 6 mm Gaussian kernel; relative CBF maps were calculated *via* control/tag subtraction performed on the ASL data. The z-scores maps were thresholded at $z > 2$ ($p < 0.05$) and the percentage signal change values observed using fPET-FDG, fMRI ASL and fMRI BOLD were calculated (Fig 2).

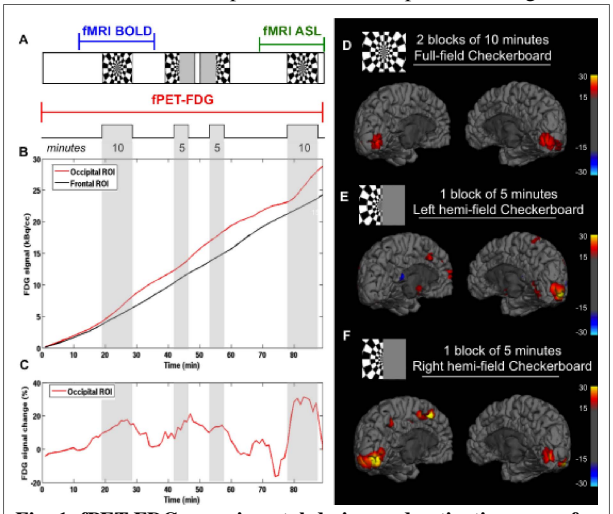

Fig. 1. fPET-FDG experimental design and activation maps for one subject. A) fPET-FDG experimental design for a 90 minute experiment during visual paradigm alternating between a full checkerboard and left and right half checkerboard, B) fPET-FDG signal in the occipital ROI (red) and in the frontal ROI (black) in kBq/cc, C) FDG signal change during the 90 minute experiment in the occipital ROI, this signal is used in the GLM analysis, D) Percentage signal change (signal change>15%) observed for a single subject during the two blocks of 10 minutes full-field checkerboard, E) during the single 5 minute block of left hemi-field checkerboard and F) during the single 5 minute block of right hemi-field checkerboard.

Results

Using the activated voxels to define a post-hoc volume-of-interest, an individual subject's time-activity curve (TAC) for visual stimulation was created and compared to a volume-of-interest that did not respond to the visual stimulus (the individual subject's frontal cortex). Changes in glucose utilization are easily observed as changes in the TAC slope (FDG utilization rate) and in the derivative signal during visual stimulus in the activated voxels (occipital region) but not in the frontal cortex (Fig. 1B,C). The mean percent increase in glucose utilization derived from fPET-FDG for our three subjects in the V1 region was 25% for the full-field checkerboard, 26% for the left hemi-field checkerboard and 28% for the right hemi-field checkerboard. The mean percent increase in CBF and BOLD in our three subjects during the full-field checkerboard activation in the V1 region was 21% and 4% respectively (Fig 2) and largely colocalized with fPET-FDG activations, as previously described [2].

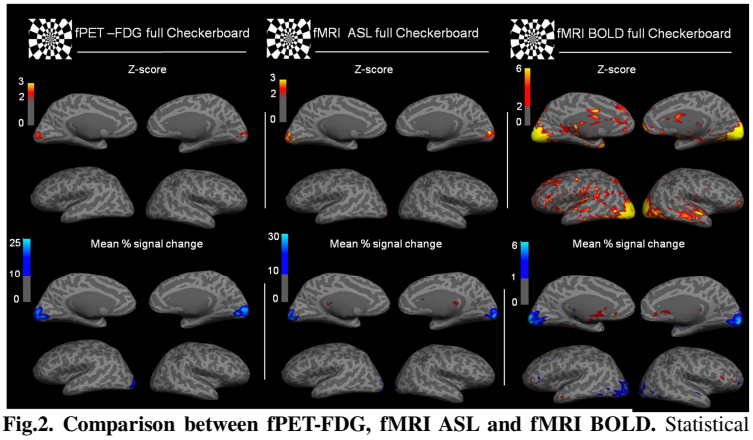

Fig.2. Comparison between fPET-FDG, fMRI ASL and fMRI BOLD. Statistical activation maps (top, yellow-red, $z > 2$) and percentage signal change (bottom, blue) during the 10 minutes full-field checkerboard of a single subject measured using fPET-FDG, fMRI ASL and fMRI BOLD

Conclusion

This study demonstrated for the first time that multiple stimuli (four in this case) can be measured dynamically during a single FDG PET scan (Fig 1). Confirmation of functional specificity is inherent in our analyses given that the contralateral hemisphere has a higher response to a hemi-field checkerboard (Fig 1 E, F) The absolute changes in FDG utilization as measured by fPET-FDG are consistent with previous studies measuring single response in a two-scan paradigm. The complementary nature of fPET-FDG to fMRI capitalizes on the emerging technology of hybrid MR-PET scanners. fPET-FDG, combined with quantitative fMRI methods, will allow us to simultaneously measure dynamic changes in glucose utilization, hemodynamics and oxygen consumption, addressing vital questions about neuronal and neurovascular relationships across tasks and disease states.

References

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