

Therapy for the Periphery



Scott Delp
Stanford University

The power of optogenetics to improve our understanding of neural circuits is clear. Applying optogenetic techniques to humans, however, remains a goal that is yet to be realized. In my laboratory, we have used optogenetics to manipulate activity in selected neurons of the peripheral nervous system, motivated by the desire to use optogenetics to excite muscle in cases of paralysis, inhibit motor neurons to reduce spasticity, and control nociceptors to treat neuropathic pain. Others have demonstrated that optogenetics can be applied to control neuronal activity in nonhuman primates or have used optogenetics in rodent models to partially restore vision. Translating these exciting results into optogenetic therapies for humans will require successfully overcoming a set of challenges. These include the identification of important disease states that are not adequately addressed by electrical stimulation, pharmacology, or other therapies, demonstration of a potent therapeutic effect of optogenetics in an animal model of the disease state, development and demonstration of safe and effective gene therapy techniques that can transduce selected neurons in humans, development and evaluation of devices to deliver light to transduced neurons in humans, and, finally, management of a clinical trial to evaluate the safety and efficacy of the optogenetic treatment. Meeting these challenges will be difficult but will allow us to harness the power of optogenetics to improve human health.

Prostheses in Sight



Sheila Nirenberg
Cornell University

New technologies come along every few years. Sometimes they are a fad, and sometimes they let us move forward in big leaps. Here, I'd like to give an example about how a specific technology—optogenetics—made a real leap possible. The example involves a treatment we're developing for restoring sight for patients with retinal degenerative diseases. Patients with these diseases need a way to get visual information to their brains. This is a two-step process. First, the information needs to be converted into the retina's neural code. Second, the code needs to be transmitted to the brain. My lab works on neural coding and had addressed the first step: converting visual images of arbitrary complexity such as faces and landscapes in real time into the retina's code. But how could we get the coded signals to the brain? Electrodes don't offer a good solution because they're too coarse: the retina's code has single-cell resolution, and electrodes would force us to blur this as each electrode stimulates 50–100 cells. This is where optogenetics came in: the resolution it provides matches the resolution of the code, and when we put the two together, we had a very effective solution. We converted the solution into a prosthetic system that can make completely blind retinas in animals behave very much like normal ones, and we're now starting to bring it through the FDA and into clinical trials.

Coping with Background Noise



Vincent Walsh
UCL

I've just read about Google's acquisition of DeepMind, and I was impressed, but not surprised, at the humility of Demis Hassabis, the founder of the \$400,000,000 AI company. He emphasizes how difficult it is to understand the human brain. This is in stark contrast to my own field, human brain stimulation. There are many claims, based on small effects under laboratory conditions, that brain stimulation can improve memory, mathematical cognition, creativity, language, or performance in athletes or military personnel. In some cases, there seems to be a lack of understanding of the conceptual and technical gulf between these lab results and what to expect in the real-world setting. Overblown statements also don't help. Human brain stimulation has proven its worth in the treatment of depression and neurodegenerative disorders, but success in other fields has so far been limited. There are dangers in not being grounded in reality; for those who can't see these patterns, I'd recommend Carl Djerassi's novel "Cantor's Dilemma" as a good fictionalization of the issues and the cost of not confronting them. The success of transcranial magnetic stimulation in depression shows that brain stimulation can make a serious contribution to health, and it may be the case that other forms of stimulation will be useful for other conditions. But, unless we take a step back now, we are in danger of spreading false hope and of masking real potential in the low signal-to-noise environment created by shouting before there is much to say.