that editors should intervene when peer-review comments are hostile. Such comments have a disproportionate impact on minorities and other marginalized groups, inducing self-doubt and harming productivity, according to a 2019 *PeerJ* paper. It's not just ethical to edit such review reports—it's essential, says Seth Leopold, editor-in-chief of *Clinical Orthopaedics and Related Research*.

Jane Alfred, director of Catalyst Editorial, which offers training on research integrity and publication ethics, thinks it's best to return reports containing hostile language and ask the reviewer to change it. Reviewers are often grateful for the chance to revise ill-considered comments, she says. But Leopold says this may be impractical at fast-paced journals, and trying to educate reviewers who make unprofessional comments is likely futile. It's better, he says, not to ask that person to review again.

Changing a reviewer's recommendation is another matter, says Howard Browman, a council member of the nonprofit Committee on Publication Ethics, which is developing guidance on how to navigate the ethics of editing reviewers' comments. "It's so obviously something you wouldn't do," he says.

Yet it apparently happened to Fidler, who stumbled on the changes to her report by accident. Although the review process was double-blinded, she recognized the paper as Hoekstra's because she had seen him present the work, on Ph.D. students' statistical reasoning, at a conference in Slovenia. So after sending in her review, she emailed him to congratulate him and tell him that her review was nitpicky but positive.

That same day, Hoekstra's paper was rejected by the journal. "The reviewers have spoken in nearly a single voice in their recommendation to me that I decline publication of the paper in its current form," wrote the editor-in-chief, George Marcoulides, a research methodologist at the University of California, Santa Barbara. Although editors may override reviewer recommendations, the normal practice is to explain this in the decision letter. Hoekstra wrote back to Fidler, attaching the two reviews he got from the journal and asking for suggestions of other journals that might publish the work.

When she saw the reviews, Fidler cottoned on. "I think we have a controversy on our hands," she wrote to Hoekstra. She downloaded her review from the online journal system, and compared it, word by word, with the review Hoekstra received. Her sentence saying her concerns were minor had been deleted. Other sentences criticizing Hoekstra's methods had been added. She emailed Marcoulides, who replied that the journal computer system sometimes blended and distorted reviewer comments.

Fidler calls that explanation "preposterous," saying it would be impossible for a technical glitch to create "perfectly grammatical sentences that are exactly opposite in meaning." She reached out to contacts at SAGE, the journal's publisher, who said they would investigate, but she heard no more from them. In an email to *Science*, a SAGE spokesperson wrote that the publisher "addressed the issue directly with the editor at the time" and that Marcoulides now double-checks reviewer comments for consistency.

Later in 2012, Marcoulides invited Hoekstra to resubmit his paper. This time, Fidler's review made it through intact, and Hoekstra's paper was accepted—pivotal for him winning a permanent job at Groningen. In an email to *Science*, Marcoulides wrote that the reviewer comments automatically attached to his decision letter were "distorted" and his edits were intended to clarify his interpretation of Fidler's assessment. "In hindsight, I should have contacted her rather than attempting to resolve the problem on my own," he wrote. He added that he still sometimes edits reports for clarity or to remove inappropriate language.

"I think it's especially important that [editors] have really hard and fast rules for themselves."

Simine Vazire, *Collabra: Psychology*

Few journals offer explicit guidance on when editing peer-review reports is and isn't permissible. Alfred says they ought to, and should also allow reviewers to opt out from being edited. No matter how well-intentioned editors may be, she says, clear policies will ensure a transparent and unbiased process. Many journals have a safeguard: They share all reviews and the editorial decision with reviewers, allowing them to see how their comments were communicated to the authors. But about 20% of the editors in the survey report that their journals do not send out either the reports or the decision letters to reviewers.

Simine Vazire, editor-in-chief of *Collabra: Psychology* and a colleague of Fidler's, argues for a bright line on the question: no edits without reviewer permission. Her journal has no policy on the issue, but she is considering proposing one. Without clear boundaries, she says, it becomes easy to rationalize changes, adding that journal editors have lots of power and little accountability. "There's no one watching over editors," she says. "I think it's especially important that they have really hard and fast rules for themselves." ■

NEUROSCIENCE

Efforts to control monkey brains get a boost

With open data project, primate optogenetics confronts stumbling blocks

By **Kelly Servick**

When neuroscientist Sébastien Tremblay set out to manipulate monkeys' brains with light, colleagues had sobering advice: "It's more difficult than it sounds."

Tremblay, who works in neuroscientist Michael Platt's lab at the University of Pennsylvania, uses light to activate or silence precise groups of neurons and probe their role in brain function. The method, called optogenetics, works well in rodents, but studies in nonhuman primates are critical if it's ever going to become a therapy for humans—to suppress seizures, for example, disrupt tremors in Parkinson's disease, or even project images into the brain of a blind person (*Science*, 8 November 2019, p. 671).

But in spite of more than 10 years of work, progress has been slow. The tools for rendering cells light sensitive were largely refined in rodents and behave unpredictably in monkeys. It's hard to illuminate enough tissue in large primate brains to reliably change animals' behavior. Researchers have devised their approaches by trial and error, often without knowing what had or hadn't worked for others.

