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Headstrong

V.S. Ramachandran is changing minds about the brain

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STAFF WRITER

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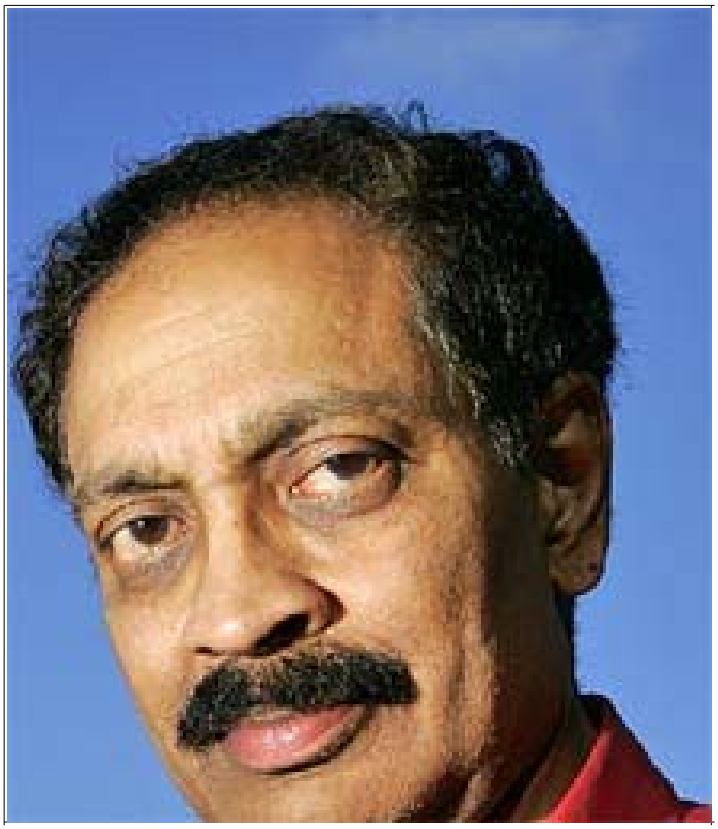
A working brain consists of 100 billion neurons (more than all the stars in the Milky Way), each connected to as many as 10,000 other neurons, the entirety combining to produce more possible states of mind than the estimated number of elementary particles in the known universe.



EARNIE GRAFTON / Union-Tribune

But numbers don't explain how the human brain actually works. Or more important, how it makes humans human. To do that, you need to look at brains that don't work quite so well.

That's the province of Dr. Vilayanur S. Ramachandran, a 55-year-old cognitive neuroscientist at UCSD who, for more than two decades, has been exploring – and explaining – some of humanity's curiouser mental conditions, from people who still feel their missing appendages to those who see numbers in colors or smell sounds to patients who believe their families have been replaced by impostors.

These are matters of the mind, but Ramachandran believes they can be

resolved through basic biology, by better understanding how the brain's multitudinous cells function together. Like his friend and mentor, the late Nobel laureate Francis Crick, Ramachandran believes that within the gelatinous brain (think warm Jell-O) exist empirical explanations for virtually everything that defines and differentiates us as human beings.

“All the richness of our mental life – all our feelings, our emotions, our thoughts, our ambitions, our love life, our religious sentiments and even what each of us regards as his own intimate private self – is simply the activity of these little specks of jelly in your head, in your brain. There is nothing else.”

Crick, who died in 2004, said much the same thing. He called it “the amazing hypothesis.” Ramachandran wants to prove it.

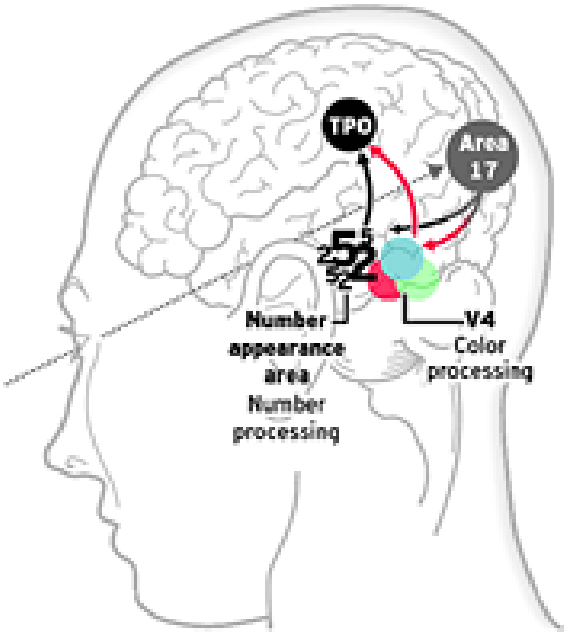
A born scientist

V.S. Ramachandran – Rama to his friends – was born in Tamil Nadu, India, in 1951. The son of an Indian diplomat, he spent much of his early life abroad, moving with his family from post to post in Asia and India.

