



SCHOOLS FOR THE BLIND in India have helped find children eligible for vision-correcting surgery.



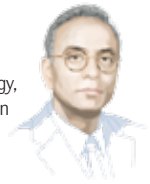
MEDICINE

ONCE BLIND AND NOW THEY SEE

SURGERY IN
BLIND CHILDREN
FROM INDIA
ALLOWS THEM
TO SEE FOR
THE FIRST TIME
AND REVEALS
HOW VISION
WORKS IN
THE BRAIN

By Parwan Sinha

Pawan Sinha, a professor of vision and computational neuroscience at the Massachusetts Institute of Technology, studies the mechanisms and principles by which the brain recognizes objects and scenes.



M

Y MOTHER USED TO KEEP A SMALL BLUE GLASS BOWL OF CHANGE NEAR the door of our house in New Delhi. When she went out, she would take a few coins as alms for the poor that one inevitably sees on the city's streets. Given how quickly you can become desensitized to the abundance of human misery in India, I was always impressed by her unwavering adherence to this ritual.

The bowl lay unused for several months as my mother battled cancer. When I went back to India in 2002, a year after her death, I noticed that it was one of the few items of hers that my father had saved. Little did I realize that it was going to change my life.

One wintry afternoon during my visit, while stepping out of the house to visit a friend, I reached in the bowl for a few coins and put them into my pocket. It was bitterly cold, and I was glad to find a cab with windows that closed all the way, never a certainty in New Delhi. After a few minutes, the cab stopped at an intersection. Traffic was surprisingly light, and I noticed a small family huddled by the side of the road. I pulled out the coins, rolled down the window and beckoned to them.

They slowly made their way to me, with the two children holding on to the woman's sari. It was gut-wrenching to see the emaciated barefoot children dressed in thin cotton rags. Compounding my discomfort, I noticed that the children, who must have been six or seven years of age, were also blind. As the small family stood shivering outside my cab, I could see the cataracts in the children's eyes. This surprised me because I had only ever seen cataracts in older people. The traffic light turned green. I put the coins in the mother's hand and watched the family disappear as the cab pulled away. For the next several days, the children's faces haunted me. I tried to learn as much as I could about childhood blindness in India. What I read was shocking.

India is home to one of the world's largest populations of blind children, estimated at nearly 400,000. The visual handicap, coupled with extreme poverty, greatly compromises the children's quality of life; moreover, mortality rates are frighteningly high. The World Health Organization estimates that up to 60 percent of children die within one year of going blind. Less than 10 percent of these children receive any education. For blind girls, the outlook is even more dire. Many are confined to home and suffer physical or sexual abuse.

Distressing as these numbers are, they became even more disturbing to me as I read that much of the suffering was needless; blindness in nearly 40 percent of the children was treatable or preventable. Many youngsters, however, never receive medical care because the treatment facilities are concentrated in major cities, and nearly 70 percent of India's population lives in villages. These circumstances mean that a blind child in a financially strapped rural family is likely destined to live a dark and tragically short life.

I took in these numbers with a sense of incredulity. After all, I had grown up in India. How could I have remained unaware of this problem? And how could such things run so counter to the popular narrative of India as a rising economic superpower? I decided to make another trip to India. I visited villages around Delhi, in the southern state of Andhra Pradesh

IN BRIEF

India is home to one of the world's largest populations of blind children, estimated at nearly 400,000. Many of these children receive no education, and girls are often victims of physical and sexual abuse.

As a neuroscientist, the author decided to try to help cataract-stricken children and young adults gain the ability to see the world far beyond the age at which developing vision was deemed to be possible.

Surgery often proved a success, even for some of those well into their 20s. The procedure also provided the scientists on the author's team with a new understanding of the functioning of the visual system.

Putting Together a New Visual World

When children and young adults of Project Prakash see the world for the first time, they have difficulty assembling parts of a scene into an integral whole. A photograph of girls dancing demonstrates the problems involved. Fragments of color, brightness and texture need to be organized by the visual system into coherent objects.



The middle illustration depicts the location of these diverse elements. Success comes when a collection of static objects, with defined borders (*right*), starts to move. The brain integrates rhythmic steps and upthrown arms into the perception of a single, integral entity, the shape of the dancers' bodies.

and in the delta of the Ganges in West Bengal. The many blind children I met convinced me that the statistics were based in fact. And the desperate poverty I saw in these villages helped me understand why so many of them remained untreated.

