This Week in The Journal

Regenerated Bipolar Cells in Fish Appear Normal

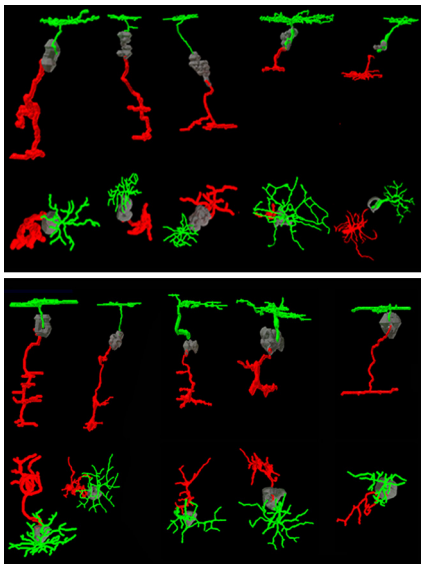
Timothy E. McGinn, Diana M. Mitchell, Peter C. Meighan, Natalie Partington, Dylan C. Leoni, et al.

(see pages 120–136)

In mature teleost fish, retinal Müller glia cells can generate new retinal neurons, which restore at least some visual ability after retinal damage. The extent to which normal circuitry is restored by these new cells is unclear, however. Answering this question is important as researchers pursue the possibility of stimulating neurogeneration by Müller glia in mammals, hoping ultimately to restore visual function in humans. Therefore, McGinn et al. examined the morphology and connectivity of regenerated bipolar cells in zebrafish retina.

The authors first injected ouabain to kill most bipolar, amacrine, and retinal ganglion cells (sparing photoreceptors and Müller cells). They examined bipolar cells 60 d later, when previous studies indicated visual behaviors had reemerged. Multiple types of bipolar cells were present at this time, although the total numbers remained much lower (10–30%) than normal. The dendritic arbors of regenerated bipolar cells were comparable in extent and branching patterns to those of controls, and they received synaptic input from a similar variety of photoreceptors. Consistent with these results, electroretinograms showed partial recovery of b-wave amplitude, which measures bipolar cell responses to visual input. Bipolar-cell axons also regenerated, stratifying in multiple layers as in undamaged retina. The axons had normal extents and numbers of branches, although some abnormal branching patterns were present.

These results suggest that retinal neurons generated from Müller glia in adult zebrafish develop relatively normal arborizations and synaptic inputs. Future work should investigate whether the synaptic output of these regenerated neurons and of other retinal neurons are also relatively normal. In addition, the extent to which functional circuitry develops in the absence of photoreceptor sparing must be determined. This last element might be especially important if this approach is to be translated into restoration of vision in humans after retinal injury.



Regenerated bipolar cells (bottom) exhibit a range of dendritic (green) and axonal (red) arbors, similar to those of bipolar cells generated during normal development (top). See McGinn et al. for details.

Nucleus Reuniens Affects Place Cell Properties

Thibault Cholvin, Vincent Hok, Lisa Giorgi, Franck A. Chaillan, and Bruno Poucet

(see pages 158–172)

Storage and retrieval of long-term memories depends on interactions between the prefrontal cortex (PFC) and the hippocampus. Although some hippocampal neurons project directly to the PFC, much communication from the hippocampus to PFC, and all communication in the reverse direction, is indirect. A major hub in PFC–hippocampal interaction is the thalamic nucleus reuniens (Re), which is extensively interconnected with both structures. The role of the Re in this circuit remains unclear, but its inactivation alters performance on spatial navigation tasks and leads to overgeneralization of fear after contextual fear conditioning. This suggests that by regulating communication between the PFC and hippocampus, Re promotes the formation and/or retrieval of specific memories (Cassel et al. 2013 Prog Neurobiol 111:34).

To investigate Re function in greater detail, Cholvin et al. produced excitotoxic lesions in Re and the adjacent rhomboid nucleus (Rh) of rats, then recorded hippocampal place-cell activity as rats explored different arenas. When rats with ReRh lesions were placed repeatedly in a familiar arena, their hippocampal neurons exhibited normal place fields: the cells were active only in a particular location in the arena. Although place fields in ReRh rats were generally less stable than normal, they became stabilized after multiple exposures to the familiar environment. When ReRh rats were placed in a novel arena, the locations of place-field changed, like they did in control rats, but the new place fields were less spatially coherent in ReRh rats. Moreover, whereas place fields remained stable across exposures to familiar and new arenas when control rats were repeatedly switched between the two, such switching reduced field stability in the familiar environment and prevented field stabilization in novel arenas in ReRh rats. Finally, whereas overdispersion (variability in firing rates across multiple transversals of a place field) was higher in familiar than in novel arenas in control rats, it was consistently lower than controls in ReRh rats in both familiar and novel arenas.

Together, these data suggest that field stability and spike variability in hippocampal place cells depends on input from the Re. Notably, previous studies have shown that inactivation of PFC also decreases hippocampal place-field stability and overdispersion, consistent with Re transmitting information from the PFC to hippocampus. This information might activate previously stored spatial maps, allowing the animal to navigate appropriately. Future work involving transient activation or inhibition of specific populations of Re neurons at specific times should further elucidate the role of this nucleus in hippocampus-dependent behaviors.

This Week in The Journal was written by Teresa Esch, Ph.D.