Global and local fMRI signals driven by neurons defined optogenetically by type and wiring.

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Public Summary:

Scientific Abstract:
Despite a rapidly-growing scientific and clinical brain imaging literature based on functional magnetic resonance imaging (fMRI) using blood oxygenation level-dependent (BOLD) signals, it remains controversial whether BOLD signals in a particular region can be caused by activation of local excitatory neurons. This difficult question is central to the interpretation and utility of BOLD, with major significance for fMRI studies in basic research and clinical applications. Using a novel integrated technology unifying optogenetic control of inputs with high-field fMRI signal readouts, we show here that specific stimulation of local CaMKIIalpha-expressing excitatory neurons, either in the neocortex or thalamus, elicits positive BOLD signals at the stimulus location with classical kinetics. We also show that optogenetic fMRI (of MRI) allows visualization of the causal effects of specific cell types defined not only by genetic identity and cell body location, but also by axonal projection target. Finally, we show that of MRI within the living and intact mammalian brain reveals BOLD signals in downstream targets distant from the stimulus, indicating that this approach can be used to map the global effects of controlling a local cell population. In this respect, unlike both conventional fMRI studies based on correlations and fMRI with electrical stimulation that will also directly drive afferent and nearby axons, this of MRI approach provides causal information about the global circuits recruited by defined local neuronal activity patterns. Together these findings provide an empirical foundation for the widely-used fMRI BOLD signal, and the features of of MRI define a potent tool that may be suitable for functional circuit analysis as well as global phenotyping of dysfunctional circuitry.