Feature: Giving blind people sight illuminates the brain's secrets

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By Rhitu Chatterjee

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NEW DELHI—Manoj Kumar Yadav came into this world with cataracts. In developed countries, a simple surgery cures this disabling eye affliction within the first few months of life. But like the vast majority of people in India, Yadav was born in a village, with limited access to health care. His parents are poor and uneducated. They didn't even realize their infant son was blind until he began to bump into things while crawling. Years later, when regional doctors examined Yadav, they told him he would never see. “So we gave up,” recalls Yadav, now 22.

“We thought there was no point in running around anymore trying to find treatment.”

Then in 2011, a team of eye specialists from New Delhi visited Yadav’s village in Uttar Pradesh state. They screened him and other blind children and kindled hope that Yadav might someday be able to see after all. That August, he and his father took a 13-hour train journey to India’s capital. Here at the Dr. Shroff Charity Eye Hospital, a surgeon excised his cataract-ridden lenses and slipped in synthetic ones in their place.

When the doctors removed the bandages a day later, Yadav’s world was filled with light, and shapes that to him were inscrutable. He couldn’t tell people from objects, or where one thing ended and another began. His brain, deprived of information from his eyes for 18 years, didn’t know what to make of the flood of visual stimuli. But over the coming months, his brain gradually learned to interpret the signals it was receiving from his eyes, and the blurry and confusing world began to come into focus.

Yadav is among hundreds of blind children, teenagers, and young adults who are now able to see thanks to a project called Prakash, which means “light” in Sanskrit. India may have the largest number of blind children in the world. Estimates range from 360,000 to nearly 1.2 million. The vast majority live in rural areas, their quality of life worsened by poverty, lack of access to health care, and a dearth of facilities for the disabled. Nearly 40% of these children are thought to have preventable or treatable blindness, caused by congenital cataracts, damaged corneas, and eye infections.

Led by neuroscientist Pawan Sinha, Project Prakash began in 2004 as a humanitarian effort to address this problem. But it also had a scientific goal. Sinha, based at the Massachusetts Institute of Technology in

Cambridge, hypothesized that the newly sighted children could help answer a question that had long intrigued him: How does the brain learn to see? Initially funded by the U.S. National Institutes of Health as an exploratory grant, Prakash has since grown into a groundbreaking effort in neuroscience. For years, physicians assumed that once a blind person passed a critical age in early childhood without vision, their brain would never be able to make sense of the visual world. Through patients like Yadav, Prakash has demolished that assumption.

"It took me about one-and-a-half years before I could see everything clearly," Yadav says. Short and slight, Yadav is polite and soft-spoken, and his eyes restlessly dart back and forth. The condition, nystagmus, is a relic of his congenital blindness. But with the cataracts gone, it doesn't keep him from seeing. "Now, I can even ride a bicycle through a crowded market," he says.

Prakash "beautifully demonstrates that there is still room for plasticity and recovery" in patients who have grown up blind, says Olivier Collignon, a neuroscientist at the University of Trento in Italy. That doesn't mean the newly sighted will be able to see as well as those born sighted, he cautions. "That is not supported by data."

Still, the surprising capacity of Prakash patients to gain substantial vision is rewriting visual neuroscience. As the medical payoff of their efforts became clear, project leaders have launched a series of studies, from low-tech tests of patients' responses to visual illusions to functional MRI (fMRI) imaging of their brains reorganizing in response to visual input. While probing how the newly sighted process visual cues, project scientists are peeling away layers of mystery about which aspects of sight come preprogrammed and which are shaped by experience.

OPHTHALMOLOGY TEXTBOOKS have long suggested that trying to give sight to teenagers who have been blind since birth is unlikely to succeed. In a series of groundbreaking studies in cats and monkeys that won them the Nobel Prize in Physiology or Medicine in 1981, Torsten Wiesel and David Hubel showed that if the brain is deprived of visual signals during a critical period soon after birth, vision is impaired for life. There have been no similar experiments in humans for ethical reasons, but scientists assumed our critical window slams shut between ages 6 and 8. That belief guided surgeons at Shroff, who turned away congenitally blind children older than 8 years.

However, Sinha unearthed a couple of studies from several decades ago that suggested congenitally blind adults could gain at least some vision after cataract surgery. Then in 2002 and 2003, while traveling across India to understand the extent and causes of blindness, Sinha met four individuals, all of whom had had cataracts removed as adolescents and had acquired some vision. The anecdotal evidence was enough to persuade Sinha that, given recent advances in medicine, Project Prakash was worth pursuing, and he convinced the Shroff surgeons to give it a try.

The team's eye specialists and health workers set up screening camps in rural areas to identify children who could benefit from surgery and nonsurgical interventions like eyeglasses, eye drops, and medication. So far, more than 1400 children have received nonsurgical care and nearly 500 children and young adults have undergone cataract operations. About half of those patients—the ones that the scientists are convinced were blind from birth—become research subjects.

