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Ann Graybiel is considered by peers to be the leading expert on the part of the brain that controls daily habits. (Globe Staff / Dominic Chavez)

MIT researcher has routine behavior on the brain

By Carol Cruzan Morton, Globe Correspondent, 6/11/2002

Nearly every morning, MIT scientist Ann Graybiel begins a daily exercise routine that often includes sit-ups, toe-touches and a 2-mile jog. It's a short and varied routine she can nearly do without thinking - and she ought to know.

Graybiel is widely regarded among scientists as the expert on the part of the brain that controls our daily habits, the basal ganglia that run the physical lessons crucial for life's daily routines. For more than three decades, she has looked at this fist-sized part of the brain nested inside the deeply wrinkled rind of the cortex. Shaped like a comet with a tail, the basal ganglia record a baby's first grasp of a cat's tail. Once people learn to ride a bike, their basal ganglia never forget.

For this pioneering work, which also has relevance for neurological disorders such as Parkinson's and Huntington's, Graybiel will receive the 2001 National Medal of Science, the country's highest honor in science, during a ceremony Thursday at the White House. She also has been named the 2002 recipient of the James R. Killian Faculty Achievement Award at the Massachusetts Institute of Technology, the top faculty honor.

"Ann has singlehandedly transformed the study of this part of the brain," said Mriganka Sur, who teaches two neuroscience classes with Graybiel and studies how the brain changes during development and in adulthood. "She is the acknowledged leader in the study of the large and complex part of the brain involved in movement."

Graybiel traces her excitement about science to her parents. Her mother was not a scientist but started reading medical books at age 5 and stayed interested in science. Her father was a cardiologist at Massachusetts General Hospital and coauthored with

Paul Dudley White the first textbook of clinical electrocardiography. During World War II, he moved the family from Chestnut Hill to Pensacola, Fla., and conducted seminal research that helped prepare astronauts for space flight. Ann joined her father at John Glenn's launch to the first manned orbit of the Earth by an American.

In northern Florida, science was first taught in the ninth grade and not to girls. Instead, Graybiel learned how to make an apron in home economics. Her parents sent her to boarding school at National Cathedral High School in Washington, D.C. She was in the first class of Radcliffe women who graduated with a Harvard degree in 1964. As an undergraduate, she settled on chemistry and biology, which might have served as a premedical major if she hadn't been so captivated by science.

She went on to receive a doctorate in psychology and brain science from MIT, and stayed and moved up through the tenured faculty track. In graduate school, Graybiel met her husband, James Lackner, now a professor of physiology at Brandeis University.

In college, Graybiel seemed "the smartest person in the world," said MIT colleague Nancy Hopkins, who was in the same class at Radcliffe. "In a room of 400 students after a lecture in physics at Harvard leaving most people in a stupor, one hand would shoot up and someone would ask a brilliant question," Hopkins said. "That was Ann Graybiel."

Three years ago, a committee led by Hopkins and composed of the 14 top tenured women professors, including Graybiel, made a splash with their report on largely unintentional but pervasive discrimination against women in the MIT School of Science in areas including hiring, awards and promotions.

Graybiel considers herself foremost a scientist, not an activist, said Hemai Parthasarathy, a senior editor at the weekly journal, Nature, who earned her doctorate in Graybiel's lab. "She just gets on with it," Parthasarathy said. "She gives practical advice for being a woman in a male field." This year, Graybiel was the only woman among 14 men also selected as recipients of the 2001 National Medal of Science.

She may be best known as the scientist who did the most to reveal the fundamental architecture of the basal ganglia. Major chemical transmitters there - such as dopamine - are distributed in a mosaic of tiny compartments composed of groups of nerve cells. The basal ganglia are life's little instruction book for routines that once took most of your brain to learn. It says, "Don't think, just do." A small cue is enough to trigger the complex pattern of any rote task, such as starting your car and backing out of the driveway. If you intended to drive to a friend's house but instead drove your daily commute route on automatic pilot, blame it on the basal ganglia.

"The basal ganglia seemed to have no special qualities until clusters of cells with special shapes were discovered by Ann," said Nobel laureate David Hubel, who studies the visual system at Harvard Medical School and has known Graybiel since her graduate school days at MIT. "It's not a homogenous mess; it's several systems clumped together."

According to Graybiel, learning a habit takes a lot of brain power, including both the cortex and the basal ganglia. Even more neurons fire during the phase of repeated

practice required to perfect a new habit and earn more rewards. After the consolidation phase stamps the pattern into a memory somewhere in the basal ganglia, the behavior can be repeated on automatic pilot, freeing the cortex to think about other things. Multitasking is made possible by this way of ingraining behaviors. Graybiel calls her theory behind the complex ingrained behavioral routines "chunks."

In the experiments, the chunks are predictably cued by a sound in the same maze where they were learned. Without the cue and in a strange setting, the animals seem to forget the habit. Graybiel compares that to the urge to smoke when people who are trying to quit enter a room where they used to keep their cigarettes.

Be it animals or people, Graybiel is a big believer in positive reinforcement, she said as she offered a selection of Godiva chocolates to a visitor. The mice in her lab, she noted, prefer Belgium chocolate. Mice rewarded by some of the world's best chocolate have contributed much to neuroscience - such as how the brain learns or forgets a habit.

The basal ganglia shamelessly wallows in the pleasurable neurochemical offerings released there. One shot of cocaine and one part of the basal ganglia begs for more. Recently, basal ganglia circuitry gone haywire has become a prime suspect in medical disorders of movement, habit and mood. The feedback loops between the basal ganglia and the cortex and other regions of the brain may be involved in disorders as diverse as Parkinson's disease, Huntington's disease, and obsessive-compulsive disorder.

"In the case of addiction, we get a surge of dopamine, a reward signal in the brain, at least early on in the additive phase," Graybiel said. "This really turns the brain on. In a habit, we probably do, too, early on, but after a while the behavior becomes autonomous. Then, even if the reward rush isn't there, we do it anyway. The interesting thing is that some of the mechanisms that lead to repetitive behaviors in an addicted state may be similar to the ones that lead to abnormal movements in some neurological disorders."

On the positive side, habits stored in a functioning basal ganglia may outlast facts stored in the thinking part of the brain that are lost to age. "As a community of humans, we have so much potential."

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