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Brain Games;
The Marco Polo of neuroscience.

BYLINE: John Colapinto

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One morning in January, a tall, gray-haired man whom I will call Arthur Jamieson arrived at the Mandler Hall psychology building, at the University of California, San Diego, in La Jolla. Jamieson is seventy years old and lives in the Midwest. He is a physician and an amateur cellist, and has been married for forty-seven years. He also suffers from a rare and bewildering condition called apotemnophilia, the compulsion to have a perfectly healthy limb amputated-in his case, the right leg, at mid-thigh. He had come to La Jolla not to be cured of his desire (like most people with the syndrome, he believed that relief would come only with the removal of the limb) but to gain insight into its cause. To that end, he had scheduled a meeting with Dr. Vilayanur S. Ramachandran, an Indian-born behavioral neurologist who is the director of the Center for Brain and Cognition at U.C.S.D., and has a reputation among his peers for being able to solve some of the most mystifying riddles of neuroscience.

Ramachandran, who is fifty-seven, has held prestigious fellowships at All Souls College, in Oxford, and at the Royal Institution, in London. His 1998 book, "Phantoms in the Brain," about rare neurological disorders, was adapted as a miniseries on BBC television, and the Indian government recently accorded him the title Padma Bhushan, the country's third-highest civilian honor. But it is the awe that he inspires in his scientific colleagues that best illuminates his position in neuroscience, where the originality of his thinking and the simple elegance of his experiments give him a unique status. "Ramachandran is a latter-day Marco Polo, journeying the silk road of science to strange and exotic Cathays of the mind," Richard Dawkins once wrote. Eric Kandel, the Columbia University neuroscientist whose work on the physiological basis of learning and memory earned him a Nobel Prize in 2000, invoked two pioneering brain scientists to describe Ramachandran's contribution to the field: "He is a continuation of a tradition in neurology that goes back to the nineteenth century, to giants like Broca and Wernicke, who gave us, from studying clinical material, enormous insights into the functioning of the human mind."

Ramachandran, who has dark skin, curly black hair, and a mustache, cultivates a slightly rebellious image, often wearing dark polo shirts and a black leather jacket. However, when he meets with patients he tends to dress more conservatively. The day that he met with Jamieson, he was wearing a wool blazer and a tie. He greeted Jamieson in his office, whose décor reflects Ramachandran's many interests outside neurology: Darwinian evolution, plate tectonics, Indian art, Victorian medicine, paleontology, optical illusions. A four-foot stone sculpture of the god Shiva stood behind his desk. On one wall, there was a three-hundred-million-year-old fossil of a mesosaur, a freshwater reptile found only in South America and Africa (and which, as Ramachandran likes to explain, is a central piece of evidence in the theory of continental drift). On a side table was an array of antique scientific items: a brass Gilbert telescope, a hand-cranked electrical machine for curing "nervous diseases," a box of glass tubes containing Victorian homeopathic medicines.

Another table held what appeared to be a smoothly sanded wooden sculpture of a woman's pelvis. Ramachandran often tells visitors that the object is a Henry Moore, before revealing, with a booming laugh, that it is actually a specimen of the world's largest seed, from the coco-de-mer palm.

Ramachandran listened closely as Jamieson talked about his condition. In a specialty that today relies chiefly on the power of multimillion-dollar imaging machines to peer deep inside the brain, Ramachandran is known for his low-tech method, which often involves little more than interviews with patients and a few hands-on tests-an approach that he traces to his medical education in India, in the nineteen-seventies, when expensive diagnostic machines were scarce. "The lack of technology actually *forces* you to be ingenious," he told me. "You have to rely on your clinical acumen. You have to use your Sherlock Holmes-like deductive abilities to figure things out."

Ramachandran suspected that apotemnophilia was a neurological disorder and not, as Freudians have theorized, a psychological syndrome associated with repressed sexual desires. After interviewing several apotemnophiliacs-Jamieson is the fifth person with the disorder whom he has studied-Ramachandran was struck by the fact that all of them said they became aware of the compulsion in early childhood, that it centered on a particular limb (or limbs), that they could draw a line at the exact spot where they wanted the amputation to occur, and that they attached little or no erotic significance to the condition. Furthermore, none rejected the limb as "not belonging" to them, as some stroke victims do in the case of a paralyzed arm or leg, and as Ramachandran had predicted they might. Instead, they said that the limb *over*-belonged to them: it felt intrusive. "If you talk to independent apotemnophiliacs, they say the same bloody things," Ramachandran told me. " 'The line for cutting is here.' 'It started in early childhood.' 'It's over-present.' They're *not* crazy."

Jamieson, who was born and raised in New York City, first remembers having an unusual relationship with his right leg when, at around the age of seven, he was waiting for a bus. He found himself thinking that if he stuck out his leg it would be crushed and severed by the bus. "What came to me was not 'No, I don't want to do that' but 'How would I ever explain this?' " he told Ramachandran. In recounting his childhood memories, he said, "One of the things that's astonishing to me is how clear these recollections are."

"These things are very salient," Ramachandran said in a resonant baritone, which carries a British-inflected Indian accent. "It's interesting to contrast these very clear-cut descriptions with these vague, Freudian notions about this whole phenomenon-that it's primarily connected with sexual stuff."

"Yeah," Jamieson said with disgust. "I've got no desire to cozy up to anyone with a stump. It's psychobabble."

Asked where he would make the cut line for the amputation, Jamieson unhesitatingly drew an index finger across the middle of his right thigh. As to whether he felt that his leg didn't "belong" to him, Jamieson was emphatic. "Somehow, for me, that just doesn't compute, that kind of language," he said. "I have always been fascinated by amputation and wished that I had one. Why? Who the hell knows?"