“There were lots of upheavals, but not in a bad way,” he says. “I thought it was a good thing. It kept me open-minded.”

As far back as he can remember, Ramachandran was curious about the natural world. When the family garden in Bangkok flooded with annual rains, he collected tadpoles and studied them, once adding thyroid hormones to the water to speed their metamorphosis into “miniature frogs.” Later in Madras, a coastal town in southern India now known as Chennai, Ramachandran systematically gathered, identified and categorized seashells with the aid of library books.

“I was socially isolated as a kid. I had friends, but I wasn't very good at sports and that sort of thing so I became quite comfortable being by myself, exploring,” Ramachandran recalls. “The world was my private playground, and in it, I was supreme. Darwin, Faraday, Huxley and other great scientists were my companions.”



Crossing senses

Ramachandran also aspired to become a scientist, perhaps in embryology – a nod to his tadpole days – but his father urged a career in medicine. “He said even a bad doctor can still make a good living.” So Ramachandran attended Stanley Medical College in Madras, from which he graduated in 1974.

Medical school taught Ramachandran how to observe and think. It also introduced him to real patients with real ailments, some neurological.

“If you're a thinking person, the liver is interesting, but nothing is more intriguing than the brain,” Ramachandran says. “I mean, there are people who deny their hand belongs to them. How can anything be more fascinating than that?”

After Madras, Ramachandran went to Trinity College at the University of Cambridge, where he studied human psychophysics and neurophysiology. Then he moved to the California Institute of Technology. In 1983, he came to UCSD.

Over the years, Ramachandran's work has attracted broad attention, not least because he pursues such unabashedly engrossing topics.

“My interests span biology,” he says, “though sometimes I feel like an anachronism, somebody from the Victorian era when there weren't so many boundaries dividing the sciences.”

He has investigated everything from aesthetics to religion to tropical flounders, always looking for connections between human brain biology and behavior, always looking for the next great revelation.

Ramachandran isn't interested in the grind of routine science, the necessary analyzing and confirming of earlier findings by other people. He wants to discover fundamental truths, an ambition that sometimes rankles others.

“You need to have tremendous confidence in your work, even a touch of arrogance, chutzpah,” Ramachandran says, smiling. “Many very fine researchers lack intellectual daring. It's human nature to want to be cozy, secure. But that can be a cul de sac. And I have really never

cared about peer approval.”

“Rama's approach is that it takes as long to do an experiment that addresses a little question as it does to do an experiment that addresses a big question, so why not pursue the big questions,” says Edward Hubbard, a colleague and post-doctorate fellow in cognitive neuroimaging at Federic Joliet Hospital in Orsay, France.

His genius, adds William Hirstein, who worked with Ramachandran at UCSD for several years and is now chairman of the philosophy department at Elmhurst College in Illinois, is finding hard evidence to harder questions.

“Rama is an imaginative person who wants to test the biggest questions, but he's also a practical experimentalist.”

In the late 1990s, for example, Ramachandran and colleagues reported that religious belief likely originates in the temporal lobes of the brain, an area that handles many high-level cognitive skills but also mediates intense emotional feelings, such as joy, terror and dread. The work was derived from studies with patients with temporal lobe epilepsy, who said they frequently had deep religious experiences during and after seizures.

Such work draws the ire of those who fear science is reducing people to mere biological mechanisms. Jaron Lanier, the computer scientist credited with popularizing “virtual reality” technology and coining the term, insists that Ramachandran does nothing of the kind.

“He is looking at the brain scientifically, at a level of detail that is new, but in such a way that he doesn't dehumanize people at all. He has a respect and awe of what it means to be human, without losing his scientific understanding.”

Three case studies:

Phantom limbs

Ramachandran's early scientific career focused on visual perception. He notes that the act of seeing is extraordinarily complex, involving more than 30 brain regions. His work helped explain how the eyes combine information to perceive depth and how shading, motion and other phenomena affect what the brain “sees.”

In the late 1980s, he shifted to other studies, specifically the mental conditions that he believed offered insight into brain function and larger mysteries like human consciousness.

Perhaps his best known work involves phantom limbs – a neurological syndrome in which 50 percent to 80 percent of amputees say they still

experience sensations – pain, warmth, cold, movement – in their missing appendages. For years, it was medical dogma that the phenomenon was related to affected peripheral nerves. Ramachandran thought the source was a changing brain.

On your brain lies a map of your body, with different sections of the brain's cerebral cortex corresponding to and with different parts of the body. “It's almost as though you have a little person draped on the surface of the brain,” said Ramachandran.

But this map is anatomically scrambled. It's not arranged like a person at all. The cortical section responsible for the face, for example, is next to the region that keeps tabs on the hands.

