Trials begin for a new weapon against Parkinson’s- Strong Red light

Alan Minson says his Parkinson’s symptoms improved after he started to use a “light helmet” in July 2019.

Light therapy can help lift moods, heal wounds, and boost the immune system. Can it improve symptoms of Parkinson’s disease, too? A first-of-its-kind trial scheduled to launch this fall in France aims to find out. In seven patients, a fiber optic cable implanted in their brain will deliver pulses of near-infrared (NIR) light directly to the substantia nigra, a region deep in the brain that degenerates in Parkinson’s disease. The team, led by neurosurgeon Alim-Louis Benabid of the Clinatec Institute—a partnership between several government-funded research institutes and industry—hopes the light will protect cells there from dying.

The study is one of several set to explore how Parkinson’s patients might benefit from light. “I am so excited,” says neuropsychologist Dawn Bowers of the University of Florida College of Medicine, who is recruiting patients for a trial in which NIR will be beamed into the skull instead of delivered with an implant.

Small tests in people with Parkinson’s and animal models of the disease have already suggested benefits, but some mainstream Parkinson’s researchers are skeptical. No one has shown exactly how light might protect the key neurons—or why it should have any effect at all on cells buried deep in the brain that never see the light of day. Much or all of the encouraging hints seen so far in people may be the result of the placebo effect, skeptics say. Because there are no biomarkers that correlate well with changes in Parkinson’s symptoms, “we are reliant on observing behavior,” says neurobiologist David Sulzer of
But proponents point to a Parkinson’s therapy named deep brain stimulation (DBS), in which electricity of a specific frequency is applied to affected brain regions. Invented by Benabid more than 30 years ago, DBS has become a standard approach for treating tremors and other severe motor symptoms in Parkinson’s patients even though its mode of action isn’t entirely clear either. The well-documented healing effect of low-level laser therapy on other tissues is also encouraging, says Michael Hamblin, a researcher at the Wellman Center for Photomedicine at Massachusetts General Hospital. In some countries, doctors routinely use lasers to treat pain or speed up wound healing.

Ten years ago, John Mitrofanis, a neuro-anatomist at the University of Sydney, was inspired to try light in Parkinson’s after a colleague told him that light in the NIR range protected retinal cells against toxins. In a 2012 study, he and colleagues showed in a mouse model of Parkinson’s that NIR light shined into mice’s heads protected dopamine-producing cells in the substantia nigra from a neurotoxin.

Excited, Mitrofanis called Benabid, with whom he once spent a year studying DBS. Benabid, “being the surgeon, said, ‘We have to develop a light device that gets close to the area,’” Mitrofanis recalls. The researchers reasoned that light shining from outside the skull would not penetrate deep enough to make a difference in larger animals.

In 2017, together with research fellow Cécile Moro, they injected 20 macaques with a neurotoxin known to cause Parkinson’s symptoms. In nine of them, they also delivered NIR to the midbrain area through an implanted device. Mitrofanis recalls how the first NIR-treated monkey behaved after a 3-week recovery period: “He was moving around like there was nothing wrong. We looked at each other and just hugged. ... It was euphoric.” Overall, NIR-treated monkeys developed fewer symptoms than the untreated group and retained 20% to 60% more of the brain cells targeted by the neurotoxin.

Mitrofanis also struck up a collaboration with Catherine Hamilton, a retired occupational physician in Tasmania who had treated her own arthritic knee by wrapping it with light-emitting diodes (LEDs). In a study of six Parkinson’s patients published last year, Hamilton, Mitrofanis, and others reported that wearing a helmet lined with LEDs improved facial expression, auditory processing, engagement in conversation, sleep quality, and motivation, though it did not have much effect on motor symptoms. “If I miss a day session, there
“is a gradual change in me,” says Alan Minson, a Parkinson’s patient living in Longford, Australia, who started to use a helmet in July 2019. “Bad dreams come back, my tolerance level goes way down, and my lethargy goes way up.”

Ann Liebert of the University of Sydney is planning a study in 120 patients using a more sophisticated helmet. In a similar effort, Bowers will randomize 24 patients to externally applied NIR or sham light and watch for behavioral and motor benefits.

Bowers will also look for signs that, as some have proposed, light boosts brain cells’ energy-producing mitochondria. Test tube experiments have shown that light can trigger the enzyme cytochrome C oxidase, which is present on mitochondrial membranes, to rev up cellular energy production, which in turn might increase blood flow and stimulate cells to churn out several neuroprotective proteins and growth factors. “But I’m not convinced a transcranial device can penetrate deeply enough to show substantial improvements,” Bowers says. She’s more hopeful about Benabid’s trial.

That study will follow 14 early-stage Parkinson’s patients for 4 years, seven of whom will be treated periodically with pulses of 670-nanometer light delivered to the brain via a thin laser diode cable. The other seven patients will not be operated on; an ethical review board ruled against subjecting them to surgery without a chance of benefit. The main objective is to prove the implant is safe, Benabid says, but the researchers will also evaluate disease progression. “It has to make a big difference,” he says. “There is no reason [to do] extensive surgery for mild improvement.”

The researchers plan to use common imaging methods to quantify the number of dopamine-producing cells in patients. But a protective effect may be hard to detect. “The major problem with all neuroprotection trials in Parkinson’s disease is that the diagnosis appears to occur after more than 50% of dopamine-producing cells are gone,” Sulzer says. Unless the improvement is huge, “the signal might be too small to detect.”

The team will also look for clinical benefits. But because researchers grade Parkinson’s symptoms by observing patients performing specific tasks, assessments are largely subjective, and symptoms vary over time; everyone has good days and bad days, Sulzer says. Because the control group will not undergo surgery, it will be especially hard to rule out placebo effects.

Yet Sulzer is giving studies like Benabid’s the benefit of the doubt. The absence of a clear mechanism isn’t a reason to dismiss the therapy, he says. “There are
many things we don’t understand,” Sulzer says. “I am skeptical and also think it is an intriguing area of pursuit.”