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COLUMN ONE | MAPPING THE MIND

Deep, Dark Secrets of His and Her Brains

Sandra Witelson had studied scores of brains looking for gender differences. Then she found one that made a difference: Einstein's.

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June 16, 2005

HAMILTON, Canada — The invitation curled from her fax machine, a courtly question scrawled above the signature of a man whose name she did not recognize.

"Would you be willing to collaborate with me on studying the brain of Albert Einstein?"

It was signed Thomas Harvey. Sandra Witelson did not hesitate.

She wrote "yes" on the piece of paper and faxed it back.

"It never occurred to me that it might be a joke," she recalled. "I knew that Albert Einstein's brain had been preserved and that it was somewhere where someone was looking after it."

For 40 years, Harvey, a retired pathologist from Princeton, N.J., had been the quixotic custodian of the 20th century's most famous brain.

In 1955, he had conducted a routine autopsy of Einstein after the 76-year-old physicist died at Princeton Hospital. The remains were to be cremated. Harvey, however, decided to preserve the organ responsible for the theory of relativity and the principle of the atomic bomb.

It was not such an unusual thing to do. Einstein's ophthalmologist had removed the scientist's eyeballs and put them in a safe-deposit box. Earlier acquisitive anatomists had preserved Galileo's finger, Haydn's head and Napoleon's penis.

For Harvey, however, more than morbid curiosity was at work. He believed that the slippery worms of Einstein's brain tissue, pickled in warm formalin, embodied some clue to the mystery of intelligence. He held on to that hope through 40 years of indecision.

Eventually, it led the soft-spoken Quaker to Witelson, a raven-haired Canadian psychologist with a taste for black leather and red showgirl nails.

She had brains, dozens of them — the largest collection of normal brains in the world.

When Witelson began acquiring human brains, sex was the last thing on her mind.

Inside her walk-in refrigerator at McMaster University here in Ontario, her collection filled three walls of metal shelves. The 125 putty-colored specimens sat in frosted jars and snap-top plastic tubs like quarts of boiled shrimp and wedges of cheese.

Every one posed a riddle that had shaped her research for 30 years: How does the structure of the brain influence intelligence?

A professor of psychiatry and neuroscience, Witelson grappled with such a fundamental mystery by studying a somewhat smaller one: why certain abilities develop on one side of the brain rather than the other.

The two hemispheres of the brain are almost symmetrical physically but can seem to be separate minds when it comes to awareness and mental processing. They even have different problem-solving styles, researchers report. Yet they work together seamlessly to produce a single mind.

By 1977, Witelson was trying to learn why language skills developed on the left side of the brain for all right-handers but on the right side for many left-handers.

To compare the two sides, she needed normal brains — more than anyone had gathered before.

For 10 years, she worked through a network of doctors and nurses, hoping to persuade terminal cancer patients to make a last contribution to medicine. Her research was funded by the U.S. National Institutes of Health.

By 1987, 120 men and women had agreed to donate their brains after death. They all submitted to thorough psychological and intelligence tests so that each brain would be accompanied by a detailed profile of the mind that had animated it.

In the prime of life, the cerebral cortex contains 25 billion neurons linked through 164 trillion synapses.

Thoughts thread through 7.4 million miles of dendrite fibers and 62,000 miles of axons so compacted that the entire neural network is no larger than a coconut.

No two brains are identical, nor are two minds ever the same.

With so many well-documented donors, however, Witelson could conduct comparative brain studies on an unprecedented scale.

She could confidently seek relationships between anatomical features and mental capacities. She could also compare right-handers and left-handers, and sort the organs by gender.

In an era when people probe the thought process with scanners, radioactive tracers and super-conducting sensors, Witelson's approach was deliberately old-fashioned.

She measured her brains.

She weighed them.

She cut them up and counted the cells.

She traced synapses, the junctures where impulses pass from one neuron to another in the hidden root cellars of the brain.

Wherever she looked, she discerned subtle patterns that only gender seemed to explain.