To test his hypotheses, Ramachandran examined amputees. One man reported feeling sensations in his missing hand when Ramachandran touched a cotton swab to his cheek.

Ramachandran realized that sensory signals from the face were also being processed by the part of the brain that had once been responsible for the now-missing hand and that higher centers of the brain were misinterpreting those signals as coming from the phantom limb.

He repeated the experiment with other patients, with the same results. Subsequent neuroimaging studies have provided proof of the brain's sensory reorganization.

Synesthesia

Synesthesia is the cross-wiring of the senses: In affected people numbers can take on specific colors, sounds can evoke specific smells. The touch of something can cause a certain taste in the mouth. Synesthesia occurs in an estimated 1 in 200 to 2,000 people.

Though first described in 1880, the syndrome was long regarded as merely odd, and perhaps not even real. Through a series of simple experiments, Ramachandran helped prove synesthesia was a legitimate

phenomenon and that every person, to some degree, possesses synesthetic abilities.

In one set of experiments, volunteers were shown large groupings of black-printed numbers, say 2s and 5s, on a white background. For most volunteers, the numbers appeared to be randomly printed. But for synesthetes who see 2s in the color green and 5s in the color red, a pattern was quickly obvious. The 2s formed the outline of a triangle in a scattered sea of 5s.

Ramachandran believes synesthesia is generally an inherited condition. It seems to run in families and appears to be more common in writers, actors and artists. But why has the gene persisted, Ramachandran wondered? To what purpose? He believes synesthesia survives because it increases brain connectivity. It improves the facility for finding associations between disparate subjects. “Evolutionarily, that's a useful ability,” he says.

To some degree, everybody mixes sensory input. Here's a Ramachandran thought experiment: Imagine two shapes – a bulbous blob of undulating curves and a jagged form, all sharp edges and corners. The shapes have names, either booba or kiki. Which is which?

The vast majority of people say the blob is a booba and the jagged object a kiki because the sounds of their names reflect their visual properties. It's an example of mild synesthesia. The brain is combining two distinctly different senses – vision and hearing – to make a choice.

Capgras delusion

Capgras delusion is much rarer than synesthesia. It is a neurological syndrome in which patients, who have invariably suffered some sort of brain trauma, adamantly insist that a spouse or family member has been replaced by an impostor. In all other aspects, they seem quite normal.

Psychiatrists once supposed the condition was Freudian, somehow linked to repressed desires. Ramachandran and Hirstein hypothesized

that it was biological, the result of a dysfunction in the brain structures that regulate emotions, including responses to familiar faces.

Their evidence is compelling. Capgras delusion seems to exist only in a visual context. An afflicted patient who doesn't respond to his visiting mother (though he concedes she looks just like his mother) will, nonetheless, happily recognize the same woman's voice on the telephone as his mother.

Ramachandran explains it this way: “What we suggest is that maybe what's gone wrong is that the fusiform gyrus (involved in face perception) and all the visual areas are completely normal in this patient. That's why when he looks at his mother, he says, 'Oh yeah, it looks like my mother,' but the wire, to put it crudely, that goes from the amygdala to the limbic system (which regulate emotion) is cut by the accident. So he looks at his mother and he says: 'Hey, it looks just like my mother, but if it's my mother, why don't I experience this warm glow of affection?' ”

Hirstein and Ramachandran tested the idea using galvanic skin response (GSR) – a method of measuring electrical resistance of the skin. For reasons not entirely clear, emotional changes alter the skin's ability to conduct electricity. In Capgras patients, Ramachandran found, familiar faces provoked no change in GSR activity.

The hidden self

The Holy Grail of neuroscience is human consciousness. That is, a scientific understanding of what creates and fuels the totality of one's thoughts, feelings and impressions.

While Ramachandran concedes there are aspects of consciousness that probably lie beyond the investigative powers of science, he thinks consciousness ultimately will be explained.

He contends that consciousness is essentially the collaborative, collective consequence of certain regions of the brain, among them the insula, amygdala, inferior parietal lobule and Wernicke's area.

“These structures provide 70 to 80 percent of humanity,” he says.

The parietal lobe, for example, handles math and metaphor – two distinctly human abilities. Wernicke's area processes the meaning of spoken words.

Currently, Ramachandran is investigating mirror neurons, brain cells (first discovered in the 1990s) that are found abundantly in humans and to a lesser extent in other primates. These cells specialize in mimicking and understanding not just the actions of others, but also the underlying intentions, emotions and social meaning of behavior.

In research published earlier this year, Ramachandran and colleagues suggested that autism may be linked to dysfunctional mirror neurons. The researchers conducted electroencephalograph recordings of 10 autistic individuals. Mirror neurons in normal brains fire both when the person performs an action and when the person observes the same action performed by someone else.

In the tested autistic individuals, however, the mirror neurons responded only to what the individual did, not when they watched others do the same thing.

