SFN 2018 abstract

Submit to session: I.04.d – Optogenetics

Non-invasive optogenetic excitation using focused-ultrasound-mediated delivery of virus-encoded Chrimson and transcranial red-light exposure

Antonios N. Pouliopoulos[1], Nancy Kwon[1], S. Abid Hussaini[2], Elisa E. Konofagou[1,3]

1. **Department of Biomedical Engineering,**
2. **Department of Pathology and Cell Biology, and**
3. **Department of Radiology**

Columbia University, New York, USA

Background, Motivation and Objective (469 characters)

In conventional optogenetics, channelrhodopsin (ChR) is encoded by an adeno-associated virus (AAV) delivered via direct injection into the brain and activated via blue-light illumination through implanted optical fibers. However, these invasive procedures are sources of morbidity and damage to the surrounding tissues and alter physiological brain responses. Here, we aimed at fully non-invasive optogenetic excitation using focused-ultrasound(FUS)-mediated viral delivery of the red-shifted ChR variant Chrimson and red light exposure.

Statement of contribution/Methods (450 characters)

AAV encoding Chrimson (peak absorption wavelength ~ 600 nm) were delivered into the brain of wild-type mice through FUS exposure in the presence of systemically circulating microbubbles. To remotely trigger neuronal activity, we transcranially illuminated the mouse brains using an LED source (635nm, beam size: 4 mm) 2 weeks after viral delivery. Mice were then sacrificed and their brains were imaged with fluorescence microscopy to confirm the presence of Chrimson and neuronal activation inferred by Arc and cFos expression.

Results/Conclusions (841 characters)

AAVs were delivered in the treated hemisphere (fig. 1A). Similar AAV delivery was achieved in both illuminated and control mice. Arc staining showed that neuronal activation occurred at areas of AAV expression, suggesting that light-sensitive channels were activated due to red light exposure. Arc activation was on average 66 ± 37 % higher on the ipsilateral side compared to the contralateral side in illuminated brains (fig. 1B). In contrast, the difference in Arc activation in non-illuminated mice was 4.57 ± 4.25 %. Although viral delivery was equivalent between illuminated and control mice ($p > 0.05$), Arc activation was significantly higher ($p < 0.05$) in mice exposed to red light. Finally, cFos upregulation overlapped with Chrimson-expressing neurons, suggesting light-mediated neuronal activation (figure 1C). Our initial findings indicate that neuronal activity can be triggered remotely *in vivo* using a combination of ultrasound and light exposure through the intact skull.

Character count: 1760/1800

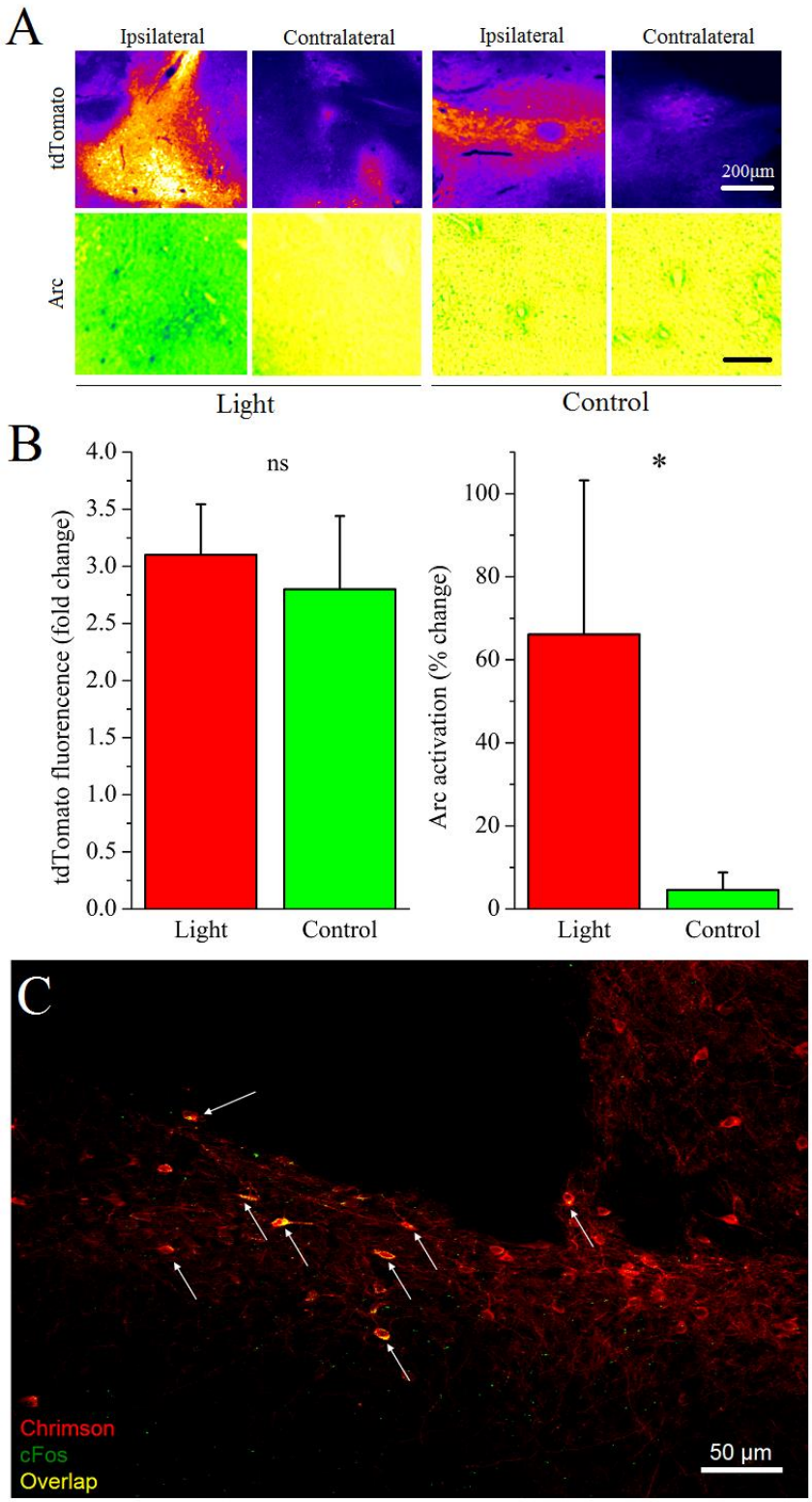

Figure 1: Non-invasive optogenetic excitation following red-light exposure. A) tdTomato fluorescence indicated successful viral delivery predominantly in the ipsilateral side, in both light-exposed and control mice. Arc staining revealed areas of increased neuronal activation only in the light-exposed group. B) tdTomato fluorescence was enhanced in the ipsilateral side compared to the contralateral side in both light-exposed and control mice, without significant differences (ns: $p>0.05$). In contrast, Arc activation was significantly higher in light-exposed mice (: $p<0.05$). Data presented as mean ± s.d.. C) cFos expression coincided with the presence of Chrimson channel.*