This Week in The Journal

An Amacrine Cell that Couples to Müller Glia Cells

William N. Grimes, Didem Göz Aytürk, Mrinalini Hoon, Takeshi Yoshimatsu, Clare Gamlin, et al.

(see pages 6018–6037)

The retina is a complex structure with an astounding number of cell types. For example, an inventory based on electron micrograph reconstructions (Helmstaedter et al., 2013, *Nature*, 500:168) indicated that there are >45 types of retinal amacrine cells. Little is known about most of these cells, including the second most common type, referred to as AC51-70. These narrow-field amacrine cells have a unique morphology, stratifying exclusively in the inner half of the inner plexiform layer. By searching the GENSAT retina database, Grimes, Aytürk, Hoon et al. identified a reporter mouse line (*Dact2-GFP*) in which similar amacrine cells were labeled. They used this line to investigate the properties of these cells.

The most unusual feature of the cells was their gap-junction-mediated coupling to Müller glia. Although gap junctions between neurons and glia have occasionally been found in the CNS, no other retinal neurons have been shown to exhibit such coupling. Indeed, although Müller cell processes ensheathed neurites of several neuron types, gap junctions were found only between Müller cells and *Dact2-GFP*-labeled cells. Therefore, the authors named these cells Müller glia-coupled amacrine cells (MACs).

MACs had center-surround receptive fields and showed excitatory responses to small light increments. Partial reconstructions of synaptically coupled cells suggested that light responses were driven primarily by type 5 and 6 cone bipolar cells. The reconstructions also indicated that MACs receive considerable synaptic input from narrowly stratified wide-field amacrine cells, which usually are GABAergic or glycinergic. Surprisingly, however, no light-evoked inhibitory currents were detected in MACs.

Reconstructions also suggested that MACs provide synaptic output to several types of bipolar, amacrine, and retinal ganglion cells. Some evidence suggested that

these synapses were glycinergic, but MACs expressed unusually low levels of the glycine transporter, and photostimulation of channelrhodopsin-expressing MACs evoked a response in only 1 of 48 ganglion cells tested.

The function of MACs remains unknown, but their coupling to Müller glia may facilitate signaling to the retinal vasculature to induce vasodilation in response to increased neuronal activity. Determining how these cells' activity is shaped by presynaptic amacrine cells and the extent to which their synaptic output influences light responses in other cells should help to elucidate their contribution to vision.

A MAC reconstructed from electron micrographs made conventional synapses onto amacrine cells (1), bipolar cells (2), and retinal ganglion cells (3), and received input from amacrine cells (4). See Grimes, Aytürk, Hoon et al. for details

Effects of Behavioral Selection on Fox Brain Volumes

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(see pages 6144–6156)

Approximately 60 years ago, a group of researchers in Russia began selectively breeding captive foxes to produce a strain that did not show fear responses to humans. The experiment was successful: not only did these foxes seem unafraid of

humans, they behaved much like dogs, actively approaching humans and continuing to be playful even as adults. In a parallel experiment, the researchers developed a strain of foxes that were unusually fearful and aggressive toward humans. It is hoped that comparing these strains with each other and with foxes bred without deliberate selection for behavioral traits will allow researchers to identify some of the genetic and neural bases of docility, sociability, and aggressiveness. So far, such studies have identified strain differences in stress hormones and their receptors, as well as in the serotonin system. To extend this work, Hecht et al. used magnetic resonance imaging to detect differences in white- and gray-matter volumes across strains.

Both tame and aggressive foxes had larger gray-matter volumes than conventionally raised foxes; there were no significant differences in total brain volume or white-matter volume across strains, however. Surprisingly, tame and aggressive foxes exhibited enlargement of many of the same brain areas relative to the conventional strain. These included frontal areas that correspond to prefrontal and motor cortical areas of dogs, as well as the amygdala, hippocampus, and cerebellum. Differences between tame and aggressive foxes were most apparent in temporal areas that may correspond to auditory, somatosensory, and multisensory areas in dogs. Although hypothalamus volume varied greatly across individuals, no significant cross-strain differences were detected. Nevertheless, additional analyses revealed that covariation in the morphology of hypothalamic and cerebellar subregions differentiated tame and aggressive foxes.

These results suggest that foxes selected for either tameness or aggressiveness show largely overlapping changes in gray matter volume. One possible reason is that approach and avoidance behaviors are controlled by similar brain areas, including areas of the prefrontal cortex that were enlarged in both tame and aggressive strains. Future work might examine whether differences between these strains emerge at a finer scale, for example, in the morphology of different classes of neurons.

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<https://doi.org/10.1523/JNEUROSCI.twij.41.28.2021>