"We actually didn't set out to find sex differences," she said. "Sometimes as a scientist, you are doing one thing and you bump into something else."

Controversial Matters

The brains in Witelson's freezer are contested terrain in a controversy over gender equality and mental performance.

Her findings — published in Science, the New England Journal of Medicine, the Lancet and other peer-reviewed journals — buttress the proposition that basic mental differences between men and women stem in part from physical differences in the brain.

Witelson is convinced that gender shapes the anatomy of male and female brains in separate but equal ways beginning at birth.

On average, she said, the brains of women and men are neither better nor worse, but they are measurably different.

Men's brains, for instance, are typically bigger — but on the whole, no smarter.

"What is astonishing to me," Witelson said, "is that it is so obvious that there are sex differences in the brain and these are likely to be translated into some cognitive differences, because the brain helps us think and feel and move and act.

"Yet there is a large segment of the population that wants to pretend this is not true."

No one knows how these neural differences between the sexes translate into thought and behavior — whether they might influence the way men and women perceive reality, process information, form judgments and behave socially.

But even at this relatively early stage in exploration of the brain's microanatomy, battle lines between scientists, equal rights activists and educators have formed.

Some activists fear that research like Witelson's could be used to justify discrimination based on gender differences, just as ill-conceived notions of human genetics once influenced laws codifying racial stereotypes about blacks, Asians and Jews.

Other experts argue that the physical differences Witelson observed may result not from the brain's basic design but from conditioning that begins in infancy, when the brain produces neurons at a rate of half a million a minute and reaches out to make connections 2 million times a second.

Spurred by learning, neurons and synapses are ruthlessly pruned, a process that continues in fits and starts throughout adolescence, then picks up again in middle age.

"The brain is being sculpted gradually through sets of interactions," said Anne Fausto-Sterling, a gender studies expert at Brown University. "Even when something in the brain appears biological, it may have come to be that way because of how the body has experienced the world."

As Witelson's research helped establish, however, the mental divide between the sexes is more complex and

more rooted in the fundamental biology of the brain than many scientists once suspected.

In the last decade, studies of perception, cognition, memory and neural function have found apparent gender differences that often buck conventional prejudices.

Women's brains, for instance, seem to be faster and more efficient than men's.

All in all, men appear to have more gray matter, made up of active neurons, and women more of the white matter responsible for communication between different areas of the brain.

Overall, women's brains seem to be more complexly corrugated, suggesting that more complicated neural structures lie within, researchers at UCLA found in August.

Men and women appear to use different parts of the brain to encode memories, sense emotions, recognize faces, solve certain problems and make decisions. Indeed, when men and women of similar intelligence and aptitude perform equally well, their brains appear to go about it differently, as if nature had separate blueprints, researchers at UC Irvine reported this year.

"If you find that men and women have fundamentally different brain architectures while still accomplishing the same things," said neuroscientist Richard Haier, who conducted the study, "this challenges the assumption that all human brains are fundamentally the same."

Yet, for the most part, scientists have been unable to document such patterns conclusively.

No one, however, had scrutinized as many brains as Witelson.

Detailing Differences

She began by studying the corpus callosum, the cable of nerves that channels all communication and cooperation between the brain's two hemispheres.

Examining tissue samples through a microscope, she discovered that the more left-handed a person was, the bigger the corpus callosum.

To her surprise, however, she found that this held true only for men. Among women there was no difference between right-handers and left-handers.

"Once you find this one difference," she remembered thinking, "it implies that there will be a cascade of differences."

As she systematically analyzed the brains in her refrigerator, she discovered that other neural structures seemed larger or smaller among men, depending on whether the man had been right-handed or left-handed.

They were relatively the same size in women. "The relationships that we were finding were always — and I do mean always — different for men and women," she said.

She narrowed her study to right-handed men and women, still looking for differences in microscopic anatomy between the left side of the brain and the right side. She meticulously counted the neurons in sets of tissue in which each sample measured 280 microns wide — about twice the thickness of a human hair — and 3 millimeters deep.

