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PHOTOACTIVATION OF INDIVIDUAL SYNAPSES IN VIVO WITH COVALENT PHOTOSWITCHES TARGETING ENDOGENOUS GLUTAMATE RECEPTORS

POSTER SESSION 01 - SECTION: OPTOGENETICS & IMAGING

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Glutamate receptors play key roles in neurotransmission at excitatory synapses and in the regulation of synaptic plasticity. We have recently developed a targeted covalently-attached photoswitch (TCP, Izquierdo-Serra et al., 2016) that allows the remote control of endogenous ionotropic glutamate receptors using light. We combined this photopharmacological effector with genetic and chemical calcium sensors to demonstrate all-optical reversible control of glutamate receptors at multiple levels of spatial resolution in the brain: we achieved the photoactivation of multiple neurons, individual neurons, and single synapses in rat hippocampal slices and in intact *Xenopus laevis* brain *in vivo*, which is challenging using other methods. We show that this compound selectively targets AMPA and kainate receptors. Labeled receptors remained functional for long periods of time (>8 hours). This allowed us to longitudinally track endogenous receptor physiology during events of synaptic plasticity, such as long-term depression (LTD). We could monitor the loss of functionality of AMPA/kainate receptors during NMDAR-dependent LTD in hippocampal neurons. TCPs are therefore a unique optical tool to label, photo-control and functionally track endogenous receptors in brain tissue without genetic manipulation.