Mechanism and circuitry underlying retinal sensitization

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Recently we have described a population of retinal ganglion cells that increase their sensitivity after the presentation of a high contrast stimulus. This process, termed contrast sensitization is a form of short-term information storage that enables ganglion cells to store the location of a previously moving object for several seconds. Effectively, sensitizing ganglion cells make a prediction that the location of a strong stimulus at one point in time will continue to be important in the near future, even after the strong stimulus ceases. To understand how the retina can paradoxically increase its sensitivity in the face of a strong stimulus, we recorded intracellularly from sensitizing ganglion cells, and found that a depolarization of the baseline membrane potential underlies the increase in sensitivity. We then fit the membrane potential fluctuations with a model that contained two independently adapting pathways: one excitatory and one inhibitory. In this model, a strong stimulus adapts the inhibitory pathway, such that subsequent stimuli are processed with less inhibition, thus increasing sensitivity. Consistent with this model, pharmacologically blocking GABAergic inhibitory transmission eliminated sensitization. To identify interneurons that generated sensitization, we recorded intracellularly from an inhibitory amacrine cell, while simultaneously recording from a population of ganglion cells with an extracellular multielectrode array. By injecting current into the amacrine cell, we measured whether amacrine transmission changed during sensitization. Initial results indicate the presence of an amacrine cell whose transmission to ganglion cells depresses during sensitization, as predicted by the model. This effect was specific, as other types of amacrine cells did not change their transmission under the same conditions. These results lead to an understanding of sensitization whereby a strong stimulus primes the circuit to form a prediction of future input by locally removing one type of inhibition.

By understanding the circuitry that underlies contrast sensitization (see figure) we will gain insight into a much larger class of neural responses: the integration of an input to create persistent activity and increased sensitivity. Such a response has been suggested to underlie aspects of working memory, and could as well play a role in certain forms of involuntary attention. Our finding of the necessity of inhibition for sensitization also provides a novel role for inhibition in adaptive encoding.

Contrast sensitization. Average response (bottom left) of a sensitizing cell to many repeats of a stimulus that changed back and forth between high (black) and low (blue) contrast (top left). Each repeat of the stimulus presented a different sequence of random intensities. On the right is the nonlinear response function for the same cell computed by passing the stimulus through a linear temporal filter (not shown) early and late during low contrast. This shows that the increase in response corresponds to an increase in the sensitivity of the cell.