Scientists ‘Inject’ Information Into Monkeys’ Brains

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By Carl Zimmer

When you drive toward an intersection, the sight of the light turning red will (or should) make you step on the brake. This action happens thanks to a chain of events inside your head.

Your eyes relay signals to the visual centers in the back of your brain. After those signals get processed, they travel along a pathway to another region, the premotor cortex, where the brain plans movements.

Now, imagine that you had a device implanted in your brain that could shortcut the pathway and “inject” information straight into your premotor cortex.

That may sound like an outtake from “The Matrix.” But now two neuroscientists at the University of Rochester say they have managed to [introduce information directly into the premotor cortex of monkeys](http://www.cell.com/neuron/fulltext/S0896-6273%2817%2931034-6). The researchers published the results of the experiment on Thursday in the journal Neuron.

Although the research is preliminary, carried out in just two monkeys, the researchers speculated that further research might lead to brain implants for people with strokes.

“You could potentially bypass the damaged areas and deliver stimulation to the premotor cortex,” said Kevin A. Mazurek, a co-author of the study. “That could be a way to bridge parts of the brain that can no longer communicate.”

In order to study the premotor cortex, Dr. Mazurek and his co-author, Dr. Marc H. Schieber, trained two rhesus monkeys to play a game.

The monkeys sat in front of a panel equipped with a button, a sphere-shaped knob, a cylindrical knob, and a T-shaped handle. Each object was ringed by LED lights. If the lights around an object switched on, the monkeys had to reach out their hand to it to get a reward — in this case, a refreshing squirt of water.

Each object required a particular action. If the button glowed, the monkeys had to push it. If the sphere glowed, they had to turn it. If the T-shaped handle or cylinder lit up, they had to pull it.

After the monkeys learned how to play the game, Dr. Mazurek and Dr. Schieber had them play a wired version. The scientists placed 16 electrodes in each monkey’s brain, in the premotor cortex.

Each time a ring of lights switched on, the electrodes transmitted a short, faint burst of electricity. The patterns varied according to which object the researchers wanted the monkeys to manipulate.

As the monkeys played more rounds of the game, the rings of light dimmed. At first, the dimming caused the monkeys to make mistakes. But then their performance improved.

Eventually the lights went out completely, yet the monkeys were able to use only the signals from the electrodes in their brains to pick the right object and manipulate it for the reward. And they did just as well as with the lights.

This hints that the sensory regions of the brain, which process information from the environment, can be bypassed altogether. The brain can devise a response by receiving information directly, via electrodes.

Neurologists have long known that applying electric current to certain parts of the brain can make people involuntarily jerk certain parts of their bodies. But this is not what the monkeys were experiencing.

Dr. Mazurek and Dr. Schieber were able to rule out this possibility by seeing how short they could make the pulses. With a jolt as brief as a fifth of a second, the monkeys could still master the game without lights. Such a pulse was too short to cause the monkeys to jerk about.

“The stimulation must be producing some conscious perception,” said Paul Cheney, a neurophysiologist at the University of Kansas Medical Center, who was not involved in the new study.

But what exactly is that something? It’s hard to say. “After all, you can’t easily ask the monkey to tell you what they have experienced,” Dr. Cheney said.

Dr. Schieber speculated that the monkeys “might feel something on their skin. Or they might see something. Who knows what?”

What makes the finding particularly intriguing is that the signals the scientists delivered into the monkey brains had no underlying connection to the knob, the button, the handle or the cylinder.

Once the monkeys started using the signals to grab the right objects, the researchers shuffled them into new assignments. Now different electrodes fired for different objects — and the monkeys quickly learned the new rules.

“This is not a prewired part of the brain for built-in movements, but a learning engine,” said Michael A. Graziano, a neuroscientist at Princeton University who was not involved in the study.

Dr. Mazurek and Dr. Schieber only implanted small arrays of electrodes into the monkeys. Engineers are working on implantable arrays that might include as many as 1,000 electrodes. So it may be possible one day to transmit far more complex packages of information into the premotor cortex.

Dr. Schieber speculated that someday scientists might be able to use such advanced electrodes to help people who suffer brain damage. Strokes, for instance, can destroy parts of the brain along the pathway from sensory regions to areas where the brain makes decisions and sends out commands to the body.

Implanted electrodes might eavesdrop on neurons in healthy regions, such as the visual cortex, and then forward information into the premotor cortex.

“When the computer says, ‘You’re seeing the red light,’ you could say, ‘Oh, I know what that means — I’m supposed to put my foot on the brake,’” said Dr. Schieber. “You take information from one good part of the brain and inject it into a downstream area that tells you what to do.”

The Blind Fish that Should Have Diabetes, But Somehow Doesn’t

*The Atlantic*, Mar 21, 2018

By Ed Yong

Millions of years ago, a small, unremarkable fish called the Mexican tetra started swimming into the caves of eastern Mexico. In the all-encompassing darkness of these limestone caverns, the tetras’ eyes, which [take a lot of energy to build and maintain](http://advances.sciencemag.org/content/1/8/e1500363), were useless luxuries. Over several generations, the cave fish lost them entirely. Today, they are born with small eyes that gradually waste away as they get older.

