bridging the Memory gap

By Mindy Baxter

Hold a piece of ice in your hand, and your brain is working feverishly. The sensory traits of the ice travel up nerve endings to your brain, where the feeling is registered.

Cold. Wet. Slippery. Hard.

But you knew how it would feel before you even touched the ice. You knew from experience. The first time you touched ice, the sensation traveled up nerve endings to your brain, where it was processed and stored. It became part of your permanent memory.

And this happens millions of times.

Memory — how it's processed and how it's stored and retrieved — is just one of many intricacies of the brain scientists and physicians are studying at The University of Texas Southwestern Medical Center at Dallas.

The Center of the Brain

A MEMORY ENTERS YOUR BRAIN not as a picture or sound or word or feeling, but rather as tiny electrical impulses traveling at warp speed on a superhighway of neurons. The impulses careen along nerve pathways in just milliseconds from your finger or ear or mouth to the center of the brain, the hippocampus. There, your brain evaluates the impulses. Is this something to keep or trash? Is it a visual image or an auditory sensation? Is it a piece of information needed again soon or something that might not be processed again for years?

Then, your brain files the information away, like another piece of paper on your desk. Sounds head toward your temporal lobes, portions of the brain located near your ears. Visuals are directed toward the occipital lobes at the back of the head. Touch is sent to the parietal lobe, which extends from your ears to the top of your head.

Of course, like most simple explanations, it's not so simple.

Dr. Munro Cullum, acting chairman of psychology and professor of neurology at UT Southwestern, says memory is a complex set of abilities and is not a unitary phenomenon.

"Memory is multifactorial. There are different types of memory and all have a different role," he said.

Can you remember your elementary school and first-grade teacher's name? What about the name of the first president of the United States? Odds are you can name those, Cullum said. Long-term or remote memories have already been firmly stored, making them less susceptible to diseases or injuries to the brain.

In contrast, the ability to form new memories is more vulnerable. Your brain doesn't place the same importance on what you had for dinner as it does your mother's name.

Memory often works like a contagion, with one memory triggering the next. Memories can be triggered by various stimuli, including things we see, feel, touch, smell and imagine.

After age 20, our brain and memory begin a slow decline. That decline doesn't usually become noticeable until our later years.

ALZHEIMER'S PATIENTS HAVE TROUBLE WITH ENCODING, WHICH INVOLVES STORING A MEMORY, AND RETRIEVAL, WHICH INVOLVES THE BRAIN FINDING AND BRINGING FORWARD A MEMORY.

Alzheimer's Disease

MEMORY LOSS both intrigues—and scares — us.

Diseases — from Alzheimer's to depression and addiction, to post-traumatic stress disorder and multiple sclerosis — can all drain memory.

In most, the hippocampus is one of the affected areas. Levels of oxygenation, medications, steroids, disease and head injury can all influence the hippocampus' effectiveness as the brain's traffic director. And without a properly functioning hippocampus, memory communication throughout the brain can break down.

"As we age, we all experience some memory loss," said Dr. Myron Weiner, professor of psychiatry and neurology, who trained in geriatrics and now specializes in Alzheimer's disease. "In general, people find if they don't force it, the information will pop up. Most people can cue themselves. Things may take a little longer to process, but it's still there.

