TOOLBOX

Choice of light-sensitive channel alters inhibitory signals

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Bright response: Beams of light can open ion channels engineered into membranes, turning neuronal activity on or off.

An innovative technique that uses waves of light to silence brain signaling in live animals can affect subsequent neuronal signals, according to a study published 24 June in *Nature Neuroscience*[1].

Optogenetics activates or silences neurons by opening light-sensitive channels engineered into the cells. The technique allows researchers to manipulate neuronal activity on cue and in a subset of neurons in live animals, and it has been used to study **mouse models of autism**.

Researchers employ different types of ion channels in optogenetics, and which they choose can influence neurons in different ways. Neurons typically maintain a negative charge inside the cell. A sudden shift toward a positive charge leads to a neuronal signal that propagates down the cell, called an action potential.

Light-sensitive channels that make the inside of the cell more positively charged trigger neural activity, and those that make the cell more negatively charged dampen it. According to the new study, however, sometimes these channels can have unexpected effects on signaling.

The researchers compared two inhibitory techniques: one that opens hydrogen channels (Archaerhodopsin-3 or ARCH), leading to an exit of positively charged hydrogen from the cell, and

one that opens chloride channels (halorhodopsin or NpHR), leading to an influx of negatively charged chloride ions. Optogenetics studies of autism typically use channel-rhodopsin receptors, which alter the levels of positively charged ions such as hydrogen or calcium.

In neurons inactivated with NpHR channel optogenetics, the chemical messenger gamma-aminobutyric acid (GABA), which typically dampens neuronal activity, instead causes the neurons to fire. This is not the case for neurons inactivated with ARCH channels.

GABA quiets neurons by opening chloride channels, so the researchers speculate that opening the channels in neurons with high chloride levels leads to an outflow of these ions, triggering activity.

Scientists should consider this effect when interpreting optogenetics results and choosing which channel to use in designing experiments, the researchers say. This could be especially relevant for autism research, as studies have linked **an imbalance in GABA signaling** with the disorder.

References:

1: Raimondo J.V. *et al. Nat. Neurosci.* Epub ahead of print (2012) **PubMed**