Endocannabinoids (eCBs) in the brain act as retrograde messengers that bind to presynaptic cannabinoid receptors causing inhibition of neurotransmitter release from the presynaptic terminal. In the mouse and human retina, cannabinoid receptors have been found in the synaptic terminals of the photoreceptors, the inner plexiform layer, and retinal ganglion cells. The functional role of eCBs and their receptors in modulating light-evoked responses of retinal ganglion cells are unknown, however. It was hypothesized that eCBs in the retina act like they do in the brain as retrograde messengers, by inhibiting the release of neurotransmitter from the photoreceptors to the bipolar cells (Reviewed by Yazulla, 2008). Thus, blocking the effects of eCBs with a cannabinoid receptor 1 (CB1) antagonist was hypothesized to increase the amplitude of light responses. As the initial study toward understanding how eCBs modulate visual responses under light adaptation, we performed whole-cell voltage clamp recordings in mouse retinal ganglion cells in a bath perfused with the CB1R antagonist O-2050. The recorded cells were labeled with Lucifer Yellow from the recording electrodes. Our preliminary results showed that bath application of O-2050 increased the amplitude of light-evoked excitatory postsynaptic currents (EPSCs) in some ganglion cells under light adaptation. This finding favored the hypothesis that eCBs function as retrograde messengers by inhibiting presynaptic glutamate release in the retina. However, our results also showed that O-2050 decreased the amplitude of light-evoked EPSCs in other retinal ganglion cells. Moreover, the modulation in amplitude of light-evoked EPSCs was found over a wide range of light intensities. Based on our limited number of samples, a correlation between the differential effects of O-2050 and morphological cell types cannot be determined. More samples are needed to draw solid conclusions. Taken together, these data suggest that eCBs in the retina act not only as retrograde messengers inhibiting the light-evoked release of glutamate in some cells, but also facilitate the light-evoked release of glutamate in other cells. Further experiments are needed to elucidate the mechanisms by which eCBs differentially modulate light responses in the retina in light adaptation.