Tremblay, Platt, and colleagues from 45 primate optogenetics labs in nine countries hope to change that with the Nonhuman Primate Optogenetics Open Database, which published its first results last week. The database contains minute details of successes and failures, many of which have gone unpublished. And if it can be sustained, it may soon include tests in monkeys of promising new optogenetic tools. The open-data approach "is tremendously powerful, tremendously useful to the community," says Hongkui Zeng, a neuroscientist who develops optogenetic tools for mice at the Allen Institute for Brain Science and was not involved in the project.

In optogenetics, researchers endow brain

Methods to influence rodent neurons using light have not translated smoothly into primate brains.

cells with a gene for one of several opsins, light-sensitive proteins from microbes. These proteins can influence the flow of ions in and out of a neuron to control whether it fires an electrical signal. Depending on the opsin, researchers can excite or inhibit neurons by shining light on them, usually via an implanted optical fiber.

Strains of mice have been genetically engineered to express opsins in their brains from birth. But for now, getting an opsin into monkey neurons means infecting the cells with a virus injected through a hole in the skull. Along with opsin DNA, the virus typically carries a sequence called a promoter, which restricts the opsin's expression to certain cell types.

There's no proven formula for getting monkey brain cells to make opsins. In the hunt for the right combination of viral strains and promoters, "we kind of entered this voodoo land," says Arash Afraz, a neuroscientist at the U.S. National Institute of Mental Health. Scientists relied on rumors of other labs' successes and failures, he says, and were afraid to vary a recipe once they got it working. Unlike with plentiful mice, researchers couldn't afford to use lots of monkeys to hone their technique, he adds. "We value them more. They have names. We view them as our colleagues, in a sense."

Afraz hopes the database, which he contributed to, will minimize wasted effort by pooling the field's failures. It catalogs 1042 viral injections performed in nonhuman primates, 552 of them previously unpublished. Seven-tenths of the experiments were in rhesus macaque monkeys. Tremblay can't be sure the database is exhaustive, but the 66 groups he invited to contribute—identified through publications and referrals from colleagues—represent the majority of labs active in the field, he says.

In a 19 October paper in *Neuron* introducing the database, the team estimates the success rate of the most commonly used vectors, promoters, and opsins in the data set. About half of the experiments in monkey brains looked for changes in neural activity after cells were hit with light; 69% found a strong effect. Of the 20% of experiments that aimed to influence an animal's behavior—to prompt an eye or hand movement, for example—nearly half saw a weak effect or none at all.

Failure likely discouraged some researchers from publishing studies, says Julio Martinez-Trujillo, a neurophysiologist at Western University and contributor to the project. His group has tried, without success, to evoke eye movements in one macaque and to impair working memory function in another. "This is the first paper that shows our experience," he says.

Such attempts probably fail in part because the virus doesn't reach enough of the brain, Tremblay says. A single injection can infect about 1 cubic millimeter of tissue—a broad swath of a mouse's brain, but a puny fraction of a monkey's. And scientists want to avoid multiple injections that could cause excessive tissue damage. Instead, some labs are trying to send the virus farther by injecting it at high volumes and pressures, a technique called convection-enhanced delivery.

Others hope to eliminate the need for brain injections by designing viruses that are small enough to cross into the brain via its tiny capillaries after being infused into a vein. In a June preprint on bioRxiv, neuroscientist and bioengineer Viviana Gradinaru and her team at the California Institute of Technology describe such an engineered virus that selectively infects the neurons of a marmoset.

Delivering light to large brains is a hurdle as well. "Say I am using a 200-micron-diameter fiber optic for stimulating my mouse brain," Afraz explains. "To scale that up, I'd have to stick a flashlight in the monkey's head." In a bioRxiv preprint last month, Afraz and colleagues describe a possible alternative: a 5-square-millimeter array of 24 light-emitting diodes (LEDs), each of which can produce as much light as a typical optical fiber. By laying this array over a monkey's cortex, researchers might illuminate a relatively broad brain area without multiple implanted fibers, Afraz says. They can also use individual LEDs to excite separate parts of the cortex in precise patterns.

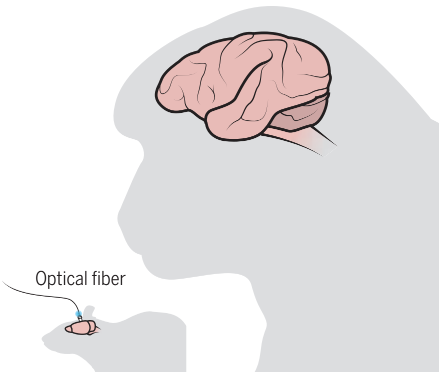
Other groups are developing more sensitive opsins so that weaker light can affect more distant tissue. In a study in mice reported on 5 October in *Nature Biotechnology*, a group led by Stanford University neuroscientist Karl Deisseroth—one of the original developers of optogenetics—used a highly sensitive opsin called ChRmine to activate neurons several millimeters below the brain's surface with light from outside the rodent's skull.

"I can't wait to test them," Laval University molecular biologist Marie-Ève Paquet says of these ultrasensitive opsins. She's part of a Canadian collaboration that tests and disseminates emerging optogenetics tools. As opsins, promoters, and viruses make their way to participating research groups, Paquet's team plans to upload its results to the new database.

To keep the database up to date, she says, "the community really has to be motivated," especially because she expects the next few years to bring a boom in studies to influence and understand the brain circuits of some of our closest animal relatives. ■

Scaling up

Monkey brains have been harder to manipulate with light than mouse brains, in part because they're much larger.



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Science

Efforts to control monkey brains get a boost

Kelly Servick

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