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THE BIONIC EYE

Can scientists use electronic implants to help the blind see?

BY: Jerome Groopman

When Connie Schoeman was growing up, her family had a country house on a lake in New Hampshire, and she loved to sit outside at night and gaze at the stars. As an undergraduate at Pembroke College in the nineteen-forties, she studied medical technology, and when she moved to California in her twenties she worked at a hospital laboratory. Connie became an expert at identifying parasites and other pathogens in clinical specimens under the microscope. One afternoon, while she was driving, Connie was hit by a car that was backing out of a driveway. "I realized that I didn't see it from the corner of my eye," she told me. An ophthalmologist examined her. Although Connie's central vision was still sufficient for her to continue lab work, her retina was pocked by heavy coal-black deposits. Tests revealed that even with glasses her vision would be no better than 20/200, which meets the legal definition of blindness. She had experienced significant loss of her peripheral field and some loss of her central field. The ophthalmologist diagnosed retinitis pigmentosa, or R.P., an inherited disease in which the rods and cones of the retina degenerate. (The rods and cones convert light into electrical impulses, which are carried by the optic nerve to the brain, where images are formed.) Connie's eyes were otherwise healthy, but with the loss of the rods her peripheral vision and light perception faded, and with the loss of the cones her central vision and color perception atrophied. "Soon I couldn't see the stars," she said. "Then, after a few more years, I couldn't see the moon."

Retinitis pigmentosa occurs in approximately one in every four thousand people, and the disease usually becomes symptomatic in early adulthood. The condition, which grows worse over time, is incurable. When Connie heard her prognosis, she realized that her work with the microscope would be impossible. She eventually went back to school, obtained a master's degree in vocational rehabilitation, and began working for the state of California as a counsellor for the blind. As her own vision deteriorated further, she learned how helpless blind people could feel. "I had to ask to be guided to the ladies' room in a restaurant," she told me. "And if I dropped something, like my keys or cash, I had to search on my hands and knees for it."

Fifteen years ago, Connie lost her vision entirely. She is now seventy-six years old, a compact woman with a lively smile and hair the color of champagne. When I met her, she was dressed in slacks and a beige blouse, and her nails were painted fire-engine red. Last November,

Connie volunteered to participate in a research study at the University of Southern California, in Los Angeles, where a device designed to restore some of the vision of R.P. sufferers is being tested. Connie agreed to have an artificial retina—a flexible, wafer-thin square grid of sixteen electrodes—implanted in her right eye. For the surgery, the eye muscles were paralyzed with injections of botulinum toxin. An ophthalmologist made an incision on the eye wall, threaded the electrode strip through the eye, and tacked it to her retina. Wires connected to the strip were buried under the skin near the eye. The wires ran to a magnetic disk sutured to her scalp just above her right ear.

"Here, you can feel it," Connie said, taking my hand and guiding it to the area above her ear. It felt like a small button.

Another piece of the device consisted of a pair of wraparound sunglasses with a miniature camera mounted on the bridge; the camera was attached to a wallet-size computer, which was connected to a coil taped above the ear, over the implanted magnetic disk. Connie put the glasses on, and the camera picked up the ambient light in the room and transmitted it to the coil in an intricate pattern of electrical impulses that were coördinated by the minicomputer. Once the impulses reached the coil, they were sent as radio waves to the magnetic disk and ultimately stimulated the electrode grid in Connie's retina. From there, the current passed through the optic nerve to the brain. In a normal eye, the cells of the optic nerve signal the brain according to a sequence known as the neural code. For Connie, that function was governed by proprietary software inside the minicomputer.

It was June, and we were in a laboratory at the university's Doheny Retina Institute, where Dr. Mark Humayun and Dr. Eugene de Juan were conducting the tests. Their research, like that of others in the field, has been highly, often hyperbolically, publicized: in 1999, Stevie Wonder, who has been blind since infancy, appeared on "20/20" with Humayun and talked about the possibility of seeing again. Some foundations that support research on blindness have been deeply concerned; they say that the device could raise false hopes, since it may succeed only where damage to the eyes is limited to the rods and cones.

