By Bernadine Healy, M.D.

It was a flashbulb memory for the University of Southern California's memory maven, Roberta Diaz Brinton. When researchers revealed in May that hormone replacement therapy increased rather than decreased the risk of Alzheimer's disease, most postmenopausal women took the news rather passively. Understandably, as they were already deflated by unhappy findings from just a year before about HRT and the heart. But Brinton was among a small close-knit group of neuroscientists who were flabbergasted.

For decades estrogen has reigned as the memory molecule—the received wisdom from aging rats, songbirds, monkeys, and even some studies in women. Many memory researchers worried these new findings from the government's Women's Health Initiative might make their own work seem obsolete. But the 52-year-old Brinton responded differently, recalls Sally Shumaker, WHI researcher at Wake Forest University and head of the memory study. Brinton called her immediately and said, "Wow, this is really exciting. You've done a terrific study. I know my work is good, so what's this telling us? Let's figure it out." Since then, she's become a constructive voice in one of the hottest health debates of our time, one that is bedeviling millions of boomers facing their own sinking estrogen levels.

Open doors. As a self-described "one-organ woman," Brinton's passion is the brain. It grabbed her interest just out of high school while she was working as a lab technician in a mental hospital. That, plus the epiphany that she was as smart as any medical student around, encouraged her to go to college at night, then on to a Ph.D. in neuropharmacology. This Hispanic woman from a working-class New Jersey family says it was fated: "God always opened one door and booted me through it."

Her own saga inspires her leadership of the Science, Technology and Research Program, or STAR, which brings low-income high school kids into USC research labs. (So far, all participants have gone to college, and most beyond.) One futuristic project that always captures their interest involves both Brinton and her husband, Theodore Berger, a biomedical engineering professor at USC. They are collaborating on an implantable memory chip that they hope someday will connect with the brain's memory center and give failing memories a boost. "We're geeks in love," she says.

Meanwhile, Brinton's main research interest is still the natural molecules that influence memory, notably estrogens. Long ago she decided to learn about remembering and forgetting by "following estrogen around the brain like Sherlock Holmes." What her sleuthing revealed is most evident under the microscope, where one can see estrogen-treated brain cells sprouting connections, wiring networks, and cooperating in creating memories: "They scream back at you, 'I'm able to do my neuron job-spec now!' " Give brain cells a drink of estrogen, she says, and then hit them with a deadly toxin like the amyloid that underlies Alzheimer's disease—and they survive. "Are they invincible? No. But they are more resilient."

But Brinton is quick to add that there is another side to this tricky hormone—estrogen can also be a neuron slayer. Her explanation: Estrogen has evolved over eons to have a "healthy cell bias." It protects robust cells but prompts the demise of weak ones. Hence the double-edged sword that might partially explain the WHI memory study. It included only women age 65 and older, some very likely having unrecognized brain cell degeneration that estrogen would not favor.

Given this new understanding, the practical questions shift to whether starting estrogen at the onset of menopause and continuing it will cause fewer cells to degenerate with age. The answer is unclear. These are "Goldilocks drugs," she says; you have to get the "porridge" just right. She's looking to tailor formulations for that group of women she dubs "estrogen dependent," who suffer serious hot flashes, sleep problems, and the verbal memory lapses she calls "whatchamacallit syndrome."
Unlike many of her colleagues, Brinton is energized by the recent shake-up of an overly simplified notion that hormone replacement is all things to all women. Now scientists must delve even deeper into the hormone well and get the answers women are still waiting for.