“Mirror neurons break down the barriers between people,” says Ramachandran. “They are the basis of empathy. They're involved in imitation and learning. They allow you to put yourself in other people's shoes, to adopt their point of view. No other species can do that.”

But Ramachandran posits that mirror neurons do even more: They permit the brain/mind to examine itself. “Just as mirror neurons allow you to take another's perspective, they allow you to see yourself, to reflect. This, I believe, is a part of what we call self-awareness.”

To be sure, there remains much to discover, and Ramachandran intends to be among the discoverers. Others think so, too.

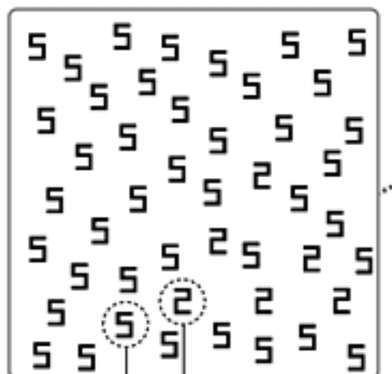
“Rama's one of the most important neuroscientists since Paul Broca (a pioneer in neuroanatomy), both in his approach and his results,” says Dr. Eric Altschuler, a former colleague and now a professor of physical medicine and rehabilitation at the University of Medicine and Dentistry of New Jersey.

“There are two kinds of genius: those who get their insight in a library and those in which it is just innate, an instinct. Rama has a deep, almost otherworldly understanding of the brain.”

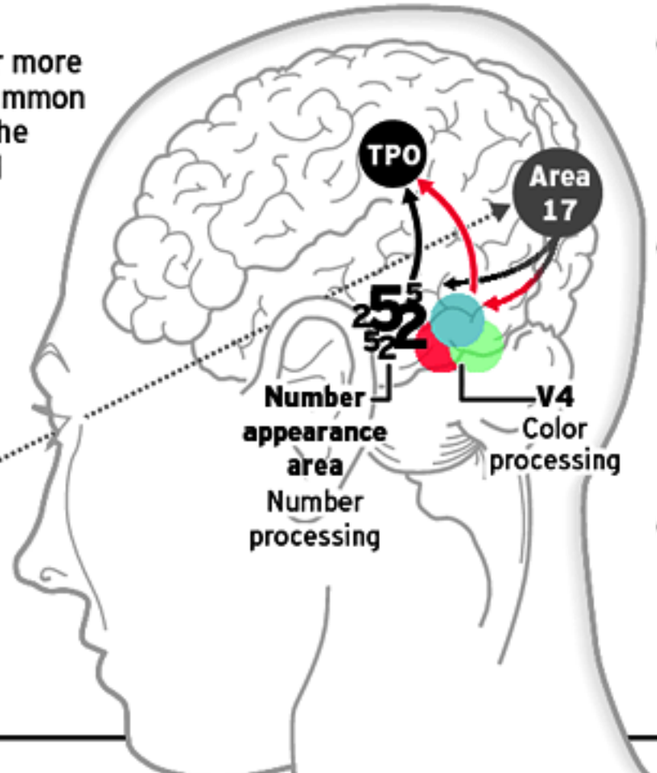
Crossing senses

Synesthesia is a condition in which people blend two or more senses, such as tasting shapes, or hearing colors. In a common form, looking at a numeral evokes a specific color for the viewer. Below is a visual test for this phenomenon, and how the brain of a synesthete may perceive it:

NON-SYNESTHETES



1 In this test, **non-synesthetes** look at a field of black 5s and 2s. For them it is difficult to discern between the two numerals without inspecting each character, one at a time.

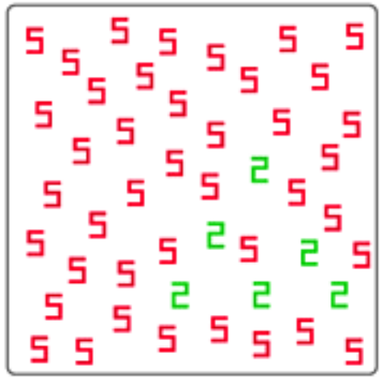


2 Human brains process visual information in steps. Information is first sent to a place called "**Area 17,**" where it is broken into simple attributes, such as color and form.

3 Color information then continues to an area called "**V4,**" which is near the area responsible for "**number appearance.**" Color and number information are further processed at a junction between the temporal, parietal and occipital **(TPO)** lobes.

4 Because color and numbers are processed near each other in the brain, it is possible that these areas are **cross-linked** in synesthetes.

SYNESTHETES



5 As a result, synesthetes may see a triangle of green 2s among red 5s in the test, though the numerals are actually black.

SOURCES: Dr.Vilayanur S. Ramachandran and Dr. Edward M. Hubbard, *Scientific American*

AARON STECKELBERG / Union-Tribune