The day I visited the lab, Connie was beginning to learn how to use the device, and a group of researchers were clustered around her. They positioned Connie at a desk in front of an open black wooden box that resembled a theatrical stage. A researcher placed a white plastic-foam cup in the center of the box. "Now scan in front of you," he instructed Connie. She rotated her head slowly from right to left.

A laptop computer was connected to the device's minicomputer; on the laptop's screen was a representation of the grid that had been implanted in Connie's eye. Activation of the electrodes by ambient light picked up by the camera would be reflected on the laptop screen. When the camera aperture was pointed toward the plastic-foam cup, part of the grid on the laptop display went from gray to white.

Connie's head moved several inches past the cup, and then she exclaimed, "There it is!" The researchers noted the delay. There is a temporal dimension to the neural code as well as a spatial one, and the minicomputer had to be reprogrammed to correct the lag in time between when the camera saw the cup and when Connie's brain interpreted the image.

The researchers then shifted the cup to a far corner of the box, about two feet away from Connie. She scanned right to left and then left to right. “Nothing,” she said. The researchers told her to try again. She still couldn’t locate it. “We need to practice more,” one of them said reassuringly.

The F.D.A. has approved use of the device outside a laboratory environment, but the university’s internal review board hasn’t yet followed suit, so after an hour Connie took off the glasses and detached the coil from behind her ear. She was exhausted, and her husband brought her a cup of coffee, which he guided to her lips. I asked Connie what she saw with the apparatus. “I see a string of lights, like the kind you drape on a Christmas tree,” she said. “But they aren’t colored, just bright white.” The first time Connie used the device, she could hardly contain herself. “The excitement hasn’t worn off when I locate something,” she told me.

The idea for an electronic device that would restore vision in patients like Connie occurred to de Juan and Humayun fifteen years ago. De Juan was a young professor of ophthalmology at Duke University who spent much of his time operating on people to repair detached retinas; Humayun was his student. A minuscule two-and-a half-millimetre tack had just been developed to facilitate these repairs, and de Juan and Humayun wondered whether the tacks could be used to safely anchor electrodes onto the delicate tissues at the back of the eye. “I loved the idea,” said Humayun, who went on to get a doctoral degree in biomedical engineering to further their work. As it happened, de Juan’s neighbor in Durham, North Carolina, was an executive at a government-sponsored consortium of companies working in the semiconductor field. De Juan and Humayun collaborated with the consortium’s engineers to build prototype electrode grids. For several years, they tested the prototypes in animals, some of which had inherited retinal diseases similar to human R.P. De Juan and Humayun moved to Johns Hopkins, and after nine years there, in 2000, took the project to the University of Southern California. A graduate student of de Juan’s from Johns Hopkins, Dr. Robert Greenberg, co-founded the company Second Sight to manufacture and market the device, which he did with the support of private investors who had developed cochlear implants.

The market for a successful prosthesis would be significant. Although R.P. is relatively rare, macular degeneration, another disorder that involves rods and cones, is common. About one and a half million of the sixty million people who are older than fifty-five suffer from advanced age-related macular degeneration that causes severe loss of vision that cannot be corrected by glasses. By 2020, two and a half million people could be affected.

De Juan and Humayun knew that the retina works more like a computer than like a camera. Its hundred and thirty million rods and cones register light and compress the analog signal into electrical pulses carried as digital signals by more than a million neurons in the optic nerve. These digital signals are received and interpreted by a computer of even greater complexity, the brain.