My experience on that winter afternoon in New Delhi marked the beginnings of a personal journey that has yet to end. I resolved to help these blind children gain sight. And as a scientist, I realized that doing so presented a valuable opportunity to answer one of the most challenging questions in neuroscience: How does the brain learn to see?

AN ANSWER IN A QUESTION

SINCE MY DAYS IN GRADUATE SCHOOL at the Massachusetts Institute of Technology, this question had both fascinated and frustrated me. How does the confusing mess of colors, brightness and textures that impinges on our retina every waking moment organize itself into a meaningful collection of objects that transforms into, say, the outlines of the arms and torso of a dancing girl—and the crisscrossing blue and green on her plaid skirt?

The main approach for studying how the visual system develops involves experimenting with infants. Although it has yielded valuable results, it also has significant shortcomings. These experiments are difficult to perform. An infant's limited ability to comprehend and respond and even to stay awake for long periods strongly limits the scope of questions that can feasibly be asked. Another complicating factor is the simultaneous changes that can occur in related but distinct brain subsystems as the child grows—such as regions responsible for motivation, focusing attention and controlling eye movements.

Knowing all of this, in the summer of 2002 I found myself grappling with two seemingly unrelated questions. How does the brain learn to make sense of visual information? And, with memo-

ries of my experience in New Delhi still fresh, how could I help provide sight-restoring surgeries to congenitally blind children?

I still remember the thrill of realizing that the two questions were complementary—one held the answer to the other. Following the progress of a newly sighted child could help us understand visual learning, and scientific funding applied to such a research undertaking could help provide treatments. I marveled at how well the two needs fit together and, somewhat self-centeredly, how relevant they both were to my life.

On returning to M.I.T., I described to my colleagues a plan to pursue research that combined these scientific and humanitarian objectives. Most were enthusiastic, but a few cautioned against embarking on such an ambitious undertaking prior to receiving tenure. I understood the risk, but I felt compelled to move ahead with the plan.

I submitted an application to the National Eye Institute (part of the National Institutes of Health). I was a little concerned that asking a U.S. government agency for money to fund surgeries in India might be a nonstarter. Also, the endeavor was logistically complex and lacked pilot data about its practicality. But the review committee saw the scientific and humanitarian potential of the work and awarded me an exploratory grant to establish feasibility. I was thrilled. This was my first NIH grant, and it reinforced in me the image of American science as a force for global good that does not shy away from encouraging risky undertakings unbound by parochial considerations.

The next step was to identify a medical partner in India where blind children could receive world-class surgical care. One ophthalmic center stood out: Dr. Shroff's Charity Eye Hospital (SCEH) in New Delhi. It had outstanding pediatric facilities, and its physicians welcomed the project as an opportunity to help blind children and to engage in research.

All the pieces were in place. Still, we needed a name, one that would reflect our dual mission of bringing light into people's lives and casting light on scientific questions. I did not have to think too long. The word for light in the ancient Indo-European language Sanskrit is *prakash*. We now had a name with an appealing touch of alliteration: Project Prakash.

WOULD SURGERY HELP?

WE UNDERTOOK the project in several stages. First, we identified children—and, in some cases, even young adults—who could benefit from treatment by setting up ophthalmic screening at camps in rural areas. A team of optometrists, ophthalmologists and other health care workers examined children for vision problems (refractive errors), eye infections and treatable blindness (primarily from congenital cataracts and damage to the cornea resulting from scarring). Children chosen as candidates for treatment went to the hospital in New Delhi for a more thorough examination, including ophthalmoscopy (to see to the back of the eye), ultrasound of the eyes, and assessment of the child's general health and fitness for surgery. Dates for surgery were then set after consultation with each child's guardian.

Cataract surgery for a child is much more complicated than for an adult. Pediatric surgery requires general anesthesia and intensive follow-up care. The surgical procedure involves breaking up the hardened opaque lens into little pieces, excising these fragments via a small incision at the edge of the cornea and replacing the damaged natural lens with a synthetic one. Project Prakash bears the roughly \$300 cost—and children return for periodic postoperative checkups.

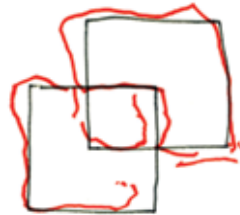
As this work got under way, one worry nagged me. I wondered whether our surgical intervention, though well intentioned, was coming too late to be of any help. Were we perhaps past a critical period early in life that requires intensive use of the eyes and visual brain circuits, an interval past which visual capacity is incapable of developing? The idea was not implausible. An English surgeon, William Cheselden, gave the first account of delayed sight onset in 1728 in a 13-year-old boy born with cataracts in both eyes. Cheselden noticed that the boy had severely impaired vision even after the removal of the occlusions.

