# Local EPI Distortion Induced by Blue Light Delivery in the Naïve Brain: Implications for Optogenetic fMRI Studies

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**TARGET AUDIENCE:** Researchers applying optogenetics stimulations to deep-brain regions with EPI acquisition methods

**PURPOSE:** Optogenetics fMRI (ofMRI) measures the BOLD response upon light induced activation of specific neural population [1], and has huge potential to answer key questions in neuroscience. Previously, it has been reported that blue light delivery in the naïve brain resulted in pseudo positive and negative fMRI response [2]. These pseudo response were attributed to NMR frequency shifts, and T1 and T2* changes. EPI is known to be susceptible to NMR frequency shifting, field inhomogeneity and T2* changes [4]. However, the effects of blue light delivery in the naïve brain on EPI distortion have not been examined. The aim of this study was to investigate the local EPI distortion induced by laser stimulation in the naïve posterior thalamus.

**MATERIALS AND METHOD: Animal Preparation:** A multimode optical fiber with a diameter of 400µm was implanted to the right posterior thalamus (-4.0mm anterior/posterior, 3.0mm medial/lateral, -6.0mm dorsal/ventral from Bregma) of Sprague-Dawley rats (350-400g, N=3). MRI data were acquired immediately after fiber implantation. **Blue Light Delivery:** 470nm blue light (20Hz, 30% duty cycle, 5/10/15mW) was delivered in a block design (Fig. 1). **MRI Protocols:** All MRI data was acquired on a 7T Bruker Scanner. Dynamic MRI data was acquired using a single-shot GE-EPI sequence with TR/TE= 1000/20ms or a single-shot SE-EPI sequence with TR/TE=1000/26, and with FOV=32×32mm$^2$, 64×64 matrix, 10 contiguous 1-mm slices and 3 different phase encoding directions (0°, 45° and 90° deflection from dorsal/ventral). High resolution T2-W images were acquired as anatomical references. **Data Analysis:** Dynamic images were realigned, and smoothed with a Gaussian kernel of 0.5mm FWHM using SPM8. A general linear model analysis was applied to calculate voxel-wise response t-maps. T threshold of 3.33 ($p<0.001$) was applied. Images from different blocks were averaged. The time series of percentage BOLD signal change were extracted and plotted.

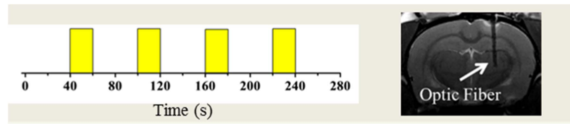


Fig.1 20Hz light delivery paradigm with 20s on and 40s off periods (left). T2-W image show the fiber implantation targeting the right posterior thalamus (right).

