This Week in The Journal

How V1 Activity Influences Perception in Mice

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(see pages 3867–3881)

Neurons in primary visual cortex (V1) respond to simple visual features, such as orientation. These responses are read out by downstream areas to make perceptual decisions. How V1 responses are combined to make such decisions is unclear. One way to answer this question is to manipulate the responses of a subset of neurons activated during a perceptual task and ask how this manipulation affects judgments.

Jin et al. used this approach to examine how mice perform an orientation discrimination task. Mice were trained to depress a lever, hold it during repeated presentations of a stimulus of a particular orientation, and release it when the orientation changed. The interval between stimulus presentations was varied to induce adaptation to the initial orientation on some trials, and the magnitude of the orientation change was varied to determine perceptual threshold. Adaptation selectively reduced the responses of neurons that were activated most strongly by (“preferred”) the initial orientation. At the behavioral level, adaptation significantly increased the perceptual threshold and reduced the number of times mice released the lever before the orientation changed (the false alarm rate).

Two populations of V1 neurons are likely to be involved in this task: one that prefers the initial orientation and one that prefers the second. When the stimulus orientation changes, the activity of the first population should decrease while the activity of second population increases. An optimal decoder might therefore monitor the activity of both populations to determine when the orientation changes. Indeed, a linear regression trained on V1 population activity used this strategy. Unlike in mice, however, adaptation did not affect the discrimination threshold and false alarm rate for this decoder. Additional analyses suggested that the reason for this difference is that mice based their perceptual decision solely on the activity of neurons that prefer the second orientation.

These data indicate that mice do not necessarily use all the information available in V1 to make perceptual choices. This does not mean that mice never use all available information, however. Whether mice use a different strategy for other tasks remains to be tested.

The enhancer element cpce drives Purkinje-cell-specific expression of GFP in zebrafish. See Namikawa et al. for details.

Purkinje-Cell-Specific Expression of Mutant Kv3.3 in Zebrafish

Kazuhiko Namikawa, Alessandro Dorigo, Marta Zagrebelsky, Giulio Russo, Toni Kirmann, et al.

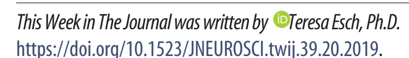
(see pages 3948 –3969)

Spinocerebellar ataxias (SCAs) are inherited diseases characterized by loss of coordination resulting from degeneration in the cerebellum. SCAs are classified into numerous subtypes based on which gene is mutated. SCA13 is caused by mutations in *KCNC3*, which encodes the voltage-sensitive potassium channel Kv3.3. This channel is highly expressed in cerebellar Purkinje cells; and because it rapidly activates at relatively depolarized membrane potentials, it enables these cells to spike at high frequencies. Although some SCA13-causing *KCNC3* mutations, such as R420H, produce nonfunctional channels that suppress activity of coexpressed functional channels, knocking out *Kcnc3* in mice does not lead to cerebellar degeneration and has only subtle effects on motor coordination. Therefore, how *KCNC3* mutations produce SCA13 remains unclear.

To investigate these mechanisms, Namikawa et al. sought to express mutant Kv3.3 channels selectively in Purkinje cells of zebrafish. Their first step was to develop a convenient means to selectively target these cells. They started with a vector containing GFP under the control of a large upstream region of *ca8*, a gene expressed almost exclusively in Purkinje cells. After determining that this region drove Purkinje-cell-selective expression, they narrowed in on a minimal regulatory element of 258 bp, which was sufficient to selectively target Purkinje cells. They named this element cpce (ca8-promoter-derived Purkinje-cell-specific enhancer element).

Notably, the cpce drove expression regardless of its orientation in the DNA strand, meaning it can drive expression of two genes at once. The authors therefore used this regulatory element to drive expression of *kcnc3a*^{R335H} (the zebrafish equivalent of human *SCA13*^{R420H}) along with fluorescent reporters in zebrafish larvae. They found that expression of *kcnc3a*^{R335H} caused progressive shrinkage and death of Purkinje cells, starting by 4 d after fertilization. Consequently, the optokinetic response to moving stripes (a cerebellum-dependent behavior) was disrupted in these larvae.

This work provides an animal model that will enable future research into the mechanisms leading to Purkinje cell death in SCA13. Importantly, the cpce also drove Purkinje-cell-specific expression in mouse cerebellar slices, allowing studies in that species as well. Moreover, the newly developed expression system will facilitate Purkinje-cell-specific manipulation of other SCA-related genes and any other gene of interest, providing a valuable tool for researchers studying Purkinje-cell function and pathology.



This Week in The Journal was written by Teresa Esch, Ph.D.
https://doi.org/10.1523/JNEUROSCI.twij.39.20.2019.