Ramachandran is one of a dozen or so scientists and doctors who, in the past thirty years, have revolutionized the field of neurology by overturning a paradigm that dates back more than a hundred years: that of the brain as an organ with discrete modules (for vision, touch, pain, language, memory, etc.) that are fixed early in life and immutable. Neurological syndromes, such as paralysis from stroke, forms of mental illness, and the perception of pain in an amputated limb (a phenomenon known as phantom-limb pain), were considered largely untreatable. But Ramachandran and other researchers have shown that the brain is what scientists call "plastic"-it can reorganize itself. Not only are different regions of the brain engaged in ongoing communication with one another, with the body, and with the surrounding world; these relationships can be manipulated in ways that can reverse damage or dysfunction previously believed to be permanent. Ramachandran's work with patients at U.C.S.D. has led to one of the most effective treatments for chronic phantom-limb pain and to a new therapy for paralysis resulting from a stroke. (In both instances, his treatment involves only a five-dollar household mirror.) It has also provided suggestive insights into the physiological cause of such mystifying syndromes as autism.

Until the mid-nineteen-nineties, Ramachandran's specialty was visual perception, but he had been interested in brain science since his days as a medical student in India. He made the switch to neurology in mid-career. "A scientist with that kind of creativity-it's rare," says Michael Merzenich, a neuroscientist at the University of California, San Francisco, whose experiments with monkeys in the nineteen-eighties provided much of the groundwork for understanding brain plasticity. "It's usually not allowed, in some sense. You're not supposed to be a butterfly like that."

Little about Ramachandran's scientific career has been conventional. He was born in Tamil Nadu, in southern India, to a Hindu family of the Brahman caste. His grandfather, Alladi Krishnaswamy Iyer, was the attorney-general of Madras and a framer of India's constitution. Ramachandran's father was a diplomat in the United Nations. However, science ran in the family. His mother had a master's degree in mathematics; one uncle was a professor of optics at the University of Sydney; another was an expert in theoretical physics and relativity.

At around the age of nine, Ramachandran began collecting fossils and seashells and became fascinated by taxonomy and evolution. He wrote to a conchologist at the American Museum of Natural History. "Here's this little kid from India sending him sketches of shells and asking, 'Are these new species?' " Ramachandran said. "And he is writing back saying, 'A, B, C, and D are well-known species; E is very rare and has not been reported from your locality and is very interesting.' So for a while I was the only conchologist in India!" Ramachandran continues to collect fossils and has gone on digs in South Dakota, where he has found specimens of trilobites and a thirty-million-year-old oreodon, a sheeplike creature. His most notable find, however, was not in the field but at the annual Tucson Gem and Mineral Show, in 2004, when he noticed on a table, amid heaps of bones and rocks, a skull that he thought could be a new species of ankylosaur, an herbivorous dinosaur from the Jurassic and Cretaceous periods. Ramachandran's friend Cliff Miles, a paleontologist, was with him and suggested that Ramachandran buy the fossil so that it could be studied and described. In January of this year, Miles and his brother Clark, also a paleontologist, announced the discovery of a new species of ankylosaur from the Upper Cretaceous period: *Minotaurasaurus ramachandrani*.

In his early teens, Ramachandran began conducting experiments in chemistry and biology in a makeshift laboratory under the staircase in the family's house in Bangkok, where his father was stationed. He also read books on the history of science and was struck by the role of intuition and play in many important discoveries: Galileo adapting a child's spyglass and discovering the moons of Jupiter, which led him to challenge the geocentric model of the universe; Faraday tinkering with a magnet and coil and discovering electromagnetism. Ramachandran often recounts these anecdotes to his students. "These stories are inspirational and fun," he told me. "But they're also telling you about how to do science."

Ramachandran's father discouraged him from pursuing a career as a researcher. "My father was intensely pragmatic," Ramachandran said. "He told me, 'Forget about chemistry and biology and all that. I know it's fun, but you're not going to make a living out of this.' " He urged his son to become a doctor, and Ramachandran duly enrolled at Stanley Medical College, in Madras. But he continued to read British and American science journals, and, in his second year, he devised an experiment that was inspired in part by conversations he had had as a child with his uncle the optics professor. The experiment addressed a question debated by experts since the time of Hermann von Helmholtz, in the late nineteenth century, about how the brain harmonizes the two slightly different images seen by each eye. For years, scientists believed that when the eyes are given conflicting information-for instance, a green image in front of one eye and a red one in front of the other-the brain accepts input from one retina at a time. Ramachandran, using an old-fashioned stereoscope and volunteers from his medical-school class, found that, when presented with a pattern that was colored differently for each eye, his test subjects continued to see in three dimensions. He concluded that a neural channel was still active in the "shut down" eye-even though his subjects were consciously seeing only one eye's color at a time. "This suggests that concepts of retinal rivalry need drastic revision," Ramachandran wrote in a report of the experiment.

He sent the report to *Nature* in December, 1971, a few months after his twentieth birthday. "To my astonishment, it was published without revision," Ramachandran told me. Soon, he published a more ambitious paper, "The Role of Contours in Stereopsis," which explored ideas about visual processing that became influential decades later. Ramachandran also wrote to one of the foremost vision scientists at the time, Dr. William Rushton, a professor of physiology at Trinity College, Cambridge, describing several original experiments that he was eager to try. The letter was passed to Oliver Braddick, a psychology lecturer who worked on vision. "The letter was obviously the product of a very fertile young mind," Braddick, who is now a professor of experimental psychology at Oxford, told me. "Perhaps a little kind of spinning off in all directions. But he had all these great ideas."

Braddick and another researcher, Fergus Campbell, invited Ramachandran to visit Cambridge for a month, at the university's expense, to conduct experiments. The results of one experiment, on which Braddick collaborated, were published as "Orientation-Specific Learning in Stereopsis," in the journal *Perception*. "Maybe fifteen years later, various people started publishing in this area of how specific developments of perceptual skills could be highly related," Braddick told me.

