This Week in The Journal

NMDA Receptors in Amacrine Cells of the Rod Pathway

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(see pages 627–650)

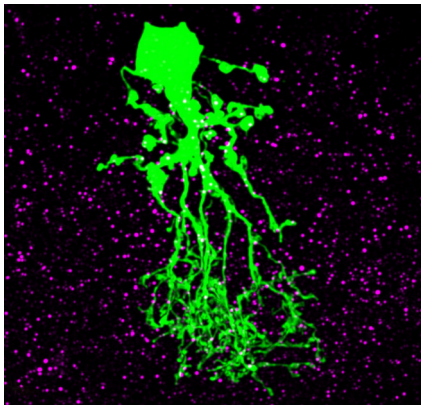
Vision in dim light is mediated by the rod photoreceptor pathway. Rods connect to rod bipolar cells, which in turn form glutamatergic synapses with AII and A17 amacrine cells. AII amacrine cells are required for transmitting information from rods to retinal ganglion cells (by way of cone bipolar cells), whereas A17 amacrines provide feedback inhibition to rod bipolar cells.

Both AII and A17 amacrine cells express NMDA receptors (NMDARs), but these are not thought to contribute to EPSCs in the cells. Veruki et al. therefore asked what the function of these NMDARs might be. They first confirmed that EPSCs in amacrine cells in rat retinal slices were generated solely by non-NMDA glutamate receptors. Nevertheless, NMDA elicited inward currents and calcium elevation in both amacrine cell types. Furthermore, NMDA increased the frequency of IPSCs in rod bipolar cells, most likely by triggering GABA release from A17 amacrines.

Notably, selectively blocking NMDARs containing GluN2B subunits eliminated NMDA-evoked responses only in AII amacrine cells, whereas selectively blocking NMDARs containing GluN2A subunits eliminated responses only in A17 amacrines. The selective expression of these subunits in AII and A17 amacrine cells was further supported by immunolabeling. Moreover, consistent with previous work suggesting that NMDARs regulate electrical coupling between AII amacrine cells and ON cone bipolar cells, GluN2B colocalized with gap-junction proteins in AII amacrines.

Importantly, NMDAR antagonists reduced baseline fluctuations in membrane currents in both AII and A17 amacrine cells, suggesting that these receptors are tonically activated by ambient glutamate. Furthermore, inhibiting glutamate uptake, which is expected to increase extracellular glutamate levels, increased high-frequency current fluctuations in both amacrine cell types, and this effect was blocked by NMDAR antagonists.

These results suggest that increases in ambient glutamate levels influence transmission in the rod pathway by acting on distinct extrasynaptic NMDAR types in AII and A17 amacrine cells. Activation of GluN2B-containing NMDARs in AII amacrine cells might regulate coupling between these cells and cone bipolar cells, and thus influence the transmission of light information to retinal ganglion cells. Activation of GluN2A-containing NMDARs in A17 amacrines, in contrast, likely inhibits further glutamate release from rod bipolar cells. Future work should investigate how these receptors influence visual processing at the network level.



GluN2B (purple) colocalizes with the dendrites of an AII amacrine cell (green). See Veruki et al. for details.

Updating Preferences during Hard Choices

Katharina Voigt, Carsten Murawski, Sebastian Speer, and Stefan Bode

(see pages 718–726)

Psychological studies in the 1950s suggested that choices not only are guided by preferences, but also influence preferences. Subjects engaged in a three-phase experiment: they first estimated the subjective value of items, then chose between items presented in pairs, and finally rerated the items. When subjects were required to choose between similarly valued items, their ratings of the items subsequently changed: chosen items were valued more, whereas rejected items were valued less. This choice-induced preference change was hypothesized to result from attempts to reduce cognitive dissonance arising from disparities between value estimates and choice behavior.

Although these and most subsequent studies were confounded by experimental artifacts (Chen and Risen, 2010 J Pers Soc Psychol 99:573), recent studies using refined methods have replicated the effect and identified brain regions involved. All these studies, however, examined brain activity during the second evaluation stage, leaving open the possibility that value estimates were updated not as a result of choice, but rather as the choice was being made.

To investigate this possibility, Voigt et al. measured brain activity during the choice stage using fMRI. Consistent with previous studies, when subjects remembered making a choice between similarly rated items, their subsequent ratings for chosen items increased, whereas ratings of rejected items decreased. Generalized linear modeling showed that activity in the dorsolateral prefrontal cortex—an area previously associated with choice-induced preference changes—predicted changes in valuation of remembered items.

Furthermore, eye-tracking data showed that during the choice phase, subjects looked longer at items they ultimately selected than at items they rejected, and the greater the difference in fixation time, the larger the change in ratings during the second valuation stage.

These results suggest that changes in valuation observed after subjects choose between similarly rated items stem partly from preference updating during the decision process itself. In fact, given that subjective values vary over time, estimating such values for isolated items is likely challenging. Comparing items side-by-side might help people define the items' subjective value more precisely, increasing the accuracy of subsequent estimates. It remains possible, however, that attempts to reduce cognitive dissonance during re-evaluation also contribute to reported changes in preference.

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