Optogenetics is the combinational method of optical and genetic approaches, which allows us to control neuronal activities in a quick and precise manner. This technique was selected as the Method of the Year in 2010 by *Nature Medicine*, and although relatively new, has already been used to reveal many novel mechanisms of how the brain works. Three recent optogenetics articles showcase the use of this powerful approach for dissecting stroke pathophysiology.

Anenberg et al (Ministrokes in channelrhodopsin-2 transgenic mice reveal widespread deficits in motor output despite maintenance of cortical neuronal excitability. *J Neurosci*. 2014;34: 1094–1104) combined optogenetics and electrophysiological approaches to show that there is a mismatch between measures of cortical excitability and motor output within 60 minutes after stroke in mice. B6Cg-Tg(Thy1-COP4/EyFP)18Gfng/J channel rhodopsin-2 transgenic mice express channelrhodopsin-2 in layer 5 pyramidal neurons, which are responsible for motor output from cortex. Channelrhodopsin-2 is a light-sensitive cation channel, and by blue light, channelrhodopsin-2–expressed neurons can be activated via membrane depolarization. In this transgenic mice, surface pial arterioles in motor cortex were occluded by the rose bengal method. The mouse group of glial archaerhodopsin were subjected to ischemic damage in cerebellum by the rose bengal method. The analyses of these transgenic mice showed that glial acidification led to release of glutamate from astrocytes, but glial alkalization suppresses glutamate release and ischemic brain damage. Using the tetracycline transactivator-tet operator system, the authors generated 2 new transgenic mouse lines, in which channelrhodopsin-2 or a proton pump sensitive proteins in astrocytes to show a causal relationship between glial acidosis and neuronal excitotoxicity after stroke. Because H+ passes channelrhodopsin-2, in this study, channelrhodopsin-2 was used as an optogenetic tool for decreasing intracellular pH. However, optogenetic activation of archaerhodopsin induces glial alkalization. The analyses of these transgenic mice showed that glial acidification led to release of glutamate from astrocytes, but glial alkalization suppressed glutamate release. Finally, the transgenic mice were subjected to ischemic damage in cerebellum by the rose bengal method. The mouse group of glial archaerhodopsin photocaivation (eg, glial alkalization) exhibited significantly smaller infarct volume, suggesting that countering of astrocyte acidosis may reduce ischemic brain damage.

During the recovery phase after stroke, newly generated neurons may provide the compensatory substrates for rebuilding circuits. A recent study by Song J et al (Parvalbumin interneurons mediate neuronal circuitry-neurogenesis coupling in the adult hippocampus. *Nat Neurosci*. 2013;16:1728–1730) used optogenetics to ask how adult hippocampal neurogenesis can generate new neurons. Parvalbumin interneurons form immature synaptic inputs onto proliferating newborn neurons in dentate gyrus in adult hippocampus. Using optogenetics approach, the authors activated or deactivated the parvalbumin interneurons and then assessed adult hippocampal neurogenesis. The authors injected adeno-associated virus with Cre-dependent expression of channelrhodopsin-2 or halorhodopsin from *Natronomonas* (NpHR) into the dentate gyrus of 5-week-old parvalbumin-Cre mice. As noted, channelrhodopsin-2 can activate neurons with blue light by depolarization. However, NpHR can inactivate neurons with yellow light by hyperpolarization of the cells. Interestingly, activating parvalbumin neurons increased the number of newborn progeny, but deactivating parvalbumin neurons decreased the neurogenesis. These data suggest that local circuit activity by parvalbumin neurons in dentate gyrus may contribute to the diatomic regulation of adult hippocampal neurogenesis.

Optogenetics can also be used for assessing glial function. Beppu et al (Optogenetics countering of glial acidosis suppresses glial glutamate release and ischemic brain damage. *Neuron*. 2014;81:314–320) expressed light-sensitive proteins in astrocytes to show a causal relationship between glial acidosis and neuronal excitotoxicity after stroke. Because H+ passes channelrhodopsin-2, in this study, channelrhodopsin-2 was used as an optogenetic tool for decreasing intracellular pH. However, optogenetic activation of archaerhodopsin induces glial alkalization. The analyses of these transgenic mice showed that glial acidification led to release of glutamate from astrocytes, but glial alkalization suppressed glutamate release. Finally, the transgenic mice were subjected to ischemic damage in cerebellum by the rose bengal method. The mouse group of glial archaerhodopsin photocaivation (eg, glial alkalization) exhibited significantly smaller infarct volume, suggesting that countering of astrocyte acidosis may reduce ischemic brain damage.

These 3 recent studies demonstrate how optogenetics may provide a powerful approach for investigating neuronal and glial mechanisms after stroke. More widespread applications of this technique in stroke models should be warranted.
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