Ramachandran returned to Madras to complete his medical degree, and in the fall of 1974 he enrolled at Trinity College to begin a Ph.D. in visual perception. "I thought they'd all be like Faraday and the great Renaissance scientists," he said of the researchers he met in England. "Ninety per cent of them are like Indian scientists, or scientists here, for that matter, or anywhere-it's a nine-to-five job. They're not moved by the great romantic spirit of science, and they're not great Renaissance people. So I was a bit disillusioned. Then I ran into Richard Gregory soon after I arrived, and I said, 'Well, at least there's some of them here!' "

Gregory was a professor of neuropsychology at the University of Bristol, the author of several best-selling books about science, and an expert in visual perception who had a special interest in optical illusions. Typical of his approach was a demonstration involving a Charlie Chaplin mask on a rotating axle, in which he shows how the brain uses prior knowledge of shape, shading, and other light effects to make sense of visual information and assemble a coherent representation of the world. Gregory's playful style irritated some of his colleagues, but Ramachandran found it electrifying. "He came to Cambridge to give a lecture," Ramachandran recalls. "He was like a magician! He is truly one of the five most amazing men I have met in my life."

During his four years at Cambridge, Ramachandran commuted regularly to Bristol to design experiments with Gregory. They have since written a number of scientific papers together, including groundbreaking work on the blind spot, the region at the back of the eyeball where the retina's photoreceptors are interrupted by the optic nerve. This region creates a gap in our vision the size of a palm held at arm's length, but, owing to several strategies of the brain, we never perceive it. Using optical illusions to trick the eyes and the brain, Ramachandran and Gregory determined how the brain "fills in" the gap, and published influential articles on stroke victims suffering from scotoma-a particularly large blind spot sometimes caused by a focal lesion in the visual cortex.

In the mid-nineties, Gregory visited Ramachandran at U.C.S.D. to undertake further experiments on scotoma, but they were unable to find a patient with a focal lesion. Instead, they spent Gregory's weeklong visit investigating a phenomenon that had long fascinated Ramachandran: the reported ability of flounder to camouflage itself against patterned backgrounds. Leading ichthyologists disagreed about whether the fish changed its appearance or whether the camouflage effect was an illusion. Ramachandran's local pet store had no cold-water flounder, so he bought five peacock flounder, a related species that lives in tropical coral reefs. The men placed the fish on the bottom of four small tanks against various backgrounds: widely spaced polka dots, a neutral gray, and two checkerboard patterns. The fish, whose natural tendency is to lie flat on the sea bottom, precisely matched on their bodies the patterns at the bottom of the tanks-and they did so within two to eight seconds, far faster than the hours and, in some cases, days reported by researchers using cold-water flounder. Ramachandran and Gregory surmised that the rapid change was an adaptive mechanism, since the species lived among bright colors and patterns. The experiment, which they meticulously documented in photographs and on videotape, effectively ended the debate on flounder camouflage-and, incidentally, throws an instructive sidelight on visual processing in human beings. Even though the fish sees the background close up and in a distorted, slanted perspective, it re-creates the pattern on its body with perfect fidelity, as viewed from directly above. Human beings, Ramachandran points out, visually process the world in the same way. "Your eyeball distorts the image-it's curved," he says. "Your lens inverts it-it's upside down. And your two eyes double it. The brain *interprets* the image."

When they wrote up the results of the experiment, Ramachandran and Gregory laced their paper with puns. In a caption for a photograph showing one fish on a polka-dot background, they wrote, "Spot the flounder," and they said that they had conducted the experiments "just for the halibut."

"So we sent this off to *Nature*," Ramachandran told me, "and back come the referees' comments: 'Brilliant paper, publish it right away, but remove all the puns.' " He laughed. The paper, "Rapid Adaptive Camouflage in Tropical Flounders," was published in a 1996 issue of *Nature*. "Since then," Ramachandran said, "I get papers on octopuses and squids and fish-because they all think I'm an expert on ichthyology!"

In 1983, Ramachandran joined the psychology department at U.C.S.D., as an assistant professor working on visual perception. In 1991, he became interested in the work of Tim Pons, a neuroscientist at the National Institute of Mental Health, who had been investigating the ability of neurons in the sensory cortex to adapt to change.

The sensory cortex is in the deeply ridged tissue that makes up the outermost layer of the brain. Until recently, much of what was known about it was the result of the work of Wilder Penfield, a neurosurgeon in Montreal who, beginning in the nineteen-thirties, had conducted a series of extraordinary experiments while performing open-skull operations on cancer and epilepsy patients. Seeking to distinguish healthy tissue from diseased tissue, Penfield touched the surface of his patients' brains with an electric probe, and, because the brain lacks pain receptors, the patients were fully conscious and able to talk to him about what they felt. As he stimulated different areas of the brain, his patients reported feeling touch sensations in specific parts of their bodies. In this way, over several decades and hundreds of operations, Penfield mapped areas of the brain according to their corresponding body parts. The "Penfield homunculus," as it came to be called, is oriented upside down: the areas corresponding to the feet and the legs are at the top of the brain, the arms and the hands are in the middle, and the face is near the bottom. Body parts with the greatest sensitivity-lips, fingertips-take up a far larger area of the cortical surface than less sensitive areas.

The regions representing separate body parts on the Penfield homunculus, like the brain centers, were believed to be unchangeable. This view came under challenge as the technology for mapping the brain improved. Whereas Penfield had used a large electrode that affected thousands of neurons at a time, brain researchers in the fifties began to use tiny microelectrodes, which could be inserted into the brains of animals to record the firing of single neurons and, thus, communication among them. In the seventies, Michael Merzenich became expert at using microelectrodes to map the sensory cortex of monkeys. In one experiment, he mapped a monkey's hand area in the brain, then amputated its middle finger. Some months later, he remapped the monkey's hand and discovered that the brain map for the missing finger had vanished and been replaced by maps for the two adjacent fingers, which had spread to fill the gap. The results, published in the *Journal of Comparative Neurology* in 1984, were decisive proof that the brain can reorganize itself-at least across very short distances of one to two millimetres.

