Brain connectivity mapping based on Positron Emission Tomography (PET) in comparison to fMRI using combined PET/MR

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Target audience:

The target audiences of this abstract are basic scientists, as well as clinicians interested in brain connectivity and multimodal PET/MR imaging.

Purpose and Introduction:

The measurement of functional connectivity (fc) of the brain has attracted tremendous interest in basic sciences as well as clinical practice. For this purpose mainly fMRI methods, utilizing the BOLD effect are applied. However, recent literature suggests that networks can also be derived from dynamic[1] and static[2] PET imaging data. Aim of this study was to examine differences between fc information derived from fMRI and new PET approaches. Especially multimodal studies might open a new domain of metabolic brain network mapping.

Material and Methods:

Rats (n=20) were studied using simultaneous and sequential PET/MR imaging. Animals were anesthetized using isoflurane, and placed on a temperature stabilized (T=37.0±1°C) animal bed. Scans were performed using either simultaneous PET/MR (7T small animal scanner, 2x2 rat brain coil, with PET insert) or sequential PET and MR acquisitions. Three different PET tracers were applied: the glucose marker [^{18}F]fluorodeoxyglucose ([^{18}F]FDG, n=8 measurements), the perfusion marker [^{15}O]H_2O (n=29) and the serotonin transporter specific tracer [^{11}C]DASB (n=8). In addition also fc-fMRI measurements (n=4) using an EPI sequence (TR=3000ms, TE=18ms, matrix size: 64x64x18, voxel size: 0.5x0.5x1.0 mm³, 300 volumes) were acquired. Independent component analysis (ICA) was applied to dynamic [^{18}F]FDG-PET and fc-fMRI data. In addition a region of interest based approach was performed. For this all datasets were segmented into 58 regions based on a rat brain template and correlation coefficients (Pearsons' R and R^2) and matrixes were calculated for the static PET data and the fc-fMRI data. fc-fMRI was studied with and without baseline correction (global signal suppression). Analysis was performed with a focus on the default mode network (DMN) in rats[3].

Results:

ICA analysis of dynamic [^{18}F]FDG-PET data showed 7 fc-networks, whereas the fMRI data indicated 9 fc-networks. The use of static PET datasets (Figure 1), shows that these networks can also be identified in fc-matrixes, e.g. Somatosensory Cortex (Ctx) with [^{18}F]FDG (R^2=0.60, P=0.02), fMRI (without global signal suppression R^2=0.77, P<0.01), fMRI (with global signal suppression R^2=0.30, P<0.01) but not in [^{15}O]H_2O (R^2=0.07, P=0.16) or [^{11}C]DASB (R^2=0.04, P=0.63). There is also a large number of off-diagonal elements, indicating function-metabolic brain networks. A structure similar to the DMN in rats was investigated using the Cingulate Ctx as reference region for the connections. Whereas [^{18}F]FDG reveals a glucose metabolism related network (P<0.05) similar to the DMN including regions such as: Amygdala (-R^2=0.81, - implies negative correlation), Cingulate Ctx (R^2=0.97), Frontal Association Ctx (R^2=0.86), Motor Ctx (R^2=0.92), Somatosensory Ctx (R^2=0.73), Hippocampus (-R^2=0.61), Thalamus (-R^2=0.27), Septum (-R^2=0.57), [^{15}O]H_2O shows that the correlation in terms of perfusion is not as emphasized between all of these regions only Cingulate Ctx (R^2=0.88), Thalamus (R^2=0.34) and Septum (R^2=0.60) show significant correlations. Finally the [^{11}C]DASB tracer identifies these regions as being not related in terms of the serotonine transporter, whereas fc-fMRI identifies many of them to be part of the DMN. Also important is the induction of negative correlations (Figure 1) by the use of a global MR signal suppression as baseline correction method.

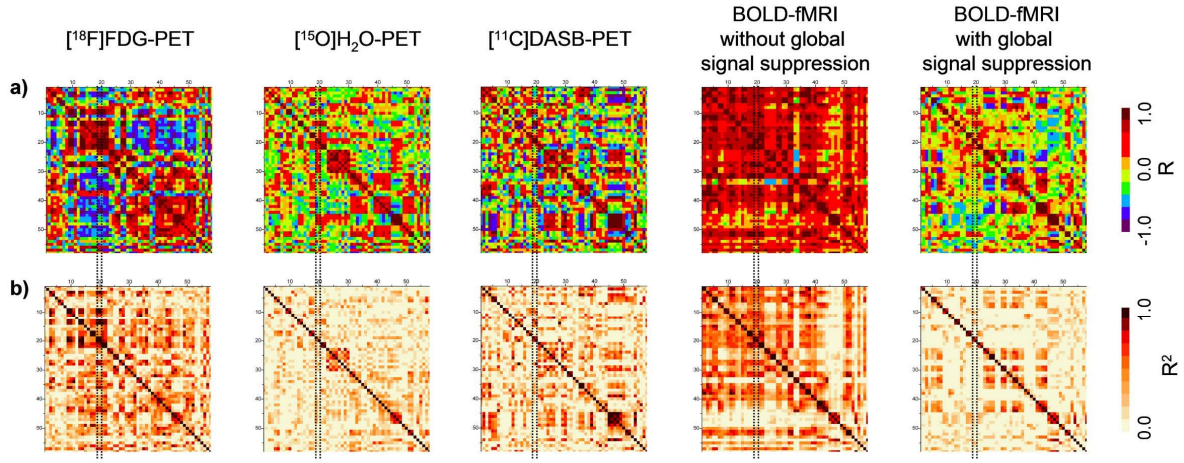

***Figure 1**: **a)** Functional connectivity matrixes (correlation coefficient R) derived from the glucose metabolism PET tracer [^{18}F]FDG, the perfusion marker [^{15}O]H_2O and the serotonin transporter tracer [^{11}C]DASB, BOLD fMRI without and with global signal suppression in rats. **b)** The respective R^2 matrixes. The PET tracers exhibit a distinctive metabolic network pattern. The dashed vertical lines identify some components of the default mode network using the Cingulate Cortex as reference region. For the clarity of the visual representation the Jackknife procedure for multiple comparison and bias correction is not displayed.*

Discussion and Conclusions:

Our results reveal that metabolic networks inside the brain can be mapped using fMRI and dynamic and static PET measurements. The applied PET tracers show, specific, tracer dependent connectivity matrixes, that are only partially similar to the information extracted from fc-fMRI. Networks such as the DMN can be traced using fMRI techniques, but also fc-PET methods. The quantitative and specific nature of PET, allows furthermore a quantification of network contributions that goes beyond correlation coefficients. Complex network measures, such as functional segregation and integration of fc-PET data appear feasible. Metabolic fc-mapping of the brain using PET data is in its infancies, however, we think that our study could impact the field toward PET functional and metabolic connectivity mapping.

References:

1. Wehrl HF et al. *Simultaneous PET-MRI reveals brain function in activated and resting state on metabolic, hemodynamic and multiple temporal scales*, Nature Med. Sep;19(9):1184-9 (2013); 2. Di X, Biswal B. *Metabolic brain covariant networks as revealed by FDG-PET with reference to resting-state fMRI networks*, Brain Connect, 2012;2(5):275-83 (2012); 3. Lu H et al. *Rat brains also have a default mode network*, PNAS, Mar 6;109(10):3979-84 (2012)