Axonal sodium channel bands shape the response to electric stimulation in retinal ganglion cells.

Electric stimulation of the retina reliably elicits light percepts in patients blinded by outer retinal diseases. However, individual percepts are highly variable and do not readily assemble into more complex visual images. As a result, the quality of visual information conveyed to patients has been quite limited. To develop more effective stimulation methods that will lead to improved psychophysical outcomes, we are studying how retinal neurons respond to electric stimulation. The situation in the retina is analogous to other neural prosthetic applications in which a better understanding of the underlying neural response may lead to improved clinical outcomes. Here, we determined which element in retinal ganglion cells has the lowest threshold for initiating action potentials. Previous studies suggest multiple possibilities, although all were within the soma/proximal axon region. To determine the actual site, we measured thresholds in a dense two-dimensional grid around the soma/proximal axon region of rabbit ganglion cells in the flat mount preparation. In directionally selective (DS) ganglion cells, the lowest thresholds were found along a small section of the axon, about 40 microm from the soma. Immunochemical staining revealed a dense band of voltage-gated sodium channels centered at the same location, suggesting that thresholds are lowest when the stimulating electrode is closest to the sodium-channel band. The size and location of the low-threshold region was consistent within DS cells, but varied for other ganglion cell types. Analogously, the length and location of sodium channel bands also varied by cell type. Consistent with the differences in band properties, we found that the absolute (lowest) thresholds were also different for different cell types. Taken together, our results suggest that the sodium-channel band is the site that is most responsive to electric stimulation and that differences in the bands underlie the threshold differences we observed.