Project Title: Retinal Prosthetic with Capacity to Produce Normal Vision  
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Background: This project focuses on the development of a novel retinal prosthetic to restore vision. Because of the severe loss of tissue in both conditions, in particular, the loss of photoreceptors, these patients have very few treatment options. For these patients, their best hope for regaining sight is through prosthetic devices. Current prosthetics, though, are still far from providing normal vision: for example, they allow patients to see bright lights and high contrast edges, but not yet natural scenes. Efforts to improve prosthetic capabilities have been focusing largely on increasing the resolution of the devices’ stimulators (either electrodes or optogenetic transducers). Investigators demonstrated that a second factor is also critical: driving the stimulators with the retina’s neural code. Using the mouse as a model system, scientists generated a prosthetic system that incorporates the code this dramatically increased the system’s capabilities, well beyond what could be achieved just by increasing resolution. Further, the results showed that the combined effect of using the code and a high resolution stimulator is able to bring prosthetic capabilities out of the realm of simple image detection into the realm of natural sight.

Objective: Develop a retinal prosthesis to restore vision after combat related eye injuries and to treat retinal degenerative diseases.

Hypothesis: A new type of retinal prosthesis, already proven successfully in mice, can produce near normal vision in humans.

Specific Aims: 1) Apply the prosthetic system developed to nonhuman primates (NHPs) and measure signal transmission through the first stages of visual processing. 2) Measure behavioral performance of the prosthetic device at the behavioral level.

Study Design: The plan is to generate a prosthetic for pharmacologically blinded NHPs to match the response of the retina to that of normal NHPs, and then to verify its performance at a behavioral level with spatial discrimination of gratings to assess visual acuity and recognition of faces and shapes judged by eye tracking and by match-to-sample tasks in trained animals. An adeno-associated virus (AAV) vector that expresses both the ChR2 gene and a green fluorescent protein (GFP) marker will be injected intravitreally or beneath the inner limiting membrane of one eye in macaque monkeys to transfect RGCs. Once the ChR2 gene has been shown to express in a fovea annulus or a parafoveal region by GFP fluorescence to light stimuli, the investigators will monitor signals from RGC axons and from lateral geniculation nucleus (LGN) neurons.

Relevance: purpose is to provide treatment for patients with advanced-stage blindness due to a) combat based eye injuries, and b) retinal degenerative diseases, the latter affecting 1.8 million people in the US (both civilians and veterans). Efforts to improve prosthetic capabilities have been focusing largely on increasing the resolution of the devices’ stimulators (either electrodes or optogenetic transducers). Dr. Nirenberg recently showed that a second factor is also critical: driving the stimulators with the retina’s neural code. Using the mouse as a model system, she generated a prosthetic system that incorporates the code - this dramatically increased the system’s capabilities, well beyond what could be achieved just by increasing resolution. Further, the results showed that the combined effect of using the code and a high-resolution stimulator is able to bring prosthetic capabilities out of the realm of simple image detection into the realm of natural sight.