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VISUAL PROCESSING

Silent motion detectors

Silent synapses express NMDA receptors (NMDARs) but lack AMPA receptors (AMPARs). These synapses remain unactivated unless presynaptic glutamate release coincides with post-synaptic depolarization that relieves NMDARs from their Mg^{2+} block. Silent synapses are prominent cellular substrates for synaptic plasticity in the developing brain, but their importance in the mature CNS is less clear. In a recent study, Awatramani and colleagues show that silent synapses on direction-selective ganglion cells (DSGCs) in the mature mouse retina have a key computational role in motion sensitivity.

DSGCs compute direction by comparing the strength of non-directional inputs from glutamatergic bipolar cells and directional inputs from starburst amacrine cells, which are both GABAergic and cholinergic. Previous ultrastructural studies suggest that DSGCs and starburst cells are driven by a largely overlapping set of bipolar cells. From this pattern of connectivity, stimuli that are too weak to elicit GABA or acetylcholine release from starburst cells would be predicted to induce non-directional responses in DSGCs; however, contrary to this expectation, direct measurements from DSGCs show that they maintain direction selectivity even for threshold stimuli. Here, Awatramani and colleagues demonstrate that silent synapses enable DSGCs to maintain direction selectivity at threshold levels.

By recording the activity of pairs of neighbouring genetically labelled starburst cells and DSGCs in response to moving-dot stimuli of varying contrasts, Awatramani and colleagues determined the sensitivities of the different inputs to DSGCs and starbursts. DSGC responses to threshold stimuli were only apparent when the cells were held at a depolarized potential (relieving the Mg^{2+} block of NMDARs) — a signature of silent synapses. By contrast, threshold stimuli activated starburst cells through AMPAR-containing synapses.

Spontaneous NMDAR-mediated activity in DSGCs was highly correlated with AMPAR-mediated activity in starburst cells, suggesting that these cells are driven by a common set of bipolar cells. In line with this, the authors used serial block-face electron microscopy to visualize single ribbon synapses of bipolar cells and indeed confirmed that some bipolar cells contact both starburst cells and DSGCs. Together, these observations suggest that individual bipolar cells send parallel inputs to starburst cells and DSGCs via AMPAR-containing and NMDAR-containing synapses, respectively.

Next, the authors used a combination of computational modelling and pharmacology to determine the functional importance of the silent bipolar cell–DSGC synapses. In large-scale multi-electrode array recordings of the spiking activity of a population of DSGCs, selectively blocking silent synapses with an NMDAR antagonist reduced DSGC responses to low-contrast stimuli more than responses to high-contrast stimuli, indicating that silent synapses are necessary for computing the direction of near-threshold stimuli.

Overall, this study characterizes the synaptic circuitry underlying motion sensitivity and illustrates how silent synapses may enable motion detection by retinal DSGCs at near-threshold contrasts. The authors note that responses to low-contrast stimuli are mediated by directional GABAergic and cholinergic inputs from starburst cells; thus, DSGC depolarization (and, in turn, the recruitment of silent synapses) in response to low-contrast stimuli probably depends on starburst-released acetylcholine.

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