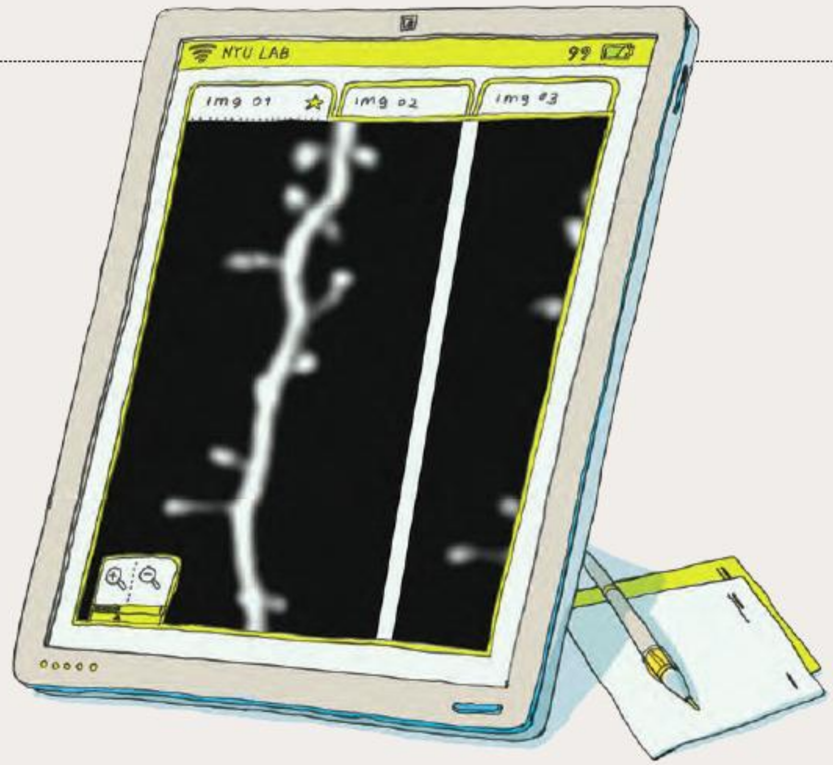

The Brain's Balancing Act

Learning by adding and subtracting synaptic connections

Dendritic spines appear like glowing knobby protrusions along the branching ends of nerve cells.

WHEN IT COMES TO LEARNING, IT'S ALL A MATTER OF GIVE AND TAKE. "We've known for a long time that the brain remodels after learning," says Wen-Biao Gan, PhD, associate professor of physiology and neuroscience. "It does this in two ways: by adding new connections to the brain's neural circuitry and eliminating old ones."

But exactly how it does this has been a mystery—until now. Using a technique he devised, Dr. Gan and colleagues at the Skirball Institute of Biomolecular Medicine have been able for the first time to view the precise changes that take place at synapses, the junctions where nerve cells communicate, in the wake of learning a new task or being exposed to a novel situation. New knowledge, explains Dr. Gan, prompts alterations specifically to the dendritic spines, the knobby protrusions along the branching ends of nerve cells. With learning, spines are gained, and others lost.

In a study published in the journal *Nature*, Dr. Gan and his associates tracked changes in the brains of mice before and after the animals experienced a new stimulus (a string of beads hung at different places along the cage) or learning a new task (running on a spinning wheel). To open a window to the brain, the team shaved away the skull over each animal's cortex, the section that plays a key role in memory. They injected the mice with a fluorescent dye that lights up the nerve dendrites. Then, using a special microscope and camera, they snapped photos of the dendrites after they ran on the wheel or encountered the newly positioned beads. The team began photographing the mice when they were a month old and followed them through adulthood.

When the team compared the photos across the months, they observed new spines emerging in response to the beads' placement or learning to run on the wheel. They saw, too, that as the mice became improved at spinning the wheel, new spines continued generating. The researchers also noted that at the same time as these new and lasting spines were created, a corresponding number of older spines, which had been formed early in the animals' development before the experiment began, disappeared.

Despite the rise and fall of dendritic spines, the animals' brain circuitry remained overwhelmingly secure. A mouse neuron can carry 10,000 spines on its dendrites. Over the months of the study, which received funding from the Alzheimer's Association, only a few hundred spines were either gained or lost on each nerve cell. The study gives a clue as to how it is possible for humans, who have hundreds of thousands of spines on one neuron, to live each day, constantly experiencing and learning new things, without losing existing memories. "The brain is a dynamic and stable organ," says Dr. Gan. "It has a way to balance." ●

—*AMANDA SCHUPAK*

IMAGE: WEN-BIAO GAN