Optogenetic-induced glutamate release in the rodent hippocampus and frontal

Francois Pomerleau, MS[1] • Peter Huettl, MS[1] • Jorge Quintero, PhD[1] • John Slevin, MD[2] • Greg Gerhardt, PhD[3]

6a

[1]Anatomy and Neurobiology, University of Kentucky • [2]Neurology, University of Kentucky • [3]Anatomy and Neurobiology, Neurology, University of Kentucky

Specific targeted control of neural systems in order to establish causality between neuronal activity and behavior has remained difficult to achieve until the recent advancements in optogenetics, which introduces light sensitive proteins (opsins) into neurons that regulate transmembrane ion conductance. Electrophysiological studies have shown that optical excitation or inhibition of neuronal activity is correlated with behavior. But to date very few studies have examined neurotransmitter release combined with optical stimulation. We have combined our expertise of direct electrochemical measurements of neurotransmitter release (glutamate) in vivo with optogenetics in order to examine glutamate dynamics in the CNS. We infused (1 µl/each) AAV5- Syn-ChR2-EYFP into the right dentate gyrus (DG) of the hippocampus and the left infralimbic (IL) region of the frontal cortex. Histological analysis using yellow fluorescence has revealed that, 5 weeks post-infusion, EYFP was present throughout the left frontal cortex and right hippocampus. There was also some evidence of bilateral distribution. We attached an optical fiber (200 µm o.d.

~200 from recording sites) to our ceramic-based microelectrode array (MEA) configured to record glutamate dynamics and lowered the assembly in DG or IL. We used constant light activation (DC: 488 nm, 1 to 10 mW) or pulses (train (TR): 10 ms; 40Hz) and directly observed light-dependent glutamate release. Glutamate dynamics were in the same range as we have previously reported using other forms of stimulation (high potassium, drug induced or behavior). We observed glutamate release in the range of 1 to 70 µM and uptake rates of 0.1 to 10 µM/sec. Recent data support that we can induce epileptogenesis with light-evoked activation of the DG. Taken together, these data support that it is possible to directly record glutamate release in vivo and control glutamatergic systems using optogenetics.