Controlled studies of visual deprivation in animals painted a similarly dismal picture. Torsten Wiesel and David Hubel, both of whom went on to win the Nobel Prize in 1981, had described the dramatic adverse consequences of early visual deprivation

FIRST SIGHT

Only the Parts, Not a Whole

A newly sighted child's tracings reveal a piecemeal view of even two-dimensional figures. Each area of overlapping boxes was perceived separately, as indicated by red squiggles. The boy also saw segments of a cow and of a ball and its shadow—all delineated in green—to be distinct objects. Consequently, he was unable to identify any of these images.



in cats. In this context, it was natural to wonder whether providing eye surgeries late in childhood would serve any useful purpose.

I felt, though, that the treatments were worth undertaking. It was risky to read too much into the old accounts such as Cheselden's. The poor surgical outcomes could well have resulted from tissue damage to the eyes, a result of crude surgical techniques, such as couching, an antiquated method for cataract removal. And most of the animal studies had looked at the suturing shut of one eye, whereas the Prakash children had suffered occlusion in both eyes. Somewhat surprisingly, depriving vision in one eye has more adverse consequences for sight in that eye than if both eyes were to be deprived together. Whether any visual function could be acquired after treatment for blindness late in childhood was still a largely open question.

NOW WE SEE

THE GREAT AMERICAN psychologist William James described an infant's perceptual world as "a blooming, buzzing confusion" that precedes the maturation of the visual system. The question for Project Prakash was whether this period—a complex bombardment of color, shape and movement that is perhaps an early stage of normal visual development—mirrors the experiences of newly sighted Prakash children, some of whom are in their 20s when they first gain sight. Does their visual system ever undergo the anarchic but necessary first steps to organize the incoming images in any meaningful fashion? The term "organization" has two meanings here. For a person to

"see," the various pieces of an image must cohere into distinct objects, a process termed *intramodal* organization. The second requirement, *intermodal* organization, has to do with the interaction of vision with other senses.

Our ability to partition an image into separate objects is so well honed that it seems effortless. We open our eyes, and the world falls into place, an orderly collection of things. Yet we have found that the experience of a Prakash child soon after gaining sight is different. The newly sighted exhibit profound impairments. They are unable to organize the many regions of different colors and brightness into larger assemblies. Many features of ordinary objects—the overlapping sections of two squares or a section of a ball delineated by the lacing on its surface—are perceived as entirely separate objects, not component parts of larger structures. It is as if the visual scene for a newly sighted person is a collage of many unrelated areas of color and

luminance, akin to an abstract painting. This perceptual over-fragmentation makes it difficult to detect whole objects.

The Prakash patients' failure raises a question that has preoccupied scientists for nearly a century: What cues allow us, as individuals with normal vision, to parse complex images correctly? The answer seems to lie in the way that the brain naturally arranges visual inputs by what are known as grouping heuristics (referred to as Gestalt cues of grouping, after the psychological research movement in the early 20th century). For instance, a basic rule programmed into the visual system induces aligned lines in an image to be grouped together because they most likely arise from boundaries of the same object.

Project Prakash is helping to lay out the landscape of what can and cannot be accomplished when a child gains vision at a late age.

None of these cues appears effective for the Prakash children immediately after gaining sight, but interesting changes occur over time. I vividly remember SK, the very first Prakash patient to give us this hint. He was a 29-year-old man we met in a cramped hostel for blind youth on the outskirts of New Delhi. A quick examination revealed that he had congenital aphakia (from *phakos*, Greek for "lens/lentil"), a rare condition in which a child is born without lenses in the eyes. The visual world for SK was highly degraded, far worse than what defines legal blindness in the U.S. He had adapted by walking with a white cane and conducting his studies in braille. Remarkably, all that was needed to correct his aphakia was a \$20 pair of glasses that could compensate for his missing natural lenses, which SK could not afford.

We had glasses made for SK and then tested his vision. What struck us right away was that contrary to our naive expectations, SK did not appear particularly thrilled about his improved vision. His visual world, our tests revealed, was a bewildering collection of many regions of different colors and brightnesses, with little to glue them together into coherent entities. Even simple line drawings, such as a circle overlapping a square, appeared to him to be a set of strangely shaped interlocking pieces (despite his prior familiarity with the concepts of squares and circles through touch). SK had a hard time delineating whole objects in photographic images. Shading and shadows, overlaps and occlusions posed insurmountable hurdles for him; every region of a different hue or luminance seemed to him to be a distinct object.