Staring through the microscope, she was baffled.

"I had the first two patients, and they were so very different," Witelson said. "I kept looking and looking at them, trying to see what the difference could be."

Then she consulted the donor documentation for each tissue sample. "Finally, I saw that one was a man, and one was a woman."

Among women, the neurons in the cortex were closer together. There were as many as 12% more neurons in the female brain.

That might explain how women could demonstrate the same levels of intelligence as men despite the difference in brain size.

"So among female brains, the cortex is constructed differently, with neurons packed more closely together," she said.

Witelson probed deeper. She knew that the human cortex was a sandwich of six layers, each packed with neurons.

She peeled away the sheets of the temporal lobe — a region associated with perception and memory — in several of her brain specimens. She discovered that the increased neural density occurred only on layers 2 and 4, which form the hard wiring for signals coming into the brain.

Then she analyzed the microscopic structure of the prefrontal cortex. There the crowding of neurons was evident only in layers 3, 5 and 6, which carry the wiring for outbound signals.

Just to be sure, she checked left-handed brains as well as right-handed brains. She found the same sex differences when she surveyed her left-handed brains.

Perhaps, she speculated, these neuron-rich layers in an area associated with perception and speech were the reason women scored more highly than men on tasks involving language and communication.

Slowly, she formed a theory: The brains of men and women are indeed different from birth. Yet the differences are subtle. They might be found only among the synapses in brain structures responsible for specific cognitive abilities.

For so long, scientists had championed the idea of larger brains as an indicator of intellect. Witelson, however, gradually became convinced that overall brain size didn't matter.

"One of the things that firmed it up for me," she recalled, "was the case of Einstein."

An Odd Pursuit

By taking Einstein's brain, Thomas Harvey had succumbed to an impulse older than medicine.

Since the days of Hippocrates, philosophers and scholars have been arguing over how the brain houses an intangible human spirit. St. Augustine was convinced that the soul lodged in the fluid-filled cavity of the organ's middle ventricle. Galen, the ancient pioneer of medicine, argued that vital spirits resided in the fourth ventricle.

When modern scientists discovered that intellect could be traced to neural tissues, brains became precious curios. Pathologists collected the brains of gifted musicians, scientists and other notables the way 18th century literary enthusiasts held onto the hearts of poets such as Percy Bysshe Shelley and Lord Byron.

Researchers at the Moscow Brain Institute measured dozens of the most brilliant brains. Vladimir Lenin, the leader of Russia's Soviet revolution, had a brain weighing about 3 pounds, they determined. The brain of writer Ivan Turgenev weighed 4.4 pounds. That of satirist Anatole France was 2.1 pounds.

At Princeton Hospital, Harvey weighed Einstein's brain on a grocer's scale. It was 2.7 pounds — less than the average adult male brain.

He had the fragile organ infused with fixative and dissected it into 240 pieces, each containing about two teaspoons of cerebral tissue. He shaved off 1,000 hair-thin slivers to be mounted on microscope slides for study.

For years, Harvey agonized over how next to proceed. His odd pursuit inspired two books: "Possessing Genius" by Carolyn Abraham and "Driving Mr. Albert" by Michael Paterniti. Through the decades, however, he drifted in obscurity.

Finally in 1985, pioneering neuroanatomist Marion Diamond at UC Berkeley persuaded him to part with four small plugs of brain tissue. Diamond discovered that the physicist's brain had more cells servicing, supporting and nurturing each neuron than did 11 other brains she studied. These unusual cells were in a region associated with mathematical and language skills.

When they published their findings, the researchers speculated that these neurons might help explain Einstein's "unusual conceptual powers."

Critics contended the study was riddled with flaws, its findings meaningless.

Eventually, Harvey mailed bits of Einstein's motor cortex to a researcher at the University of Alabama, who reported that the cortex appeared to be thinner than normal but with more tightly packed neurons.

Had it simply been compacted by time and storage conditions?