An artificial retina, they realized, would have to be equipped with both the hardware to process electrical information and the software to communicate with the brain. Heavy demands would be placed on this hardware and software. People see over a wide spectrum of wavelengths and various illuminations, and process ambient light as color, shading, and depth. To replicate

this process, the computer would have to work very fast and process vast amounts of data. "There are roughly 1.2 million fibres in the optic nerve, each connected to a neuron, which at maximum can fire off two hundred pulses per second," Humayun told me. "So one eye can send the brain up to two hundred megabits per second."

The design of a retinal prosthesis presented even more substantial obstacles. The electrical energy generated by such a device must not give off so much heat that it burns the sensitive tissues of the eye. The wires and connections need to be made of inert and durable metals that resist the salty vitreous liquid of the eye without irritating its sensitive structures. Moreover, the eye, a one-inch ball, moves back and forth rapidly and exerts powerful torque forces on anything that is attached to the retina. And the retina is roughly a quarter of a millimetre thick, its resilience similar to that of a piece of wet Kleenex. This device would have to be both strong and flexible, able to move fluidly with the eye without tearing it apart.

In the late nineteen-eighties, as de Juan and Humayun embarked on their retinal device, Dr. Joseph Rizzo, a neuro-ophthalmologist working at Harvard's Massachusetts Eye and Ear Infirmary and the director of the Center for Innovative Visual Rehabilitation at the Boston Veterans Administration Medical Center, and John Wyatt, a professor of electrical engineering at M.I.T., began experimenting toward the same goal.

Rizzo and Wyatt placed temporary electrode grids on the retinas of five blind subjects with R.P. and on one person with a normal retina, who was going to lose her eye because of a surrounding cancer. They then sent electricity to the grid through a wire—a simple experiment in comparison with de Juan and Humayun's camera, computer, and magnetic disk. Contrary to their expectations, however, Rizzo and Wyatt found that there is not always a one-to-one correlation between stimulating the retina and causing a visual percept. A single stimulus could result in a cluster of small percepts; an array of stimuli did not always lead to the perception of an anticipated pattern; and stimuli in the shape of letters, say "T" and "L," did not yield recognition. This last test was particularly confounding, since even the patient whose retina was healthy couldn't identify the letters. "That these odd findings were reproducible shows that the real problem is our own inability to figure out what is going on," Rizzo said. "Creating vision is a herculean task. We decided to look at each building block from a single cell to a cluster of cells and then to examine how that cluster influences what you see." De Juan and Humayun, initially unaware of Wyatt and Rizzo's work, leaped ahead, putting a permanent device into the eye and stimulating it with a camera to see what would happen.

Three patients with R.P., including Connie Schoeman, are participating in de Juan and Humayun's study. Harold Churchey, a seventy-six-year-old man, was the first. He has had the device for eighteen months. It had been more than fifty years since he had any vision in the implanted eye. I watched a videotape of the first time that Harold was tested with the retinal prosthesis at the Doheny institute. Like Connie, he scanned an image against a black background. "I see a line going up and down and I see a line going across," he told Humayun. "And they meet at the bottom." Harold was looking at a large white block letter "L." "He couldn't tell it was an 'L,'" Humayun said. "He couldn't piece it together. But how many letters have that configuration? We were sitting on the edge of our chairs, waiting for him to say it was the letter 'L.' But he couldn't figure out the image. We ended up giving him the answer. At that

moment, we realized that, for the device to be of any use, people's brains needed to be retrained."

Harold practiced with the device twice a week for the first three months. I watched another tape of his testing after the training. The letters "H," "L," "I," and "C" were sequentially projected in white against a black background in groups of ten. He scanned each group and was asked to identify the letters in order. The likelihood that he could do this by guessing was one in forty. Nine out of ten times, he scanned the sequence correctly.

Then, during a two-day testing session earlier this month, the researchers allowed Harold to venture outside the laboratory with a more portable version of the apparatus. They wanted to see how he would get along with the implant in the real world.