Pons, at N.I.M.H., was curious to know whether the brain could accomplish more dramatic reorganizations, across greater distances. He wondered what happened in the brains of monkeys that had lost brain input from an entire hand and arm, and he thought that he could procure some animals to test. In 1981, a member of PETA had infiltrated a Maryland lab where a researcher studying stroke paralysis had severed the sensory nerves in a group of macaque monkeys which connected the animals' arms to their spinal cords-a procedure known as deafferentation. PETA released photographs of the monkeys, and the animals were seized and placed in the custody of the National Institutes of Health. By 1990, the monkeys had grown old and were about to be euthanized. Pons successfully appealed to the N.I.H. to allow him to conduct a final experiment on four of them.

Pons anesthetized the first animal, opened its skull, and inserted electrodes into the brain-map area for the deafferented arm. He stroked the corresponding limb. As expected, the brain electrodes recorded no activity, since no messages were being sent to the brain from the arm. But when Pons stroked the monkey's face the neurons in the map of the deafferented arm began to fire. The experiment showed that the neurons in the face map had invaded the area of the hand-and-arm map, which had been inactive for twelve years. Fourteen millimetres of the monkey's arm map had been reorganized to process sensory input from the face. Pons repeated the experiment on three more monkeys, and published the results in *Science*, in 1991, as a paper titled "Massive Cortical Reorganization After Sensory Deafferentation in Adult Macaques."

Ramachandran read Pons's paper, and wondered whether it could help solve the long-standing medical puzzle of phantom limbs. Many amputees continue to experience sensations-often painful-from a missing limb, and the phenomenon has baffled scientists since it was first reported, in the sixteenth century, by the French surgeon Ambroise Paré. Ramachandran says that his interest in phantom limbs was a natural extension of his work in visual processing. "I was interested in the 'filling in' of the blind spot and other holes in the visual field; how the brain deals with undersampled regions-gaps," he said. "This resulted in my asking, 'How do you "fill in" a missing limb?' " Pons's monkeys seemed to offer a clue.

"Often, the best experiments begin as jokes," Ramachandran told me. "I joked with my students. I said, 'Hey, this means that if I touch the monkey's face the monkey should feel it in the hand.' And they all laughed, and I said, 'Hey, why not?' Then they said, 'Well, how do you train a monkey to tell you what it's feeling?' And I said, 'Why do you need a monkey? Let's try it on a person.' "

Ramachandran arranged to examine a seventeen-year-old boy whom he calls Tom, who had recently lost his left arm, just above the elbow, in a car crash. In a basement lab at Mandler Hall, Ramachandran lightly stroked Tom's cheek with a Q-tip. Tom said that he felt the touch in his cheek, but also in his phantom thumb. A touch on the lip he felt on his phantom index finger, a touch on the lower jaw in his phantom pinkie. Ramachandran realized that every time Tom moved his face and his lips-smiling, talking, frowning-the nerve impulses from his face activated the "hand" area in his cortex. "Stimulated by all these spurious signals," he later wrote, "Tom's brain literally hallucinates his arm."

Ramachandran immediately telephoned his wife, Diane Rogers-Ramachandran, and told her, "Come in right now. You've got to see this guy."

Rogers-Ramachandran is also a scientist, specializing in vision and experimental psychology. She and Ramachandran met in the late nineteen-seventies, at a vision conference in Florida. She was then a graduate student at the University of North Carolina, Chapel Hill. They married in 1987. (They have two boys: Chandramani, who is nineteen, and Jaya, fourteen.) Rogers-Ramachandran rushed from their home in nearby Del Mar to watch the experiment. In the course of a few hours, she and her husband mapped Tom's phantom hand on his face. In a later experiment, they applied warm water to Tom's cheek. He felt heat in his phantom hand. When the water trickled down his cheek, he felt it running down his phantom arm. Ramachandran and his wife published their findings in 1992, in *Science*.

Rogers-Ramachandran, a vivacious woman with bright-blue eyes, continues to collaborate with her husband on papers, and they write a regular science column for *Scientific American Mind*. She says that it has sometimes been a challenge to be married to a man of Ramachandran's mental energy and intellectual curiosity. "Like, when we got married," she said one evening, over dinner at a restaurant with her husband and Jaya, "we went to England for our honeymoon, and spent the whole time going to bookstores and collecting prints, books, scientific instruments. Never went to a play! None of those things! The collecting! He went from scientific instruments to fossils, to learning about his Indian heritage, to art. You say, 'Well, can't we just go walk on the beach?' "

She mentioned Ramachandran's abstracted air-it's as if he were constantly mulling over an abstruse neurological conundrum. I knew something about this. On the first day of my visit to U.C.S.D., Ramachandran was unable to remember where in the parking lot he had left his car and finally had to activate the alarm on the remote control to locate it. His embarrassment suggested that this was the first time such a thing had happened. Yet, during the six days that I spent with him, it happened every time. When I told this story to Diane at dinner, she snorted.

"When we leave a place, he'll go into the parking lot, and a lot of time he'll just start walking," she said. "He has no idea where he's going. He just walks. One time, I picked him up from a trip-"

"Oh, don't tell him that," Ramachandran said.

But Diane went on. "He reached in his pocket and he said, 'Oh, my God, I had a rental car in that city! I completely forgot! I have the keys and I didn't turn the car in!' Another time," she continued, "I got a call from Sears and a woman said, 'There's a man here who says he's your husband and he's trying to purchase something on this credit card.' I said, 'Ye-e-e-s.' And she said, 'We're kind of concerned if it's really your husband, because he doesn't know your birth date.' I said, 'Oh, *that's* my husband!' "

"Ha-ha-ha-ha-ha!" Ramachandran boomed. "That *is* a good story."