DNA testing revealed nothing. The preservative fluids apparently had scrambled Einstein's genetic code.

Then in 1995, Harvey happened across Witelson's work. He read her research paper on gender differences and neuron density in the Journal of Neuroscience.

"It was impressive," he recalled. He was even more intrigued to learn about her collection of brains. He was 84, still hoping that his tissue samples had something to teach about the neural geography of genius. To make ends meet, he was working in a plastics factory. Worrying about Einstein's brain, like the years, had become a burden.

Harvey carefully packed it in the back of his battered Dodge and drove north to Witelson's laboratory. "I had the brain in a big jar," Harvey, now 94, recalled.

At midnight, he crossed over the Rainbow Bridge by Niagara Falls into Canada.

Customs officials asked if he had anything to declare. Just a brain in the trunk, he told them.

They waved him through.

Pieces Fall Into Place

Witelson could barely contain her curiosity.

Einstein's brain — so far from ordinary in its intellectual achievement — might reveal a telltale anatomical signature. Size alone certainly could not account for his brain power.

"Here was somebody who was clearly very clever; yet his overall brain size was average," Witelson said. "It certainly tells you that, in a man, sheer overall brain size can't be a crucial factor in brilliance."

For a moment, she was like a schoolchild picking candies from a Valentine's Day sampler. She judiciously selected 14 pieces of Einstein's brain. She took parts of his right and left temporal lobes, and the right and left parietal lobes.

Never had Harvey given away so much brain.

Witelson and her colleagues carefully compared the 40-year-old tissue samples with dozens of normal male and female brains in her collection. She also compared them with brains from eight elderly men to account for any changes due to Einstein's age at the time of his death.

She found that one portion of Einstein's brain perhaps related to mathematical reasoning — the inferior parietal region — was 15% wider than normal.

Witelson also found that it lacked a fissure that normally runs along the length of the brain. The average human brain has two distinct parietal lobe compartments; Einstein's had one.

Perhaps the synapses in this area were more densely interconnected.

"Maybe this was one of the underlying factors in his brilliance," she said. "Maybe that is how it works."

She took it as confirmation of her suspicions about the anatomy of intelligence. If there were differences affecting normal mental ability, they would show up in the arrangements of synapses at particular points in the brain.

Einstein, she was convinced, had been born with a one-in-a-billion brain.

"We suggest that the differences we see are present at birth," Witelson said. "It is not a consequence of environmental differences."

She turned again to the brains in her refrigerator. Wherever she looked, she began to see evidence of how microanatomy might underlie variations in mental abilities.

As she matched the brain specimens to the intellectual qualities of their owners, she discovered that differences in the size of the corpus callosum were linked to IQ scores for verbal ability, but only in women. She found that memory was linked to how tightly neurons were packed, but only in men.

Witelson determined that brain volume decreased with age among men, but hardly at all among women. Moreover, those anatomical changes appeared to be closely tied to a gradual decline in mental performance in men. "There is something going on in the male brain," she said, "that is not going on in the female brain."

Brain Conquers All

Last year, a worried farming couple brought their youngest child to McMaster University Medical Center.

They were no longer certain whether their child was a girl or a boy. The youngster had traits of both, as occurs

in about one in 5,000 births. In this child, nature had devised a living test of gender and the brain.

The medical experts determined that the child's body was a composite of normal and abnormal cells. Some had a girl's usual complement of two female sex chromosomes. Many, perhaps due to a mutation, had only one female chromosome and consequently were almost male.

"Which cells got to the brain?" wondered Witelson, who was called in as a consultant. "You have to consider the sex of the brain."

The doctors all suspected the child's brain was masculine. There was no way to know for sure. They could not safely take a sample of neural tissue to biopsy.

Until recently, reconstructive surgery based on a doctor's best guess was the rule in such cases. But in Hamilton, they counseled patience, Witelson recalled.

"We said, 'Let the child's behavior tell us what sex the child is.' "

Given time, she believed, the brain would reveal itself.