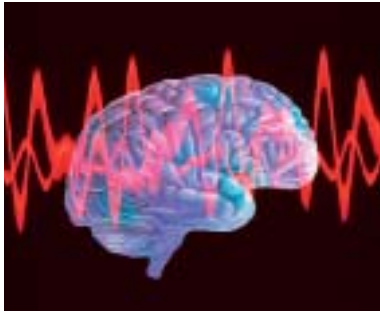


A Noisy Brain Is a Normal Brain

BACKGROUND ACTIVITY IN THE BRAIN MAY BE MORE PREVALENT—AND MORE IMPORTANT—THAN PREVIOUSLY THOUGHT.



Neural activity in the brain changes gradually, even when nothing new is being learned.

New research from H. Sebastian Seung's laboratory at the Massachusetts Institute of Technology (MIT) suggests that scientists still have quite a bit to learn about learning.

The researchers were following up on intriguing observations made by MIT collaborator Emilio Bizzi while studying behavioral tasks of macaques in 2003. Bizzi's group saw slow changes in neural activity even while the macaques were performing familiar tasks, during which no learning was going on. Previously, scientists had assumed that slow changes in neural firing corresponded to learning of motor activities, but these changes in neuron firing rates produced no corresponding changes in motor behavior.

It was Uri Rokni, a postdoc in Seung's lab, who realized that these slow changes in the macaque brain, dubbed background

noise, were distributed randomly. The changes were seen during the learning tasks as well and could represent the existence of an unstable neural network in the motor cortex. For decades, scientists have thought that the process of learning can be detected as changes in a stable neural network: when there is no learning, there are no changes in firing rates. According to Seung, the background noise was surprising. "Then the question became how to interpret [it]," he says.

One idea is that there are two components in the brain—a teacher and a tinkerer. The tinkerer is constantly adjusting things, which produces the background noise; the teacher goes back and fixes or optimizes the changes. According to Seung, "if you get rid of the noise, which is made by the tinkerer, you get rid of any ability to learn."

Rokni developed a simple mathematical model to represent how changes in neural activity during the familiar tasks could be irrelevant to behavioral performance. His hypothesis is rooted in the notion that the motor cortex is a redundant network, meaning that it uses more neurons than it needs. As a result, changes that produce background noise can affect the wiring of the brain without affecting motor behavior. ■ —LINDSEY PUJANAUSKI

IN BRIEF

The findings in mice are likely relevant to human prostate cancers, says Hynes, because other researchers had found Protein 4.1B to be reduced in metastatic prostate cancers compared with normal prostate tissue.

HANDICAPPING TUBERCULOSIS BACTERIA

HHMI investigator William R. Jacobs Jr. and colleagues at the Albert Einstein College of Medicine have produced a genetically altered strain of tuberculosis-causing bacteria that elicits a stronger immune reaction than the current vaccine, bacillus Calmette-Guérin (BCG).

Approximately 2 billion people worldwide are infected with tuberculosis (TB) and more than 1.6 million die each year from the disease. The bacteria that cause TB are becoming increasingly resistant to current treatments.

Mycobacterium tuberculosis, the bacterium responsible for tuberculosis, lives in immune cells in the lungs called macrophages. The pathogen uses an enzyme called superoxide dismutase A (sodA) to hide infection from the macrophage.

Jacob's team disabled sodA activity by deleting the gene responsible for shuttling the enzyme out of the bacteria. The mutant bacterial strain caused increased cell death, or apoptosis, in macrophages

grown in culture. In general, increased apoptosis activates cytotoxic T lymphocytes, which attack the pathogen.

When scientists infected mice with the two strains of bacteria, they observed that cytotoxic T lymphocytes proliferated much more in mice infected with the apoptosis-inducing strain. This means that the immune system was better able to detect and respond to infection by the mutant strain than by the normal bacteria. In addition, when mice were injected with either the mutant strain or BCG and then exposed to the TB pathogen, the mutant strain appeared to be more effective at preventing manifestation of the disease.

The team published their findings in the August 2007 *Journal of Clinical Investigation*.

CULTURE MATTERS TO EMBRYONIC CELL LINES

When it comes to generating neurons, researchers have found that not all embryonic stem (ES) cell lines are equal. In comparing neurons generated from two embryonic stem cell lines approved by the National Institutes of Health, scientists uncovered significant differences in the mature, functioning neurons. The discovery implies that culture conditions—which have yet to be identified—during human ES cell generation can

influence the developmental properties of the cells.

HHMI investigator Thomas C. Südhof at the University of Texas Southwestern Medical Center at Dallas and colleagues published their findings in the August 21, 2007, issue of the *Proceedings of the National Academy of Sciences*.

ES cells are developmentally immature cells capable of self-renewal and of differentiating into any type of bodily tissue. Researchers believe they can generate neural, cardiac, and other cells that can be implanted to restore damaged tissue.

The researchers developed a culture technique that induced newly produced neurons to establish synapses, or communicating junctions, with one another. Electrophysiological studies showed that the neurons derived from the two cell lines differed in the type of synapses that formed and when, and the neurons used different chemicals (neurotransmitters) to communicate with one another. The researchers also found differences in gene expression of microRNAs—snippets of genetic material believed to regulate stem cell differentiation.

The findings present a strong argument for developing more ES cell lines, the researchers say, since the causes for the functional differences they found remain unknown.