I could not resist asking whether Ramachandran had since learned Diane's birthday. They have been married for twenty-two years.

"I know she's a Leo," he said, slowly, eying her from across the table.

"I'm not a Leo," Diane said. "*You're* a Leo."

"No," he corrected himself. "Virgo! Virgo!"

"Yup," she said.

"August 18th," he said, with confidence.

"No," Diane said. Then she turned to me. "See, he gets the month, because it's the same as his."

"It's not the eighteenth?" Ramachandran asked.

"No."

"Twenty-second?" he offered.

"No."

At this point, Jaya asked, "Do you know *my* birthday?"

Ramachandran looked helplessly at his son and shrank into his seat. "It doesn't mean I don't love you," he said.

In 1994, Ramachandran published a paper in *Nature* that is now considered a landmark in the field of neuroplasticity. He described experiments that he had conducted with U.C.S.D.'s multimillion-dollar magnetoencephalography machine, which records the changing magnetic fields caused by brain activity. (Though he calls himself a "technophobe," Ramachandran occasionally uses high-tech gadgetry, chiefly as a means to support his hunches.) The high-resolution MEG scans clearly showed that in the brains of arm amputees the area associated with the face had invaded the area associated with the missing arm-"the first direct demonstration of massive reorganization of sensory maps in the adult human brain," Ramachandran wrote.

His most startling revelation about the brain's capacity for reorganizing itself was yet to come. It emerged from his efforts to address phantom-limb pain, which afflicts up to ninety per cent of amputees. Some report feeling that they are clenching their phantom fist so hard that their phantom fingernails are digging into their phantom palm. Phantom-limb pain can be so agonizing that some sufferers commit suicide.

For more than a century, doctors theorized that the pain was psychological or originated in the stump-in swollen nerve endings called neuromas. Some resorted to repeated amputations, making the stump shorter and shorter. When this didn't work, they tried severing the nerves at the spinal cord and even disabling parts of the thalamus, an organ at the base of the brain that processes pain. All to no avail. "They can chase the phantom farther and farther into the brain, but of course they'll never find it," Ramachandran once wrote. The phantoms, as he had shown, are *produced* in the sensory cortex, where neurons for the face have invaded territory once reserved for the arm.

Ramachandran posited that the phantom sensations are also created by higher brain centers, produced by a complex interplay among the sensory cortex, the motor cortex in the frontal lobes, and a "body image" map in the right superior parietal lobule, a section of the cerebral cortex just above the right ear. One of the main tasks of the right superior parietal lobule is to assemble a coherent body image from touch signals ("I feel my fingers touch the cup"), visual signals ("I see my hand reaching for the cup"), and nerve signals from the muscles, joints, and tendons ("I feel my arm extending toward the cup"). Even though amputees no longer received these signals from the nonexistent limb, Ramachandran believed that memories of these inputs remained in the nervous system and the brain.

Reviewing the histories of amputees, Ramachandran noticed that many who suffered from cramping or clenching spasms had experienced, before their amputations, a period during which the limb was immobilized, sometimes for months, in a sling or a cast. He theorized that a kind of "learned paralysis" was burned into the brain's circuitry, as repeated commands from the patients' brains to move the limb were met with touch, visual, and nerve evidence that the limb could not move. When the limb was later amputated, the patient was stuck with a revised body-image map, which included a paralyzed phantom whose neural pathways retained a memory of pain signals that could not be shut off. Ramachandran wondered what would happen if such a patient was presented with evidence that the phantom could move ("I see my hand reaching for the cup"). If the brain could be tricked into thinking that the phantom was moving, would the cramping sensations cease?

His first test subject was a young man who a decade earlier had crashed his motorcycle and torn from his spinal column the nerves supplying his left arm. After keeping the useless arm in a sling for a year, the man had the arm amputated above the elbow. Ever since, he had felt unremitting cramping in the phantom limb, as though it were immobilized in an awkward position.

In his office in Mandler Hall, Ramachandran positioned a twenty-inch-by-twenty-inch drugstore mirror upright, and perpendicular to the man's body, and told him to place his intact right arm on one side of the mirror and his stump on the other. He told the man to arrange the mirror so that the reflection created the illusion that his intact arm was the continuation of the amputated one. Then Ramachandran asked the man to move his right and left arms simultaneously, in synchronous motions-like a conductor-while keeping his eyes on the reflection of his intact arm. "Oh, my God!" the man began to shout. "Oh, my God, Doctor, this is unbelievable." For the first time in ten years, the patient could feel his phantom limb "moving," and the cramping pain was instantly relieved. After the man had used the mirror therapy ten minutes a day for a month, his phantom limb shrank-"the first example in medical history," Ramachandran later wrote, "of a successful 'amputation' of a phantom limb."

Ramachandran conducted the experiment on eight other amputees and published the results in *Nature*, in 1995. In all but one patient, phantom hands that had been balled into painful fists opened, and phantom arms that had stiffened into agonizing contortions straightened. "People always ask, 'How did you think of the mirror?' " Ramachandran told me. "And I say, 'I don't know!' There was a mirror in the lab, so that must have been in my mind, and I said, 'Let's try it.' It's not any more mysterious than if you say something 'popped into' your mind."

Dr. Jack Tsao, a neurologist for the U.S. Navy, was doing graduate work in physiology at Oxford

University when he read Ramachandran's *Nature* paper on mirror therapy for phantom-limb pain. "I said, 'Why the heck should this work? It doesn't make sense,' " Tsao told me. Several years later, in 2004, Tsao began working at Walter Reed Military Hospital, where he saw hundreds of soldiers with amputations returning from Iraq and Afghanistan. Ninety per cent of them had phantom-limb pain, and Tsao, noting that the painkillers routinely prescribed for the condition were ineffective, suggested mirror therapy. "We had a lot of skepticism from the people at the hospital, my colleagues as well as the amputee subjects themselves," Tsao said. But in a clinical trial of eighteen service-members with lower-limb amputations, in which six were given mirror therapy and the twelve others were evenly divided between two control therapies (a covered mirror and mental visualization), the six who used the mirror reported that their pain decreased (and, in some cases, disappeared altogether). In the two control groups, only three patients reported pain relief, and others found that their pain increased. Tsao published his results in the *New England Journal of Medicine*, in 2007. "The people who really got completely pain-free remain so, two years later," said Tsao, who is currently conducting a study involving mirror therapy on upper-limb amputees at Walter Reed.