On the first day, they led him into a conference room on the third floor of the institute. Heavy wood panelling ran along the lower half of the walls, and a set of large windows looked out on trees and a clear blue sky. At the front of the room was a pair of oak doors. The researchers seated Harold in the middle of the room and instructed him to orient himself. "I turned my head to the right and all the electrodes came on," he later recalled. "I said, 'I presume that's a window.' And they said, 'Yes.' I was well pleased."

With the simple array of electrodes, Harold was able to identify the heavy double doors or tell, for instance, where the molding on the wall ended and the more reflective white surface began. "I tried to find a dark spot, and that would probably be a door or a cupboard," he said.

The next day, the researchers took Harold outside. This was the first time that a patient had ever left the building with the device. The researchers asked him to look at traffic and describe what he saw. He could distinguish the shade and the size of the cars, and the direction in which they were travelling.

"In the very beginning, the doctors didn't guarantee me anything," Harold said. "But the first time they gave me the implant I knew they were on the right track."

The success of the sixteen-electrode grid makes de Juan and Humayun confident that soon a device with sixty to a hundred electrodes can be implanted. "Sixty to a hundred isn't reading and driving, but it provides pretty clear motion and size," de Juan said. "A dot-matrix printer is a five-by-seven array, and can easily make any letter of the alphabet. At sixty to a hundred, you're able to see big letters." This device is being tested in animals but hasn't yet been tested in people. De Juan and Humayun's ultimate goal is a thousand and twenty-four electrodes, a thirty-two-by-thirty-two grid. "This will allow you to read and recognize faces," de Juan said. "We currently can make a grid like that; we can even make a grid of a million electrodes. That's not the problem. The problem is matching the electronics to the patients' own circuits."

I went to Humayun's laboratory and tested a simulator that projected a thirty-two-by-thirty-two grid, to get a sense of the clarity of vision that might be possible with a more advanced—and still unavailable—implant. The device looked like the wraparound metal viewfinder worn by Geordi, a blind character in "Star Trek:The Next Generation." I put it over my eyes and moved my head around the lab, looking at the scientists next to me and then at a stack of papers on the desk. My field of vision was divided into small boxes, like the pixelated

images on a computer screen. I could distinguish faces only in gross terms. I located a Federal Express envelope on the desk, and I could easily read the logo—the capital "F" and "E" are 2.6 inches tall, and the lower-case "e," "d," and "x" are 1.8 inches—but smaller print was a blur.

Unlike Connie, I experienced no lag time between scanning the FedEx envelope with the simulator's camera and becoming aware of the image. That's because my neural code is intact. When light from the camera passed through the lenses of my eyes and activated my rods and cones, it was compressed onto the neurons of my optic nerves and digital signals were seamlessly sent to my brain. The software that substitutes for the rods and cones has to somehow reduce the input from the normal hundred and thirty million rods and cones to—in the best-case scenario—a thousand and twenty-four electrodes.

"That the brain can make sense out of just a thousand electrodes—thirty-two times thirty-two, or a thousand and twenty-four, points of light—is staggering," Humayun said to me. "And that's the part that people don't understand. They ask: How in the world can someone build an eye? How can this actually happen? But they don't realize that we can connect a grid to the world's most powerful computer, the brain." The brain, it appears, is capable of correcting the imperfections inherent in the device and its software.

Dr. Alan Chow, a pediatric ophthalmologist, and his brother Vincent, an electrical engineer, believe that it is possible to restore some sight by using the existing neural code rather than simulating it with a computer. Their company, Optobionics, which is based in Illinois, is developing a wireless chip with photoelectric cells that, they argue, can convert the light that passes through the eye into electrical pulses in the retina. Their current chip, which is affixed to the retina, is about two millimetres in diameter and less than the thickness of human hair, or about a thousandth of an inch. The surface of the chip is covered with some five thousand microscopic solar cells, known as microphotodiodes. "When we initially went to the manufacturers"—in the late eighties—"they asked, 'Where are the wires?' and we said, 'There are no wires,'" Chow told me. He said that he wanted a simple device that "would not be cumbersome for the patients." Chow also likens the eye to a computer. "In R.P., you can think of the photoreceptors as the keyboard, with all the other components of the computer still intact," he said. "With our device, we are trying to replace only the keys. Other devices that use electronics from the outside are more complicated, as if you were getting into the computer's C.P.U., its microprocessor. No one really understands how to replicate the digital signal from the retina to the optic nerve yet, so we prefer to rely on the cells that are still functioning."