Interestingly, this confusing soup of regions gelled into meaningful structure with the introduction of one particular visual cue: motion. Images that were hopelessly confusing for SK when static became interpretable when their constituent parts moved. Videos of SK inspecting an image show an almost magical transformation brought about in response to motion.

We followed SK's experiences with vision for several months. He continued exhibiting difficulties in interpreting static images.

Just as we had begun to resign ourselves to the idea that SK's image-parsing abilities might be permanently compromised, things changed. A year and a half after the initial intervention, without any training other than his exposure to the visual world around him, SK made marked improvements. He was now able to correctly parse static images and even expressed the happiness he felt about his improved vision. It was a tremendously gratifying conclusion to a chapter that had held us in great suspense.

In subsequent studies with others much younger than SK, we found a recapitulation of his experience. Many months after encountering difficulties on the image-parsing task, they begin to succeed in organizing their perceptions into coherent objects. The time needed to acquire this skill appears to depend on the age at which the child received treatment, with younger children learning more rapidly than older ones.

What underlies this improvement? Theory suggests that motion may play the part of a "teacher," training the visual system to parse images even when they are static. With the rule "things that move together belong together," a person's visual system can eventually learn to group images via static attributes such as color and orientation.

The brain, of course, does more than pick out the elements of a visual scene. It also connects to the realms of sound, touch, smell and taste—creating a sensory panorama via intermodal organization. How sight is linked to sound and other senses has preoccupied philosophers and neuroscientists for centuries. In 1688 Irish scientist William Molyneux wrote to British philosopher John Locke: "Suppose a man born blind, and now adult, and taught by his touch to distinguish between a cube and a sphere of the same metal.... Suppose then the cube and sphere placed on a table, and the blind man be made to see: query, whether by his sight, before he touched them he could now distinguish and tell which is the globe, which the cube?"

Locke included Molyneux's question in the 1692 edition of his famous monograph entitled *An Essay on Human Understanding*. Molyneux's query crystallized a series of fundamentally important questions: How do we link the different senses into a unified perception of reality? Are we born with this mental mapping of the world, or does it need to be learned through experience? Can it be acquired late in life? The pursuit of these ideas by Locke, George Berkeley, David Hume and other empiricists now bears on many of the issues vital to contemporary neuroscience.

In assessing whether the Prakash children can come to associate vision with the other senses, we have had an opportunity to directly address the Molyneux question. We work with children right after their sight surgeries and have them participate in a "match-to-sample" experiment. The child sees or touches a simple object on a blank background (the sample) and subsequently has to choose it from a pair of two different objects presented visually or by touch.

The case of YS, an engaging eight-year-old boy, with dense congenital cataracts in both eyes, provides an illustrative example. Like most Prakash children, YS was feeling comfortable by the second day after surgery and ready to work with the research team.



SCREENING CAMPS: Outreach sessions in schools and villages seek out children who might benefit from eye surgeries.



GETTING READY: A child submits to an ophthalmological exam to further determine suitability for treatment.

In the test, an intervening sheet ensured that YS could not see his hands. He would be given one object (the “sample”) to feel in his hands and then give back. He would then take the sample and another object in his hands and be asked to return the former. YS had no trouble at all picking out the sample for all object pairs presented to him. Similarly, in the purely visual domain, his performance was flawless. Yet in the crucial transfer task, recognizing visually what he had felt by hand, his performance plummeted. Four other children we worked with exhibited the same pattern of results.

Such findings lead us to believe that Molyneux’s question most likely has a negative answer—no discernible transfer of information from touch to vision takes place immediately after onset of vision. Interesting as this result seems, there is perhaps an even more intriguing addendum.

When we tested YS a week later, we were stunned to discover that his performance on the transfer task had climbed from being no better than would have been predicted by chance to achieving a near-perfect level. Two other children we followed also exhibited similar improvements. In periods as short as a few weeks, the Prakash children begin to achieve proficiency in visually identifying an object they had felt by touch, pointing to a latent ability for rapid learning to associate different senses. Taken together, these studies suggest that many years of congenital blindness do not preclude the development of sophisticated visual ability at a relatively advanced age. That realization turns out to be good news for us from both the scientific and clinical perspectives. It suggests that neural plasticity—the ability of the visual system, for one, to adapt to new experiences—exists even late in childhood or in young adults and that, based on our experiences, children would benefit from eye surgeries.