Buoyed by these successes, in the mid-nineties Ramachandran abandoned his work in visual perception to devote himself to neurology. "Vision was getting overcrowded," he told me. Neurology seemed like virgin territory. Much of the specialty was concerned with describing strange syndromes, rather than with explaining their cause or alleviating symptoms. "You've got a hundred papers saying, 'My God, they can move their phantom'-but it stayed at that level, a descriptive level," Ramachandran said. "We said, 'Look, we can do experiments. What if you do *this* to the patient?' And I took that same style to other syndromes. Then the sky was the limit. No one was studying these things."

Gradually, Ramachandran began to specialize in rare conditions and disorders, including the Capgras delusion, in which an otherwise lucid victim of a head injury insists that close loved ones (spouses, parents, children) are impostors. Freudians had theorized that Capgras patients were suffering from unbearable Oedipal desires aroused by the blow to the head, but Ramachandran demonstrated that severed neural pathways between the facial-recognition areas of the visual cortex and the emotional centers of the brain were responsible for the disorder. He also investigated post-stroke syndromes, in which patients deny that a paralyzed limb has become immobile or, in a more severe version, insist that the paralyzed arm or leg belongs to someone else. Ramachandran traced the delusion to damage in the right superior parietal lobule, the body-map region, where the discrepancy between the absence of signals from the limb to the brain and the presence of the limb on the body results in a defensive rationalization that the arm or leg must be someone else's. A few years ago, Ramachandran began studying apotemnophilia, the compulsion to amputate a healthy limb. He is, he said, "ninety-five per cent sure" that he has figured out the cause of the disorder. His consultation with Arthur Jamieson strengthened this conviction.

After interviewing Jamieson in his office, Ramachandran led him to a lab for a Galvanic Skin Response, or GSR, test, which would reveal how Jamieson's legs reacted to a mild pain stimulus. He escorted Jamieson into a small room that held only a table, a desktop computer, and two chairs. He asked Jamieson to sit with his back to the computer. Then David Brang, one of Ramachandran's graduate students, attached a sensor to the middle two fingers of Jamieson's right hand using a Velcro strap. The sensor would measure the reaction of Jamieson's sympathetic nervous system by monitoring the sweat on his fingers. With a sterilized pin, Brang pricked Jamieson's legs at random points, waiting a few seconds between each prick. A scrolling graph on the computer screen registered Jamieson's responses.

The unaffected leg-the left one-and the right leg above where he wished to have it amputated showed a normal response: the graph at first shot upward with each prick, but with further pricks it ceased to rise, then began to flatten out, indicating that Jamieson's nervous system was getting used to the stimulus. But when Brang pricked Jamieson anywhere on the leg *below* the amputation line, his nervous system responded with increasing distress, the graph climbing higher and higher with each prick.

The experiment seemed to support Ramachandran's theory about the disorder. He believed that people with apotemnophilia had a deficit in the right superior parietal lobule, where the body-image map is assembled. According to this notion, Jamieson was missing the neurons in the map that corresponded to his right leg from the mid-thigh down. He had normal sensation in the unwanted part of his leg-he felt the pin prick. But when the pain signal travelled to the right superior parietal lobule there was nothing in the body-image map to receive it.

"So there's a big discrepancy-a *clash*-and the brain doesn't like discrepancies," Ramachandran said. "When a discrepancy comes in, it says, 'Shit! What the hell is going on here?,' and it kicks in and sends a message to the insular part of the brain, which is involved in emotional reactions-so you're getting this crazy GSR." In apotemnophilia sufferers, the discrepancy causes a feeling of distress that is no less agonizing for being below the level of conscious awareness.

In the past two years, Ramachandran has tested four other apotemnophiliacs using MEG brain scans. "You touch them anywhere in the body and the right superior parietal lobule lights up, as you would expect," Ramachandran said. "But if you touch him here"-he gestured to a point on Jamieson's leg below the amputation line-"nothing happens." Ramachandran said that the experiment needed to be repeated by other researchers, but, he added, "This takes a spooky psychological phenomenon and, as Shakespeare said, gives it a 'habitation and a name.' " Furthermore, the findings suggested to Ramachandran a possible method for alleviating the oppressive sensations in the unwanted limb.

Later, he asked Jamieson to stand in a corner of his office and placed a three-foot-high mirror in front of him, in such a way that in place of his right leg Jamieson saw his left, which he held bent at the knee. Jamieson gazed into the mirror. "Astonishing," he said. For a moment, the leg looked "right."

The mirror was a less risky kind of sham amputation than the method that Jamieson had recently adopted: injecting anesthetic to block the sciatic nerve of his right leg, shutting down the touch sensation. (As a physician, Jamieson had learned how to perform the nerve block.) The anesthetic provided up to five hours of relief, Jamieson said. Apotemnophiliacs, like transsexuals, anorexics, and others with body-image disorders, often do not seek a "cure" for their condition, and Ramachandran spoke gingerly when he suggested that using both the mirror and the drug could potentially yield powerful results. "It's conceivable-nobody knows-but if you do this repeatedly, and I'm not suggesting that you try this, because I know you don't want to be 'changed,' but if you do it repeatedly, both the injections and the visual amputation, it might actually eliminate this desire," he said.

