Our tools for noninvasively probing the brain are limited in number and often ambiguous in nature. Although the ultimate goal of neuroimaging is to provide quantitative information about brain biology in health and disease, a necessary step in this process is to develop a thorough understanding of our imaging tools. PET/MR scanners enable simultaneous measurements of neurochemistry and function in ways that benefit both modalities and enable novel biomarkers from the combined information [1].

Although fMRI brings considerable assets to brain mapping studies, the assumed linkage between the response of the blood supply and neural activity is neither immutable nor specific. To address the relationship between fMRI and neural activity, PET offers a window into function on the brain side of the blood-brain barrier. One focus of our initial studies using simultaneous PET/fMRI has been to mimic a classical ex vivo paradigm that forms the foundation of modern receptor theory and drug characterization: correlations between receptor occupancy and function in vivo. Using a highly specific antagonist to displace dopamine at D2-like receptors, we showed that the induced fMRI function was consistent with a linear model of receptor occupancy versus dose and in the domains of space of time [2]. By understanding these relationships at individual receptors, it is possible to create and calibrate multi-receptor models of function induced by endogenous neurotransmitters, using displacement of PET radiotracer as an index of relative synaptic neurotransmitter level [3].

Simultaneous PET/fMRI also shows potential for clarifying aspects of biology underlying PET receptor-based imaging. For instance, the PET index of binding potential conflates receptor density and basal neurotransmitter level. By using fMRI to report the function induced by displacement of dopamine using a targeted antagonist, one can form a relative index of basal neurotransmitter level from the ratio of fMRI and PET responses [2]. Additionally, a large body of literature demonstrates that the sensitivity of PET signals in displacement paradigms is highly variable according to the specific PET radiotracer and the nature of the challenge (agonist vs. antagonist). Simple multi-compartmental models predict that agonist-induced receptor internalization, a leading candidate mechanism for the observed variability in PET studies, should produce a temporal divergence between fMRI and PET responses using an agonist challenge. In fact, this divergence is observed using a D2 agonist, and model estimates of the receptor internalization rate match ex vivo measurements [4].

In addition to receptor-based studies, simultaneous PET/fMRI provides an ideal platform for studying the coupling of cerebral flow, oxygen utilization, and glucose metabolism. In particular, recent advancements in the ability to dynamically measure changes in glucose metabolism [5] will enable correlations between fMRI-derived CBF and CMRO2 with PET FDG uptake on a time scale of minutes, rather than state-variable studies.

In summary, this presentation will attempt to show 1) how PET can be used to inform interpretations of fMRI signal, 2) how concurrent fMRI can shed light on PET binding potentials and displacement responses, 3) how fMRI and PET can work together to study cerebral metabolism and receptor-based brain function in vivo.

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