Map the light-driven fMRI signal in combination with in vivo recording

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Target Audience Scientists who are interested in combining fMRI with genetic tools to study brain function in animal models.

Purpose There are handful studies to combine optogenetics with fMRI to study the brain function in the rodent brain [1, 2, 3]. We also reported the light-driven fMRI signal through the callosal fibers by fiber optic-mediated optical stimulation in the rat brain [4]. In this work, we aimed to establish a robust light-driven fMRI platform mediated by fiber optic inserted into the deep layer cortex. Meanwhile, we performed the in vivo recording to characterize the light-evoked local field potential from the activated cortex. This platform will allow us to target specific cell types, e.g. excitatory neurons, inhibitory neurons, and glia cells, by optical stimulation, and study the coupled fMRI signal from the local cerebrovasculature directly with single-vessel fMRI [5, abstract # 6229, 2015].

Methods All images were acquired with a 14.1 T/26cm horizontal bore magnet (Magnex), interfaced to an AVANCE III console (Bruker) and equipped with a 12 cm gradient set, capable of providing 100 G/cm with a rise time of 150 us (Resonance Research). A transreceiver surface coil with 10 mm diameter was used to acquire fMRI images. ChR2 was expressed by AAV5 virus in the barrel cortex with CaMKII promoter for optical stimulation. Fiber optic (400μm) was inserted into the deep layer cortex for optical stimulation. The optical pulse was modulated with frequency from 1 to 10Hz. The pulse duration was tested from 1ms to 50ms. And the light power was set from 0.05mw, 0.25mw, 1mw and 1.8mw, which will not lead to the heating-induced pseudo fMRI signal. The block design was set with light on for 5s, 15s and 30s. Light-driven data were acquired from 2 rats. Local field potential was recorded by the ERS module from Biopac. Animal surgical procedures were described previously [6]. The light pulse was delivered through the 470nm laser (2Hz, 6s duration, pulse duration=45ms, 15 epoch). AFNI software was used to perform the linear regression analysis to acquire functional maps.

Results Fig 1 shows the fiber optic insertion into the deep layer cortex, where the ChR2 was expressed by AAV viral vectors. The fiber optic trace was also visible in the brain slice for immunostaining. The light-driven fMRI signal was detected in the barrel cortex close to the fiber tips, where the time course from the activated cortical ROI was shown for different light on duration (Fig 1B). Fig 2. The time course of the light-driven response with different frequency, pulse duration and power level was represented. Fig 3 demonstrated the local field potential recorded in the FP-S1 by optical stimulation.

Conclusion We detected the robust fMRI signal and local field potential in the cortex expressing ChR2 after optical stimulation through inserted fiber optic.

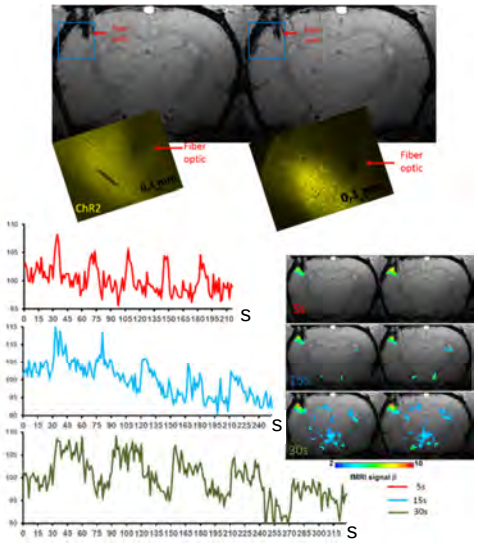

Fig 1. A. Fiber optic implantation into deep layer cortex with immunostaining slice for ChR2. B. The light-driven fMRI signal time course with different light on duration and the functional beta maps.

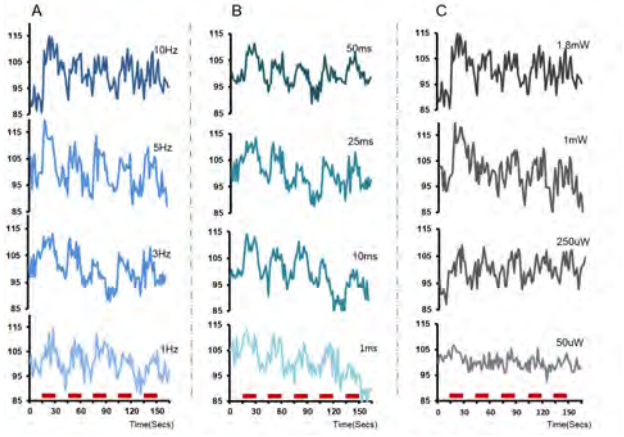

Fig 2. Multiple time course of the light-driven fMRI signal. **A**. fMRI signal at different stimulation frequencies (pulse duration: 25ms, power level: 1.8mw). **B**. fMRI signal at different pulse duration (3Hz, 18.mw). **C**. fMRI signal at different light power (25ms, 3Hz). The red dash line show the paradigm of optical stimulation.

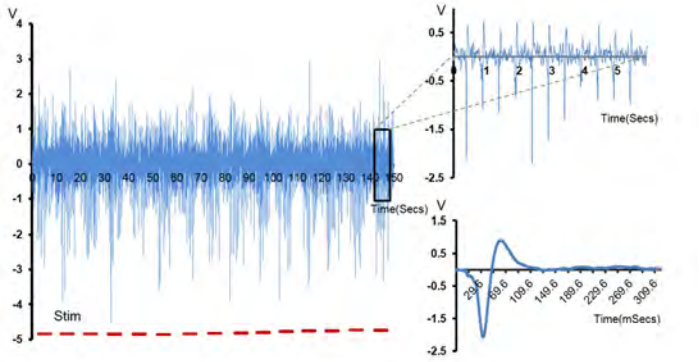

Fig 3. Optical stimulation evoked Local field potential. The red dash line show the paradigm of optical stimulation (2Hz, 6s duration, pulse duration=45ms, 15 epoch).

Reference 1. Lee et al. Nature, 465:788–792 (2010). 2. . Kahn et al. ,J Neurosci. 31:15086–91 (2011). 3. Gerits et al. Current Biology, 22:1722–26 (2012). 4. Yu et al. ISMRM, 0578 (2013). 5. Yu et al. ISMRM, 4360 (2014); 6. Yu et al. Neuron. **74**: 731-42 (2012).