Ramachandran describes his approach to science as "opportunistic": "You come across something strange-what Thomas Kuhn, the famous historian and philosopher of science, called 'anomalies.' Something seems weird, doesn't fit the big picture of science-people just ignore it, doesn't make any sense. They say, 'The patient is crazy.' A lot of what I've done is to rescue these phenomena from oblivion." Ramachandran is conscious of the fact that this focus might lead some to think that he works on the margins of his field. "Now, you could say that about Oliver," he told me, referring to his friend and colleague Oliver Sacks, the neurologist and author of "The Man Who Mistook His Wife for a Hat." "'Oh, he studies spooky things,'" Ramachandran went on. "That's bullshit. This man has deep insight into the human condition. He's a poet of neurology." Ramachandran says that his own interest in oddities is not for their own sake but for what they can tell us about the normal brain, including, he said, "very enigmatic aspects of the brain that few people have dared to approach, like what is a metaphor? How do you construct a body image? Things of that nature."

In 1999, Ramachandran turned his attention to synesthesia, an intermingling of the senses that causes some people to see each letter of the alphabet in a particular color. Others identify musical notes with colors; still others mix touch sensations with strong emotions, so that sandpaper might evoke disgust, velvet envy, wood grain guilt. Vladimir Nabokov described his letter-color synesthesia in "Speak, Memory": "I see *q* as browner than *k*, while *s* is not the light blue of *c*, but a curious mixture of azure and mother-of-pearl." As an artist, Nabokov was, according to Ramachandran's research, eight times more likely to have synesthesia than someone who is not an artist; the fact that Nabokov's mother also had the condition suggested a genetic component. (The phenomenon runs in families.)

The most common synesthesia is number-color. Ramachandran believed it was not coincidental that the fusiform gyrus, where number shapes are processed in the brain, lies next to the area where colors are processed. He suspected that a cross-wiring in the brain, similar to that in phantom-limb patients, was responsible. Brain scans confirmed his hunch: in synesthetes, there are excess neural connections between the two brain centers. This suggested to Ramachandran that the syndrome arises from a defect in the gene responsible for pruning away the neural fibres that connect the various centers of the brain as it develops early in life. "What do artists, poets, and novelists have in common?" Ramachandran asked me. "The propensity to link seemingly unrelated things. It's called metaphor. So what I'm arguing is, if the same gene, instead of being expressed only in the fusiform gyrus, is expressed diffusely through the brain, you've got a greater propensity to link seemingly unrelated brain areas in concepts and ideas. So it's a very phrenological view of creativity."

In the mid-nineties, Ramachandran read a paper by Italian researchers who had discovered that a set of neurons in the frontal lobes of monkeys fired not only when the monkeys reached for an object but also when they observed another monkey performing the same action. Ramachandran wondered if these so-called "mirror neurons" also exist in humans-a difficult thing to test, since the Italians had inserted electrodes into the brains of living monkeys, a technique that it is impossible to use on people. But Ramachandran knew of experiments from the nineteen-fifties in which noninvasive EEG scans were used. These had shown that deliberate movements in humans suppress a kind of brain activity in the motor cortex called mu waves. Ramachandran and a postdoctoral fellow, Eric Altschuler, ran EEGs on volunteers as they observed another person performing an action such as opening and closing a hand. The tests showed that merely witnessing an action in others caused mu-wave suppression in the watcher-evidence that mirror neurons exist in humans, too. Other researchers have since confirmed that people have several systems of mirror neurons, which perform different functions.

"So let's take the broader theoretical implications of this," Ramachandran said one afternoon, while we were visiting the San Diego Rehabilitation Institute at Alvarado Hospital, where he had examined a paralyzed stroke patient suffering from limb denial. He was sitting in the hospital cafeteria with the clinic's medical director, Lance Stone. "These mirror-neuron experiments are showing that, through and through, the brain is a dynamic system not only interacting with your skin receptors, up here"-he pointed at his own head-"but with *Lance!*" He pointed across the cafeteria table at Dr. Stone. "Your brain is hooked up to Lance's brain! The only thing separating you from Lance and me is your bloody skin, right? So much for Eastern philosophy." He laughed, but he wasn't kidding. Ramachandran has dubbed mirror neurons "Gandhi neurons"-"because," he said, "they're dissolving the barrier between you and me."

Ramachandran wondered whether mirror neurons were implicated in autism, a condition whose primary characteristic is severe social impairment, including an inability to imitate and a lack of empathy. Ramachandran, Altschuler, and Jaime Pineda, a U.C.S.D. colleague, ran EEGs on autistic children. They got normal mu-wave suppression when the subjects moved their own hands. But when the children watched another person move his hand, their brains didn't respond. At a neuroscience conference in 2000, Ramachandran and his co-authors presented their findings and speculated that autism was caused by a deficit in the mirror-neuron system. The idea initially met with resistance from autism researchers, some of whom argue that the disorder is caused primarily by deficits in the cerebellum. Unlike his earlier foray into ichthyology, Ramachandran was entering a sphere of science fraught with politics. "The trouble is, it's a minefield," he told me. "The parents are involved. There's big money involved. Suppose you invested your life in saying that the cerebellum is what's going on, then someone comes along and spends one year on it and says, 'It's the mirror-neuron system'?"

In the past nine years, however, mirror neurons have become a central topic in autism research. Almost at the same time as Ramachandran, a group in Scotland had also suggested the link. Among those who have provided further evidence are researchers at the Helsinki University of Technology, who used MEG scans to show mirror-neuron deficits in autistic teen-agers and adults. Lindsay Oberman, a former graduate student of Ramachandran's, who now works as a postdoctoral fellow at Beth Israel Deaconess Medical Center, at Harvard University, has begun using a technology called transcranial magnetic stimulation-a technique that triggers targeted areas of neurons in the brain-to influence brain plasticity in autistics. "So far, we have done some amazing things," Oberman has written. "We have found evidence that we can improve the functioning of the mirror-neuron system and some communication skills following repeated application of TMS."