Their recent studies show that experience isn't critical for certain visual functions. Instead, the brain appears to be prewired to interpret at least some simple aspects of the visual world. The evidence comes from tests of visual illusions that are also helping settle a longstanding debate about why the brain misinterprets particular kinds of images.

When our perception of an image differs from reality, we experience a visual illusion. Some neuroscientists think the innate wiring of our brains is responsible for illusions; others think they are a product of learning. Resolving this debate has proved difficult, says Susana Martinez-Conde, a neuroscientist at the State University of New York Downstate Medical Center who studies illusions. "Babies can't report on visual experience," she says. "And it wouldn't be ethical to deprive a baby of visual experience to test this." The answer was "anybody's guess," she says—until Project Prakash started studying the newly sighted children, whose vision, when first acquired, is close to a newborn's.

In 2010 and 2011, Sinha's team picked nine children from those about to undergo cataract surgery. The subjects had been blind since birth, according to the parents and surgeons at Shroff Charity Eye Hospital. Soon after their bandages were removed, the scientists showed them the Ponzo illusion. First demonstrated more than a century ago, this illusion typically involves lines converging on the horizon (like train tracks) and two short parallel lines cutting across them.

Although the horizontal lines are identical, the one nearer the horizon looks longer. The dominant explanation for the Ponzo illusion is that it is a result of the brain's experience interpreting 2D images as 3D scenes, with the individual elements of images perceived to be at various depths and distances.

"That learning leads us to associate these two identical lines in this illusion as being at two different distances from us," Sinha explains. The brain interprets the line nearer the apparent horizon as farther away and therefore longer than the other identical line.

If the Ponzo illusion were the result of visual learning, the Prakash kids wouldn't fall for it. But to the team's surprise, the children were just as susceptible to the Ponzo illusion as were control subjects with normal vision: They consistently found the line closer to the horizon longer, the team reported in Current Biology in May.

The kids also fell for the Müller-Lyer illusion, a pair of lines with arrowheads on both ends; one set of arrowheads points outward, the other inward toward the line. The line with the inward arrowheads seems longer. "All we can say based on these results is that it's not experience," Sinha says. "It's something else. It's probably being driven by very simple factors in the image that the brain is probably innately programmed to respond to."

Martinez-Conde is willing to hazard a guess at how the Müller-Lyer illusion works. Her past research has shown that our eyes tend to notice corners more than straight lines. Perhaps, she says, our brain focuses on the corners of the outward arrowheads, making the line between them look shorter than the line with inward arrowheads. “But this should be taken with a big grain of salt because I don’t have any data to prove it.”

Whatever the mechanism, the new study adds to growing evidence “that we are not blank slates when we’re born,” Martinez-Conde says. Other evidence comes from a recent study by Amir Amedi, a neuroscientist at the Hebrew University of Jerusalem, and colleagues in which they used fMRI to compare the visual cortex of congenitally blind individuals with that of normally sighted ones. They found that the basic organization of the visual cortex of congenitally blind people is similar to that of the normally sighted, and both have similar connections between different parts of the cortex.

That means “we’re born with this machinery for seeing that in a way doesn’t require visual experience to emerge,” Amedi says. “The visual system comes with certain connections and computational biases.”

SUCH PREWIRING MAY HELP the Prakash children gain functional vision in the months following surgery, Amedi speculates. But experience and learning seem to play a bigger role in visual acquisition. “There is growing evidence that [even] adult brains can change in structure and function,” says Brigitte Roeder, a neuropsychologist at the University of Hamburg in Germany. For example, studies have shown that adults who regularly play action video games become better at certain visual tasks, like reading the fine print on a prescription bottle or tracking several friends moving through a crowd.

More relevant to the Prakash children is the ability to create a mental image of a 3D space. “Spatial imagery is very important in our lives,” says Prakash team member Tapan Gandhi, a neuroscientist at the Indian Institute of Technology, Delhi, in New Delhi. “If I ask you, think about your kitchen, where you’ve kept what, you can visualize it. This is very important for our daily lives.” But blind people aren’t adept at imagining spaces. When tested for this ability using a matrix and movable pegs, Prakash children before surgery perform poorly compared with normally sighted people, Gandhi says. Soon after surgery, however, they start to improve at spatial imagery tasks. Vision must be crucial to helping the brain create mental maps of spaces, he says. And the brain either does not have a critical window for this ability, or the window remains open until much later in life, Gandhi and colleagues reported in the 12 March 2014 issue of Psychological Science.

