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Presentation Abstract

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Title:	Modulation of fear behavior via optical fiber arrays targeted to bilateral prefrontal cortex
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Abstract:	In recent years we have developed optogenetic molecular reagents for neuroscience, starting with channelrhodopsin-2 (ChR2) and N. pharaonis halorhodopsin (Halo/NpHR), as well as other novel and useful reagents to be described at this conference (Arch, spHalo, and Mac), that enable neural circuits to be activated and silenced with different colors of light. At the hardware level, however, many neural circuits of interest possess complex 3-dimensional shapes. To enable sophisticated neural manipulations, including 1) perturbation of complexly-shaped brain regions such as hippocampus and amygdala, 2) bilateral manipulations of neural structures, and 3) well-timed manipulation of multiple brain regions to study synchrony and plasticity, we recently developed inexpensive, end user-fabricatable arrays of blue LED-coupled optical fibers ("fiber arrays") that enable easily-customized deployment of light to multiple sites in the brain. Each optical fiber (200 microns in diameter, with maximal radiant flux of >200 mW/mm2 at the fiber tip) can illuminate a volume within the brain up to a cubic millimeter or so in size. Here we apply our optical fiber array system to study prefrontal regulation of fear extinction, selectively activating excitatory neurons without driving fibers of passage. Lentiviruses carrying the gene for the blue-light responsive excitatory cation channel, ChR2, were bilaterally injected into mouse infralimbic cortex (IL). After two weeks to permit ChR2 expression, they received three tones (30 s duration) coterminating with a footshock (1 s duration, 0.5 mA magnitude). One

day later, all subjects received 10 more tones (ITI = 60 s) without footshock (extinction phase), in a context different from the conditioning context. Data suggest that simultaneous bilateral delivery of a 500 ms train of 125 Hz blue-light pulses (4 ms in duration each) to the IL, starting 100 ms after tone onset, resulted in reliably-reduced fear responding to conditioned tones, relative to controls. We anticipate that the ability to manipulate complex 3-dimensional neural substrates with light will greatly advance the understanding of how neural circuits contribute to normal behavior as well as in animal models of neurological and psychiatric illness.

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