LECTURE

Searching for Mechanisms of Retinal Direction Selectivity

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Abstract. A classic example of a complicated neurocomputation carried out by a relatively simple neuronal circuitry is that some mammalian retinal ganglion cells respond selectively to direction of motion. Search for the mechanisms of direction selectivity in the mammalian retina started some 35 years ago. It has been shown that direction selectivity is caused by an asymmetrical inhibition induced by GABA acting on $GABA_A$ receptors. However, the physical circuitry underling this computation is still not clear. A few recent breakthroughs provide important evidence for the sites where the computation takes place. (Keio J Med 49 (4): 159–161, December 2000)

Key words: Motion detection, neurocomputation, electrophysiology, retina

Initial Direction

Following the discovery of direction selective (DS) ganglion cells in the rabbit retina,[1] Barlow and Levick[2] carried out a series of elegant studies on the mechanisms of direction selectivity. In one of the most powerful experiments, they flashed 2 bars in sequence to mimic a motion. When the bars advanced in the preferred direction, the cell responded to both bars, when the bars advanced in the null direction, the cell only responded to the 1st flash, showing an asymmetrical inhibition propagating in the null direction. Later experiments mapped the inhibitory area to every spot in the receptive field, showing a cardioid shaped inhibitory zone displaced towards the null side.[3] Pharmacological experiments showed that the directional inhibition could be abolished by GABA antagonists such as picrotoxin[4] and bicuculline,[5] indicating this inhibition is caused by activation of $GABA_A$ receptors. In addition, specific antagonists against NMDA or L-AP4 receptors reduce the amplitude of the DS cells' response, but not direction selectivity, while AMPA/Kainate receptor antagonists abolish direction selectivity.[6] This suggests that the directional GABA inhibition is mainly driven by AMPA/Kainate receptors.

Wrong Directions

Horizontal cells

It was first proposed that the axon-bearing horizontal cells might be responsible for direction selectivity, since the projecting axon could function as a means to mediate the feed-forward lateral inhibition.[2] However, this proposal quickly became unlikely due to three main reasons. Firstly, there are probably not enough axon-bearing horizontal cells to cover the entire retina with a coverage factor of 4 to be responsible for 4 cardinal directions seen in the rabbit retina.[7] Secondly, the horizontal cell outputs feedback to photoreceptors, but direction selective bipolar cells have never been reported in the mammalian retina. And thirdly, the axon terminals of the axon-bearing horizontal cells exclusively contact rods while direction selectivity persists over a wide illumination range.

Starburst amacrine cells

Starburst amacrine cells have been suspected to play a major role in direction selectivity for several decades for many beneficial reasons. Starburst cells synthesize and release neurotransmitter ACh,[8,9] and ACh directly excites DS cells.[10] In addition, enhancing the ACh effect abolishes the direction selectivity.[11] Dendrites of starburst cells cofasciculate with dendrites of the DS

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