The first Optobionics implant was performed in June, 2000, and ten people with R.P. have now undergone the procedure. These patients suffered from visual disabilities ranging from four times the legal definition of blindness (about 20/800) to no light perception whatsoever. In May, 2003, Chow presented his recent findings at a meeting of researchers in Fort Lauderdale, Florida.

Paul Ladis is a forty-six-year-old retired machinist who has R.P. He had the chip implanted in early November, 2002. In kindergarten, he had difficulty seeing the blackboard and, as an older child, had reduced night vision, but his vision didn't become significantly impaired until he reached his twenties. As a machinist, he worked on sheeting and aluminum, with heavy

tools, for fifteen years, but it has now been a decade since he practiced his trade. Paul has a ready laugh and a strong Chicago accent. “I am an extremely cautious guy,” he said with a chuckle. “Everyone I worked with at the machine shop got hurt—deep cuts and lost fingers. I was the only one, even with my poor vision, who was never injured.” Paul’s level of sight before receiving the chip was minimal. “I could barely see a light bulb in front of my face,” he said. Two of his three brothers also have R.P., and last year on a July 4th picnic the brother whose vision was intact told Paul that he had seen a television program on Chow’s work. The next day, Paul’s wife went to the Optobionics Web site, and, after careful consideration, Paul decided to apply for participation in the trials. He went through forty hours of preoperative testing before undergoing the surgery on his right eye, which was performed at Rush-Presbyterian–St. Luke’s Medical Center, in Chicago.

One night, about two weeks after the operation, Paul was having a snack in the kitchen when he noticed something bright at the edge of his vision. “I looked around, and saw this light, and realized that I had left the refrigerator door open,” he said. “If I hadn’t seen it, I would have walked right into the open door, like I’ve done a thousand times before. For me, that was quite an achievement. It was fabulous.” Now, he said, “I’m able to see contrast a lot more. I can see different shades of dark and light.”

But Paul’s apparent improvement in visual perception isn’t the same from one day to the next. He estimates that for three to four days of the week his retina is “on.” The other days, his sight is only slightly better than it was before the chip was implanted. Paul said that blind people don’t really see black, as is often assumed. “When I was fifteen or sixteen, I would look at the night sky and realize that it wasn’t black anymore but a fuzzy gray,” he told me. “Now, on the good days, when my vision seems better, I can see black again.” And now, if one of his daughters is wearing a striped shirt and his retina is “on,” he can detect her movement as she goes by him.

In the initial stages of R.P., the ability to see fluctuates, and Chow believes that the chip has returned Paul to an earlier phase of the disease: “It’s almost like we’re turning the clock backward.” In all the patients who have the chip, Chow said, there has been moderate to substantial improvement in a variety of visual functions. However, four patients who have had the prosthesis for more than two years have reported regressing from their peak visual performance with the chip.

There is considerable skepticism about whether the Optobionics implant alone can generate enough current to stimulate the optic nerve and produce any vision at all. Eberhart Zrenner, an eminent German scientist who is leading a competing research team, wrote in *Science* in February, 2002, that Chow’s model doesn’t have the necessary power to activate nerve cells. John Wyatt, the M.I.T. professor, agrees. “The physics won’t give you that,” he said. “You cannot get more energy out of a photodiode than you put in, because there is no battery in there, no amplifier.” Even if a person stared directly at the sun, he said, he doubted that the implant could generate enough electrical current to trigger neurons. Chow’s patients could be experiencing a placebo effect, or, he said, “there may be biological restoration of some kind that’s occurring.” The small amounts of electricity, too low to stimulate the optic nerve, could cause the remaining cells in the retina to release chemicals that boost their function. “But it’s not enough to make the nerve cells in the retina fire,” Wyatt said. “I’ll be happy to stake my whole career on that.”

