

The Power of One

ALTERING A SINGLE NEURON CAUSES A SURPRISINGLY SWEEPING CHANGE IN THE RAT BRAIN.

Maybe the flapping of a butterfly's wings in Brazil can't really cause a tornado in Texas, but this whimsical idea may be an apt analogy for how the brain works. Perturbing one single neuron, HHMI researchers have discovered, can change the electrical landscape of the whole brain.

Yang Dan, an HHMI investigator at the University of California, Berkeley, didn't set out to show this. She wanted to probe how the strength of connections between neurons changes over time. So she and her colleagues set up an experiment: they would activate single neurons one at a time in a rat brain and then measure local connections from nearby neurons.

They found that instead of just tweaking how it interacted with other nearby neurons, activating any one neuron flipped the anaesthetized rat's entire brain between two states. In one state, which resembles deep sleep, brain waves are slow and synchronized throughout the brain. In the other state, which resembled rapid eye movement (REM) sleep—a less deep state of sleep—neurons were less synchronized and fired faster and more often. The flip worked in both directions.

"This is surprising," says Dan, "because it shows that the weight of a single neuron is so much greater than we thought. It's the power

of the individual." There are 100 billion neurons in the human brain, she points out, with only weak connections between them. But with each neuron connected—albeit weakly—to thousands of other neurons, a signal can spread like wildfire.

Why activating a single neuron would cause such a drastic change throughout the entire brain, Dan can't fully explain. "So far what we have is a fascinating observation," she says, "but in terms of explanations we only have speculation."

Dan's research, published in the May 1, 2009, issue of *Science*, suggests that the cortex—the part of the brain where her team was perturbing neurons—plays an important role in controlling the state of the brain. Previously, scientists had focused mostly on other areas—the hypothalamus and brain stem. To further flesh out the issue, Dan hopes to study rats that are awake, rather than anaesthetized. ■ —SARAH C.P. WILLIAMS



The frequency of brain waves sets two states of the brain apart.

IN BRIEF

HEARTBEAT TO HEARTBEAT

The first beats of an embryo's heart do more than pump blood, HHMI investigators George Q. Daley and Leonard I. Zon, both of Children's Hospital Boston, have shown. The force of the beating heart triggers production of blood stem cells, which give rise to new red and white blood cells. The effect can be mimicked with drugs, the researchers also discovered.

Daley first noticed in 2001 that streaming a fluid across embryonic stem cells compels them to develop into blood cells. A later collaboration—with a scientist who invented a system to expose cells to different degrees of fluid flow—helped Daley take a closer look. They put embryonic stem cells into the setup and showed that when fluid flowed over the cells with the same force as blood in a developing heart, blood stem cells formed.

Meanwhile, Zon was looking for compounds that boost the production of blood stem cells within bone marrow, to treat patients with weak immune systems or blood diseases. To test thousands of drugs for whether they increase blood cell production, Zon used a technique that stains new blood stem cells purple. In 2007, his team found a class of compounds

that did just that. The compounds, it turned out, also increased blood flow, corroborating Daley's observation. Since then, Zon has discovered drugs that allow developing zebrafish embryos that lack a beating heart to produce blood cells. Daley's results appear in the June 25, 2009, issue of *Nature* and Zon's results are in the May 15, 2009, issue of *Cell*.

LISTERIA'S TWO SIDES

With the flick of a few genes—some on, others off—the bacterium *Listeria monocytogenes* can turn from a harmless soil dweller into a dangerous human pathogen. HHMI international research scholar Pascale F. Cossart has made headway into understanding this transformation by investigating what parts of its genome *Listeria* expresses in different environments.

Cossart, at the Pasteur Institute in Paris, compared *Listeria* grown in the lab with bacteria from the intestine of *Listeria*-inoculated mice as well as bacteria from inoculated samples of human blood. Her team also compared normal bacteria with bacteria genetically altered to be less virulent.

The analysis turned up many surprises, says Cossart. First, they revealed that different groups of genes are expressed in

the soil-dwelling and in the human pathogen versions of the bacteria. They identified one protein—SigB—that controls genes *Listeria* use to adapt to the intestines and another protein—PrfA—that helps the bacteria survive in the blood. The bacteria switch between expressing SigB and PrfA, depending on which surroundings they sense.

More surprisingly, the scientists found that some of the genes important to the switch don't code for proteins—they are small noncoding RNAs. They also discovered long antisense RNAs and other RNA elements that highlight new regulatory mechanisms in bacteria. The findings appear in the June 18, 2009, issue of *Nature*.

ULTRAVIOLET'S CELLULAR KILLER

When a cell is exposed to ultraviolet radiation from the sun, two things can happen: the cell can stay alive but accumulate DNA mutations that may lead to cancer, or the cell can sacrifice itself, preventing the spread of the possibly cancer-causing mutations. An HHMI researcher has unraveled the molecular pathway that leads a cell to head down the self-sacrificing path.

Alberto R. Kornblihtt, an HHMI international research scholar at the University of