On the last day of my visit with Ramachandran, I attended the lab discussion that he holds, each Monday, with his postdoctoral and graduate students at the Center for Brain and Cognition Laboratory, on the second floor of Mandler Hall. The lab, a room of modest size, was dominated by a long central table heaped with the strange tools of Ramachandran's trade: a foam-rubber hand of the type you buy at a horror shop (for a demonstration that Ramachandran likes to do to show visitors how the brain projects touch sensations onto objects that are not part of the body); a mirror ball of the type that M. C. Escher liked to draw; a boxed set of the BBC miniseries of Sherlock Holmes (for inspiration); several plastic minimizing lenses (Ramachandran has found that viewing a painful arm or leg through a lens that makes the limb look smaller dramatically reduces pain); a reflective metal tube that could be twisted into various amoebic shapes (when I asked if this puzzle had "experimental significance," Ramachandran said, "No," then quickly corrected himself: "Well, it's fun"); a series of oddly shaped metal boxes outfitted with slanting mirrors (for inducing perceptual distortions in those who peer through the eyeholes); and a plaster cast of *Minotaurasaurus ramachandrani*, a creature that resembles a medieval gargoyle, with three nasal openings on either side of its ridged and crenellated head. Ramachandran has asked one of his postdocs, Paul McGeoch, to perform a CAT scan of the skull in order to learn about the creature's olfactory lobes, and, in this way, to test Ramachandran's theory that his ankylosaur's heightened sense of smell might allow the beast to sniff out mates or carrion from a great distance (although it was more likely a vegetarian).

Seated around the table were members of Ramachandran's research group. Most were in their middle to late twenties, except for a man in his eighties with a British accent: John Smythies, whom Ramachandran introduced to me as the person who launched the drug revolution in the sixties. Smythies demurred, explaining that as a postdoc at Cambridge in the fifties, while performing psychopharmacology experiments involving mescaline, he had merely introduced Aldous Huxley to a colleague, who then administered to Huxley the hallucinogens that led him to write "The Doors of Perception," which later became a bible of the Woodstock generation.

Ramachandran, who was dressed in his usual black leather jacket and dark polo shirt, took a seat at the table and fielded questions from his students, helping them to refine their methodologies and using the brisk interchanges to hone ideas for research. At one point, Lisa Williams, a Ph.D. student who specializes in schizophrenia-a disorder that Ramachandran first began exploring about a decade ago-mentioned, in passing, the difficulty that schizophrenics have in differentiating between phenomena that are internally and externally generated.

"Oh!" Ramachandran cut in. "Speaking of that, I have an idea-I'm sure it's been done-but you know that when people think to themselves you get unconscious movements of the vocal cords? Now, has anybody done that with schizophrenia to see if it's enhanced?"

"I don't know," Williams said. "I'll look that up."

If such enhanced subvocalization occurs when schizophrenics think, that would support Ramachandran's view of the brain as an organ in dynamic equilibrium-and of mental illnesses as resulting from a neurological disruption that destroys that equilibrium. In the case of schizophrenia, whose sufferers often complain of "hearing voices," Ramachandran suspected damage or deficit in a sensory mechanism in the vocal cords which, when normal people think, sends a signal to the brain indicating "This is simply a thought; no one is actually saying this." If this mechanism was damaged, the subconscious movement of the vocal cords could be interpreted as an outside voice speaking in one's head.

"By the way," Ramachandran continued, "I have a theory that if you take people with carcinoma of the larynx, and you remove the vocal cords, and they think to themselves, they may actually start hallucinating. A prediction."

This remark prompted Laura Case, a first-year graduate student who has focussed on autism, to speak. "That could be interesting in autism, too," Case said. "Because if they lack the robust mirror activation for actions, which they do-"

Ramachandran interjected, "Then they confuse-so they may confuse their own vocalizations with somebody else's! And people have linked autism to schizophrenia. The old theory was that it was early-childhood schizophrenia! Was that a coincidence?"

The discussion proceeded in this freewheeling manner for more than an hour, with Ramachandran seizing on notions that seemed to offer fruitful possibilities for further investigation and tactfully deflecting those which he thought were dead ends. When the discussion ended, at 6 P.M., and Ramachandran's students had departed, I asked him if he thought that his work was aimed at constructing a "grand unified theory" of the brain. He said that neuroscience was still too young a discipline for such an ambition. Nevertheless, in recent years he has increasingly focussed on the biggest mystery of the brain: consciousness. Mirror neurons play a role, he thinks. "One of the theories we put forward," he said, as he packed up his bag, "is that the mirror-neuron system is used for modelling someone else's behavior, putting yourself in another person's shoes, looking at the world from another person's point of view. This is called an allocentric view of the world, as opposed to the egocentric view. So I made the suggestion that at some point in evolution this system turned back and allowed you to create an allocentric view of yourself. This is, I claim, the dawn of self-awareness."

Still, Ramachandran said, deciphering how consciousness works will take a supreme creative leap. "It may require a radical revision of the way in which you perceive the universe, the world, the brain," he said, as he stepped into the hallway and locked the lab door behind him. "Just like Einstein had to change your complete perspective in order to really understand time, saying it's part of the whole space-time manifold. Things don't 'pass through' time-that's a human illusion. But, if it requires that, some genius is going to have to come along and solve it." He opened the door to the stairwell and started down. "What we're hoping," he went on, "is that we can grope our way toward the answer, finding little bits and pieces, little clues, toward understanding what consciousness is. We've just scratched the surface of the problem. When I say 'we,' not just our lab but the entire world of neuroscience."

By now, we had reached the ground floor of Mandler Hall and were walking outside, past clusters of students. Ramachandran was still speaking excitedly-he had veered into a knotty digression about the brain's role in the evolution of language-when he glanced up and realized that we had reached the parking lot. He stopped talking and looked out over the sea of automobiles.

"Uh-oh," he said.