The tetras’ eye sockets, however, don’t go to waste; they can use them to store fat. Blind cave fish are stockier than their cousins that live on the surface, and some have fat-filled humps. “You dissect them and you see that their body cavity is full of visceral fat that surrounds their organs,” says [Misty Riddle](https://connects.catalyst.harvard.edu/Profiles/profile/34212292), from Harvard Medical School. [Some of them eat more](https://www.ncbi.nlm.nih.gov/pubmed/26170297) than their sighted relatives, but even when the two groups are fed the same amounts of food, the blind ones put on more weight. These are sensible adaptations for living in caves, where food is scarce and starvation is always just around the corner.

Now, Riddle and her colleague Ariel Aspiras have discovered [another bizarre metabolic trick](http://nature.com/articles/doi%3A10.1038/nature26136) that may help the cave fish cope with a world of little food. They’ve relinquished the tight control that most animals exert over the levels of glucose (sugar) in their blood. Instead, they allow those levels to fluctuate wildly, in a way that’s reminiscent of type 2 diabetes. And yet, these fish have none of the health problems that diabetic humans experience.

When humans eat a meal, our blood sugar spikes. Our pancreas reacts by releasing insulin, a hormone that tells the liver and other organs to start absorbing the extra glucose. When we fast, our blood glucose drops, and the pancreas releases glucagon, a different hormone that prompts the liver to release glucose instead. Through the actions of these two hormones, we keep our blood sugar at an even keel.

In the blind cave fish, that keel is broken. Their blood glucose, rather than swelling and dipping in gentle waves, spikes and crashes instead. It typically stays at a much higher level than that of the surface fish. It remains high if the cave fish go without food for a day. And it falls off the charts if they starve for a week.

That’s not because they have something wrong with their pancreas. Instead, their muscles are unusually insensitive to insulin. In humans, insulin resistance and high blood sugar are two of the defining traits of type 2 diabetes—a disorder that can lead to long-term problems like heart disease, strokes, and [kidney failure](https://en.wikipedia.org/wiki/Kidney_failure). But the cave fish “are happy, normal, and healthy despite having this extreme elevation in their blood glucose,” Riddle says. “We were really shocked to see that.”

Her surprise deepened when she and her colleagues worked out why the fish are resistant to insulin. The hormone works by sticking to a protein called the insulin receptor, like a key entering a lock. The cave fish have a mutation in this receptor, which likely changes the shape of the lock so that the insulin key no longer fits. Riddle and Aspiras confirmed this by using a gene-editing technique called CRISPR to introduce the same mutation into the insulin receptor of zebra fish—a species that’s commonly used in laboratory studies. These modified zebra fish became insulin-resistant and put on more weight, just like the blind cave fish.

This is a very strange result, for two reasons. First, insulin is a growth hormone that’s important in the development of fat cells. Humans who have broken insulin receptors are typically extremely thin, as if they were in a permanent state of starvation. In tetras, those same broken receptors seem to have the opposite effect.

Second, the very same mutation that Riddle and Aspiras found in the cave fish causes [Rabson–Mendenhall syndrome](https://en.wikipedia.org/wiki/Rabson%E2%80%93Mendenhall_syndrome) in humans—a severe, diabetes-like illness that manifests in infancy and typically kills people before their third birthday. The cave fish, however, can live as long as their surface-dwelling cousins—if not longer. Some of the animals in Riddle’s lab have been alive for at least 14 years. “At that age, they look similar to a surface fish that’s 3 years old,” she says. “We don’t really have high enough numbers of the old fish to say that they age more slowly, but it certainly seems that they’re not aging prematurely.”

Indeed, the cave fish probably have several such adaptations. Riddle and Aspiras did most of their work on tetras from two caves, Tinaja and Pachón, which are part of the same mountain range. But in Molino cave, which is part of a different range, the cave fish evolved independently. They *also* have high blood-sugar levels, but they don’t have the same insulin-receptor mutations. They must have their own unique techniques for changing their response to insulin.

By learning more about these adaptations, the team hopes to better understand how diabetes manifests in people, and perhaps find ways of treating it. It wouldn’t be the first time, either. Byetta, a drug that’s commonly used to manage type 2 diabetes, was developed after studying the [saliva of the Gila monster](https://www.theatlantic.com/science/archive/2016/10/arizonas-adorable-monster/504470/) lizard.

“The [cave fish] study supports the idea that using therapies to enhance insulin sensitivity may prevent or delay the onset of type 2 diabetes,” says [Juleen Zierath](https://ki.se/en/people/julzie), from the Karolinska Institute. Still, she notes that most humans live in a very different world to that of the cave fish—one of ample nutrients. When we cut down on calories, we tend to become moresensitive to insulin, not less. As such, it’s unclear what lessons we can draw from the cave fish.

[Anna Krook](https://ki.se/en/people/annkro), also from the Karolinska Institute, agrees. After all, she notes that even mammals like mice and humans can react to the same insulin-receptor mutations in very different ways, which should give us pause before extrapolating from one animal to another. “We can and should use this opportunity to gain important insights about life with high glucose, but in the end it may not always translate across species,” she says.