Chow says that he is used to dealing with skeptics. He asserts that the implant does produce the electricity required to stimulate retinal neurons. But he also acknowledges that the chip's greatest benefit may be its ability to "wake up" dormant rods and cones throughout the eye. "About half the patients see light directly over the implant," he said. "But the most significant improvement occurs in the areas surrounding it."

He argues that testing for a placebo effect by implanting an inert chip would be unethical, since it would subject the patient to extensive surgery, as well as to the risks of having a foreign body in the eye, when there is no expected benefit. In studies performed on rats, which he presented at a recent conference, Chow used inactive chips as controls, and, while there was some effect in terms of preserving electrical activity in the animals' retinas, he states that the degree of signalling was much less than had been observed with the activated photodiodes. He hopes that in the coming months his work will be independently tested at the Atlanta Veterans Administration Medical Center, which is affiliated with Emory University, and at Rush-Presbyterian– St. Luke's Medical Center.

For de Juan and Humayun, the problem remains how to generate high-resolution images in the brain from grids of only a thousand electrodes. "The neurons are there, and they are functional," Humayun told me. "Currents can be generated that aren't so high that they burn the neurons when we get to a grid of a thousand. But do we know enough about the neural code? All the neurons are synched in your eye, tied together in a neural network. Spatial processing is well understood. The retina is like a keyboard: if you stimulate here, the light is seen over there. But what about temporal sequencing? What kind of patterns of pulses do we need to send down the optic nerve?"

As Connie Schoeman's testing demonstrated, the patient's input is essential. When she experienced a delay between the time it took the camera to pick up the image of the plastic-foam cup and the time it took her brain to form an image of the cup, the researchers realized that they would need to rewrite the software. "You can imagine how it would be if we tested only animals," Humayun said. "We'd never get the feedback that we do from patients, who can tell us that we're off. This is how we're going to break the neural code and learn how to design software that allows an electronic device to talk to the brain through the optic nerves."

Wyatt thinks that although scientists will never be able to reproduce this vastly complex code, in the end it may not matter. "The neural code is the eight-hundred-pound gorilla in the living room," he said. "But the brain is the angel in the living room. When the brain receives the artificial electronic pulses from the device, it may learn how to adapt to make something coherent." In effect, because the brain is malleable, particularly in people who have had long-standing sensory deprivation, it may "re-write" the natural neural code to conform to the device's input.

"The important thing is not, bang, you turn on the camera and somebody who has been blind for fifty years can see. That's just not reality," Humayun said. Retraining the brain is what's required. And not only retraining the brain but also retraining the brain to perceive at a lower resolution, since the input is not as detailed as what comes from a normal retina. Cochlear implants require a learning curve—about two months of intensive training—similar to that of the

retinal prosthesis. And, Rizzo says, any device needs to be an improvement over the seeing-eye dogs and canes that blind people now rely on to navigate.

Three months after sitting with Connie Schoeman, I spoke with her about how much progress she had made, and confirmed her report with data from Humayun. She told me that she was now able to correctly identify objects. “These strings of Christmas lights allow me to distinguish one object, like a knife, from another, like a plate,” she said.

When I asked her what this meant for a blind person, she said, “It’s the beginning, and it’s really, really exciting. I’m waiting for permission to have the device at home. Then I’ll see how much use I can get out of it.”

It is unclear to what extent the sixteen-electrode grid will benefit Connie. The model with a thousand and twenty-four electrodes would probably be more functional, allowing her to see faces and letters with greater resolution. Humayun insists that it’s only a matter of time before the necessary advancements are made. “It’s an engineering problem,” he said. “It’s not like cold fusion or time travel.”