Brain Researcher Defies Conventional Wisdom on Estrogen

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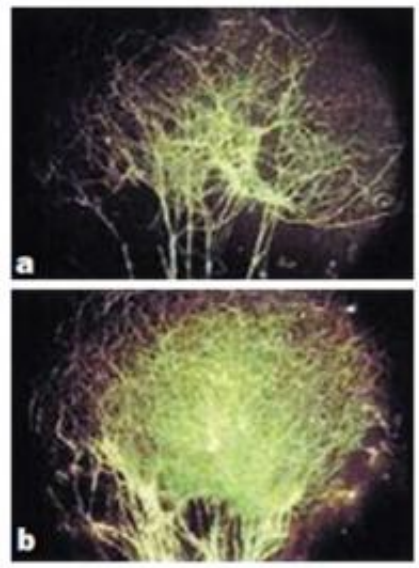

These images show the effect of estrogen on the growth of brain cells and circuitry: a) mouse brain tissue without estrogen, and b) with the addition of estrogen.

(PhysOrg.com) -- When Dominique Toran-Allerand started studying the effects of estrogen in the brain some 40 years ago, her research was considered so unconventional as to be unbelievable. One of her first papers, she recalls, was met with a four-page single-spaced rejection letter from the *Journal of Brain Research*.

“There is a lot of dogma in science,” she sighs. “When you’re challenging

dogma, it makes your work more difficult to prove."

Today, the estrogen-brain connection is an accepted part of neuroscience , and Toran-Allerand's work is considered groundbreaking. Now 75, this professor of pathology and cell biology in obstetrics and gynecology at the College of Physicians and Surgeons continues to examine estrogen's effects from her laboratory on the 16th floor of the P&S building. She is currently working on an NIH-supported project grant with colleagues at the University of North Texas.

"She has continued to shape our understanding of how estrogen affects the brain, making numerous seminal discoveries in the process," said Mehar-van Singh, an associate professor and assistant dean of biomedical sciences at the University of North Texas Health Science Center. Singh worked with Toran-Allerand as a post-doctoral fellow and continues to do so today on the new NIH project grant. His own specialty focuses on hormone neurobiology. "Her work is relevant to our understanding of how certain parts of the brain develop, how estrogen influences mood, and how estrogen's actions may impact the aging and/or diseased brain."

Such recognition seemed far off in 1973, when Toran-Allerand started examining a little-understood strand of neuroanatomy. Although the idea of examining estrogen was suggested by her department chair at the time, Raymond Vande Wiele—a visionary whose own preliminary experiments suggested the brain might be influenced by hormones—her male counterparts thought it a waste of time. "When something is new, it's extraordinarily difficult to get people to accept the possibility that this might actually exist."

In fact, Toran-Allerand's experiments found that after estrogen was introduced into the brain cells of mice, the hormone appeared to stimulate cell growth and development. It turns out that estrogen

stimulates more interactions between nerve cells, aiding cognition. As soon as she saw those results, she was hooked.

“Estrogen is very important for the brain to function normally. That’s hard for people to accept, because it’s true for both males and females,” she said. “It’s not just a hormone that is important for reproduction; it’s a hormone that’s very important for the well-being of the brain in both sexes.” For men, estrogen is converted from their own testosterone in the brain.

Subsequent studies have further demonstrated estrogen’s effects on the brain and its development and cell viability. Researchers at the University of California, San Francisco, for instance, found that estrogen is directly responsible for the development of brain circuits in males that guide aggressive and territorial behaviors. And at the University of Rochester, scientists recently demonstrated that estrogen plays a role in how the brain processes sound and that it may possibly control other sensory processes as well. Estrogen can also delay or prevent Alzheimer’s disease or memory loss.

Born in Paris, Toran-Allerand emigrated with her family to New York during World War II. After graduating from Albany Medical College in 1959, the only female medical student in her class, she was also the lone female neurology resident at the Neurological Institute. Classmates gave her a hard time. “They would call me nurse in front of the patients,” she recalled. “Women just weren’t accepted then.”

But she knew from the start that she wanted to do research. “I really liked neuroanatomy. God knows why,” she said with a laugh. “I just found the brain very interesting.”

Toran-Allerand is still challenging conventional wisdom. Her current research concerns the effects of two different forms of estrogen on the

brain. One, 17beta-estradiol, is made in the ovaries and has reproduction functions. The other, 17alpha-estradiol, is made in the brain but has no apparent purpose. “For me, this just doesn’t make any sense,” she said. “Why would the body go through the trouble of making something if it had no function.”

Her early findings show that 17alpha-estradiol is better able to stimulate the formation of nerve cells and appears to be “a powerful antidepressant made locally in the brain,” she said. The next step is to explore whether the brain can make enough of this hormone to effectively control or treat depression in women and men, and whether it could prevent or treat postpartum depression.

Despite 40-plus years of study, Toran-Allerand said there is still much to learn about estrogen, and she has no plans to retire. Indeed, her fierce approach to her research is on display in her small office.

Taped to a file cabinet is a quote by the German philosopher Arthur Schopenhauer, which Toran-Allerand refers to often. “All truth goes through three stages,” it reads. “First, it is ridiculed. Then it is violently opposed. Finally, it is accepted as self-evident.”

Provided by Columbia University