The team found similar adaptability in the ability to distinguish a human face from facelike images. Soon after surgery, Prakash patients cannot tell the difference. That too contradicts dogma: Homing in on faces is one visual capability that scientists think is innate. But after a few weeks, the newly sighted can identify a human face and start to recognize different faces. The team has also found that their patients quickly learn to connect touch with sight. In other words, they are soon able to recognize objects they touched while blindfolded when they see those objects from a distance.

But plasticity has its limits. Collignon and his colleagues studied a group of adults in Canada who were born with cataracts but had corrective surgery before they turned 1. Despite at least 2 decades of restored sight, every individual had slightly impaired vision. Their 3D perception and their ability to detect movement were also compromised, according to unpublished results. The researchers found that the brains of these individuals appear to be wired differently: Unlike normally sighted people, their visual cortexes also process sound, they reported in August in Current Biology.

“What is really striking here is that we are speaking of people who are deprived [of sight] for a few weeks to a few months, but it leads to longstanding reorganization of the brain to respond more to sound,” Collignon says. Prakash patients, who are blind for years, are also likely to have their visual cortex reorganized, he says, which could hinder recovery. “They have a trace of their past [in their brains], and their past is blindness,” he says. “These people will never be able to recover vision like someone who’s seen before.”

Sinha’s findings confirm this. The Prakash patients do not develop vision as sharp as normally sighted people’s. “Despite following these kids for several years, we do not find a progression of acuity to normalcy," Sinha says. That suggests a critical window for acuity that closes sometime before they turn 8—the youngest age Prakash has so far treated.

Yadav's experiences are typical. "I can read newspaper headlines with my glasses," he says. But 4 years since his surgery, he still has trouble reading the finer print in newspapers and books.

The window also seems to close early for contrast sensitivity: the ability to discern contrasts, shades, and patterns, one of the most basic functions of vision. In one test, Sinha's team shows Prakash kids four patterns—a house, a square, an apple, and a circle—and asks them to identify the patterns as they change in size and contrast. Normally sighted people can detect these patterns for a range of sizes, if the contrast is above a certain threshold.

For Prakash kids, their contrast sensitivity improves significantly up to several months after surgery, but never reaches normal levels. They remain stuck at detecting a limited range of sizes, and only when the contrast is fairly high.

Graham Crouch

Manoj Yadav bicycles to work in Gorakhpur, India. “I can ride a bicycle even in a crowded market,” he says.

Taken together, the findings demonstrate that there is no single critical period governing vision, says Amy Kalia, a postdoctoral fellow with Sinha. “Is vision recoverable or not,” she says, “is a more complex story.”

Training could help the Prakash children recover more visual function, says Uri Polat, a neuroscientist at Tel Aviv University in Israel. “The window doesn’t shut,” he says. “It becomes less sensitive.”

In 2004, Polat was the first to show that training can restore eyesight in adults with amblyopia, or lazy eye. A lazy eye prevents normal development of the visual cortex during early childhood. Patients have impaired binocular vision, as well as poor acuity and contrast sensitivity; the diminished sight was considered irreversible after age 10. Polat had patients look at a computer screen with variations of a Gabor Patch image, which has blurry black-and-white patterns that change in size and contrast. After just a month of training, his patients had better acuity and contrast sensitivity.

Amedi agrees that training is key, but thinks that it should involve touch and sound, too—senses that blind people rely on to navigate the world. His research has shown that to interpret sound or touch, they rely on parts of their visual cortex normally dedicated to vision. For example, they use the same part of the brain for braille that the sighted use for reading. Project Prakash plans to open a residential school next year to rehabilitate and educate children after cataract surgery using physical exercises and multisensory experiences.

ULTIMATELY, the Prakash team wants to reveal how restoring vision alters the visual cortex. They are beginning to probe changes in the brain with fMRI. When they image the visual cortex of a patient before and 2 days after surgery, different areas of the cortex appear to be working in synchrony. “So if you have high activity in one part of the cortex, you’ll have similar activity in another part of the cortex,” Sinha says. “It’s as if much of the visual cortex is pulsating together.”

However, just a couple of months after surgery, the fMRI picture starts to change. Different regions of the visual cortex light up differentially, suggesting a division of labor. Pictures of human faces shown to patients, for example, activate an area of the cortex known to respond to faces in normally sighted people.

“It makes a lot of sense,” Amedi says. “When they start processing visual information, they cannot perform tasks. They cannot identify an object, a person. It is all the same nonsense to them." But as time goes by, and the brain learns to distinguish objects, shapes, and faces, different areas of the visual cortex start to specialize.

Sinha, for one, did not expect these changes in the brain. "I was amazed by just how much, how massive the changes are and how quickly it happens, and how late in life it can happen," he says.

He also didn't expect the gusher of results the project has generated. "I was worried that having to work with fairly old children, we were setting ourselves up for failure."

Instead, the project has brought hundreds of young people like Yadav into the light—while putting the field of visual neuroscience in a new light as well.

To view a slideshow about Project Prakash, please click here.