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The ability to control and manipulate neuronal activity within an intact mammalian brain is of key importance for the mapping of functional circuitry and the basic understanding of neural computation. Several innovative approaches have recently been established for high-speed, light-induced activation or silencing of neurons through the use of light-sensitive, cation permeable channelrhodopsin-2 (ChR2) and light-driven chloride pump (NpHR). Here we report the generation and functional characterization of many lines of transgenic mice that express ChR2-YFP fusion proteins in defined subpopulation of neurons in various regions of the nervous system. We express ChR2-YFP in subsets of projection neurons using the neuron-specific Thy1 promoter and target ChR2-YFP to parvalbumin positive interneurons using BAC transgenic approaches. We show that illumination of ChR2-positive neurons in brain slices produces photocurrents that generate action potentials within milliseconds. Furthermore, the frequency of light-evoked action potentials can be precisely controlled up to 30 Hz. Photostimulation also evoke synaptic transmission between neurons. Using focal illumination of the cerebral cortex we demonstrate the same highly reproducible, light-dependent activation of neurons and precise control of firing frequency in vivo. Thus, these mice provide a genetic tool for precise spatial and temporal manipulation of neural activity with light to explore function and dysfunction of complex neural circuits in the mammalian brain.

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