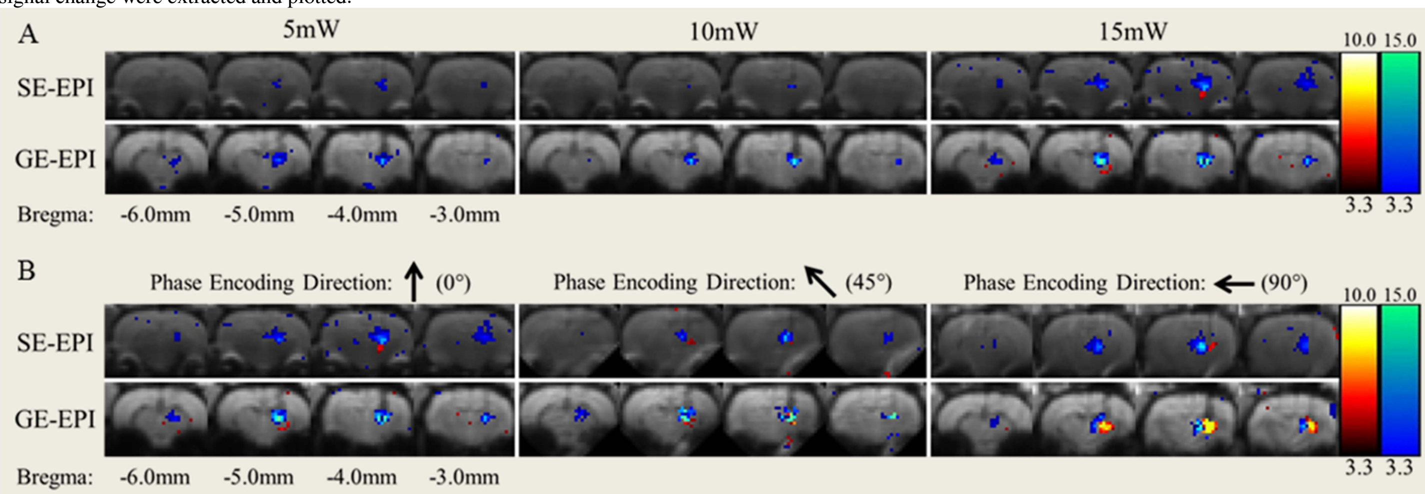


Fig. 2 The t-maps showing pseudo positive and negative fMRI response induced byblue light delivery using (A) different laser powers with a fixed phase-encoding direction (0deg), and (B) different phase-encoding directions at a fixed laser power (15mW).

**RESULTS:** Blue light in all laser powers tested resulted in pseudo negative fMRI response at the fiber tip (Fig. 2A). Stronger pseudo negative fMRI response was observed with higher laser power (Fig. 3A & Fig. 4). GE-EPI acquisition yielded stronger pseudo negative fMRI response compared to SE-EPI acquisition (Fig. 2A & Fig. 3). Pseudo positive fMRI response was only observed using 15mW laser power (Fig. 2A). Pseudo positive and negative fMRI responses were observed in all phase encoding directions (Fig. 2B). The pseudo negative fMRI response was at the fiber tip, while the pseudo positive fMRI response was adjacent to the pseudo negative fMRI response along the phase encoding direction.

**DISCUSSION AND CONCLUSION:** The light delivered in the naïve brain may cause local heating, which will induce NMR frequency shifts [2]. NMR frequency shifts can result in an increase of field inhomogeneity, causing a mismatch between the local field homogeneity during the light on and off periods. The possibly local decrease of T2 considering an increased local temperature could cause local signal intensity decrease in the SE-EPI images. The local decrease of T2* due to increased field inhomogeneity and the possibly decreased T2 should cause local signal intensity decrease in the resultant GE-EPI images [2, 3]. The temperature increases with laser power; therefore, stronger pseudo negative fMRI response is expected while using higher laser power. In addition, GE-EPI is more sensitive to field inhomogeneity than SE-EPI, hence, stronger pseudo negative fMRI response is observed using GE-EPI. The field homogenous mismatch could also cause local phase changes, which induces local geometric distortion in EPI [4]. The signals at the fiber tip may be stretched along the phase-encoding direction and could resulted in a slight signal increase adjacent to the fiber tip. The pseudo positive fMRI response can contaminate the true local BOLD activation in optogenetics fMRI studies. Several techniques could potentially alleviate such pseudo response, e.g. using parallel imaging [5], or applying dynamic phase correction methods [4]. Recently, ultra-high field animal MRI scanners are gaining popularity as they yield higher signal-to-noise ratio. However, signal distortion will be more prominent at higher field strengths under the same shimming system/quality, and the pseudo positive fMRI response may be stronger. This brings attention to a possible confounder which must be taken into account when ofMRI experiments are designed.

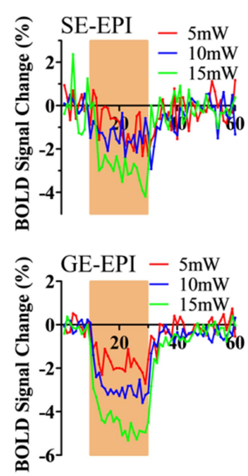


Fig. 3 The averaged pseudo negative fMRI time series induced by different light power. The shade indicates the 20s light delivery. Stronger pseudo negative fMRI response was observed with higher laser power. GE-EPI acquisition method also yielded stronger pseudo negative fMRI response compared to SE-EPI acquisition.

**REF: 1.** Lee JH, Nature, 2010. **2.** Christie IN, Neuroimage, 2013. **3.** Vesanen PT, JMR 2013. **4.** Jezzard P, Neuroimage, 2012 **5.** Larkman DJ, Phys Med Biol., 2007.