This knowledge has laid the foundation for a continuing in-

depth research program on visual development in late childhood. Working with Prakash participants ranging in age from six to older than 20 years, we have conducted assessments of a broad range of visual functions. The findings from these tests so far indicate that some key aspects of vision, such as acuity (how fine a visual pattern can be resolved), spatial contrast (changes in acuity as image contrast shifts) and optical stability, are compromised by extended deprivation. These deficits appear to be permanent because these measures do not reach normal levels even a year later.

When we look beyond these basic measurements toward so-called higher-order visual functions, however, we find evidence of significant skill acquisition—in particular, an ability to differentiate objects in an image and to link with other senses. The Prakash children also exhibit improvements in their ability to detect faces and mentally reason about the spatial arrangement of objects they observe.

THE NEW LANDSCAPE

THESE FINDINGS are beginning to give us a sense of the landscape of what can and cannot be achieved when a child gains vision at a late age. On the one hand, visual functions do not fade irretrievably if eyes and brain areas for visual processing are not subject to intensive use during the “critical period” that is believed to last for the first few years of childhood. On the other hand, early visual experience is undeniably important for the normal development of abilities such as high-resolution vision.

Early results provide a launchpad for a rich set of new investigations, some of which may be quite far removed from blindness. Based on the studies in Prakash, we are developing software for automatically discovering categories of visual objects in videos—faces, for instance. Moreover, the kinds of deficits we



IN SURGERY: A physician carefully excises cataracts, allowing a child to see clearly for the first time since birth.



FITTED FOR SEEING: A girl receives a postsurgical exam with the optometrist to get a prescription for eyeglasses.

have found in children integrating visual information soon after sight recovery bear similarities with those reported in studies of children with autism. This tentative link has now unfolded into a series of studies in my laboratory that seek to probe the causes of sensory-processing disorders in autism.


The journey ahead promises to be even more exciting than the terrain we have covered so far. A question that we have recently embarked on concerns the relation between the brain's structure and how it functions. We plan to use functional magnetic resonance imaging to look at changes in the cerebral cortex of a newly sighted child, comparing what happens when treatment begins at different ages to determine how late in life the brain can reorganize itself. We may also be able to determine, in cases where surgery is performed relatively late, whether other senses—touch or hearing, for instance—may have hijacked the area of cortex usually reserved for visual processing.

Project Prakash faces major challenges, foremost of which is to expand its outreach and treatment programs and to enable the integration of the children into mainstream society. Our plans to tackle these challenges are ambitious; we propose to start by setting up the Prakash Center for Children—a facility to integrate medical treatment, education and research. It will contain a pediatric hospital, a state-of-the-art neuroscience research center, and a rehabilitation unit for newly treated children to allow them to receive maximum benefits from their treatment.

The project's outreach effort has to date provided ophthalmic screening for about 40,000 children residing in some of northern India's poorest and most neglected villages. Around 450 visually impaired children have received surgical care and follow-up, and more than 1,400 have undergone pharmacological and optical treatments. Given the magnitude of the problem, however, this is only a beginning.

My students and I derive great satisfaction from the findings that have emerged from Project Prakash, but the work has also affected us on a deeper, more personal, level. Each blind child with whom we have worked has presented a unique story of hardships and social isolation. Equally unique is the change each child's life undergoes after treatment. SK moved back to his home state with renewed hopes for achieving his cherished goal—to be a schoolteacher. JA, who was treated at the age of 14, can now, six years later, navigate the chaos of Delhi traffic on his own.

The mother of three boys, all of whom were born with cataracts and received treatment last year, is no longer taunted by her village neighbors as carrying a curse. Two brothers who have had sight for just a few months after enduring over eight years of congenital blindness are now excited about the prospect of moving to a school for sighted children.

Such transformations serve as a testament to the power of collaboration: the debt Project Prakash owes to the scientists, clinicians, educators and sponsors who came together to advance both clinical and basic science. And I personally, of course, owe a debt of gratitude to a blue glass bowl and the very special person to whom it once belonged. 

MORE TO EXPLORE

Pawan Sinha on How Brains Learn to See. TED, November 2009. www.ted.com/talks/pawan_sinha_on_how_brains_learn_to_see.html

The Newly Sighted Fail to Match Seen with Felt. Richard Held et al. in *Nature Neuroscience*, Vol. 14, No. 5, pages 551–553; May 2011.

Project Prakash Web site: www.projectprakash.org

SCIENTIFIC AMERICAN ONLINE

Watch the children of Project Prakash at ScientificAmerican.com/jul2013/prakash