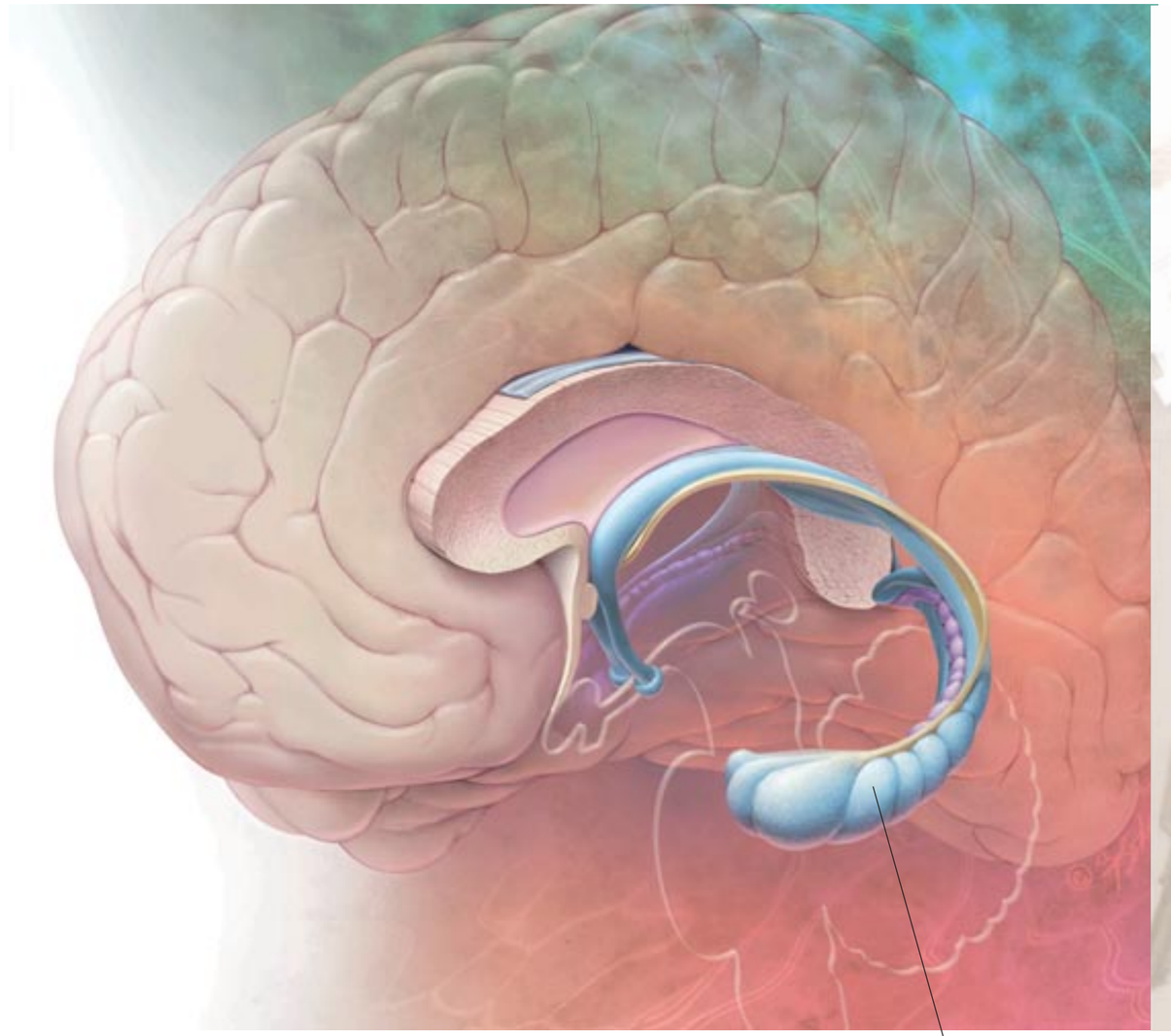
"But pronounced memory loss is not normal. It's really a matter of degree. You reach a certain threshold. It's like heart disease. Lots of us have cholesterol in our vessels, but we don't all have diagnosed heart disease. It's only at a certain point that heart disease is diagnosed. The same is true for Alzheimer's disease and memory loss."

Holder of the Ardine S. Ard Chair in Brain Science and the Dorothy L. and John P. Harbin Chair in Alzheimer's Disease Research, Weiner sees patients in UT Southwestern's Alzheimer's Disease Center, one of 29 funded by the National Institute on Aging. He estimates that more than half of his patients come to him not because they recognize they are experiencing loss, but because their families do.

"We used to see most Alzheimer's patients about four years after the onset of disease," he said. "But it's closer to three years now. More people are knowledgeable."

Alzheimer's patients have trouble with encoding, which involves storing a memory, and retrieval, which involves the brain finding and bringing forward a memory.

Patients with Alzheimer's, after being told a story about a boy in a rowboat fishing on a lake, might retell the story with plausible but incorrect or unrelated tangents, according to Cullum. Suddenly, the boat might be an ocean liner in the Gulf of Mexico.



THE HIPPOCAMPUS, WHERE EMOTION AND MEMORY ARE REGULATED.

"In Alzheimer's the information has trouble getting in and may become distorted, and this is compounded by deficits in retrieval," he said.

Four percent of people at age 75 have Alzheimer's disease, but by age 85 the average has climbed to 50 percent — and even higher if there is a family history. With each passing year the risk rises. And with life spans increasing in the United States, Weiner said specialized facilities like the Alzheimer's Disease Center at UT Southwestern play a key role in identifying and managing a growing public-health problem.

"Simply put, the country cannot afford institutional care for all of these patients," he said. "We would bankrupt the health system. With family support groups and other assistance, many families can maintain their loved ones at home."

Weiner finds that many patients are happier at home, as well.

"Certainly, caring for an Alzheimer's patient is stressful and difficult," he said. "It's not rewarding like caring for an infant, where advances are made every day. You're always giving more because the patient is always losing more."

Other Diseases of the Brain

ALZHEIMER'S MAY BE the best known of the memory thieves, but there are other diseases that rob memory as well.

People with Parkinson's disease often experience memory problems.

"In Parkinson's patients, the information is getting in, but they have trouble getting it out," Cullum said.

Brain scans of multiple sclerosis patients show lesions that can lead to memory loss. MS patients also can have memory problems as the side-effect of medications or of fatigue or depression. Sometimes antidepressants or drugs that stimulate the brain can help.

In MS patients, as in Parkinson's patients, memory retrieval is affected rather than encoding, said Dr. Elliot Frohman, associate professor of neurology and ophthalmology and head of UT Southwestern's MS program.

"Memory is central to much of what we do, but especially to learning," Frohman said. "Without the ability to learn, we lose the ability to be productive. If we had to take the time to reassemble every task we do every day in our minds, we'd be in quicksand."

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—Dr. Munro Cullum

Neurons and Signaling

THE BRAIN IS composed of trillions of nerve cells. These brain neurons communicate constantly with each other through electrical activity and chemical signals. Even while we sleep, our neurons are firing away, telling each other and our bodies what to do with thousands of messages each second.

But a neuron won't act when it has received a message from only one neuron. It must receive messages from several different neurons before it reacts. If one neuron dies, communication does not stop; only as more and more neurons become injured or diseased does communication stall.

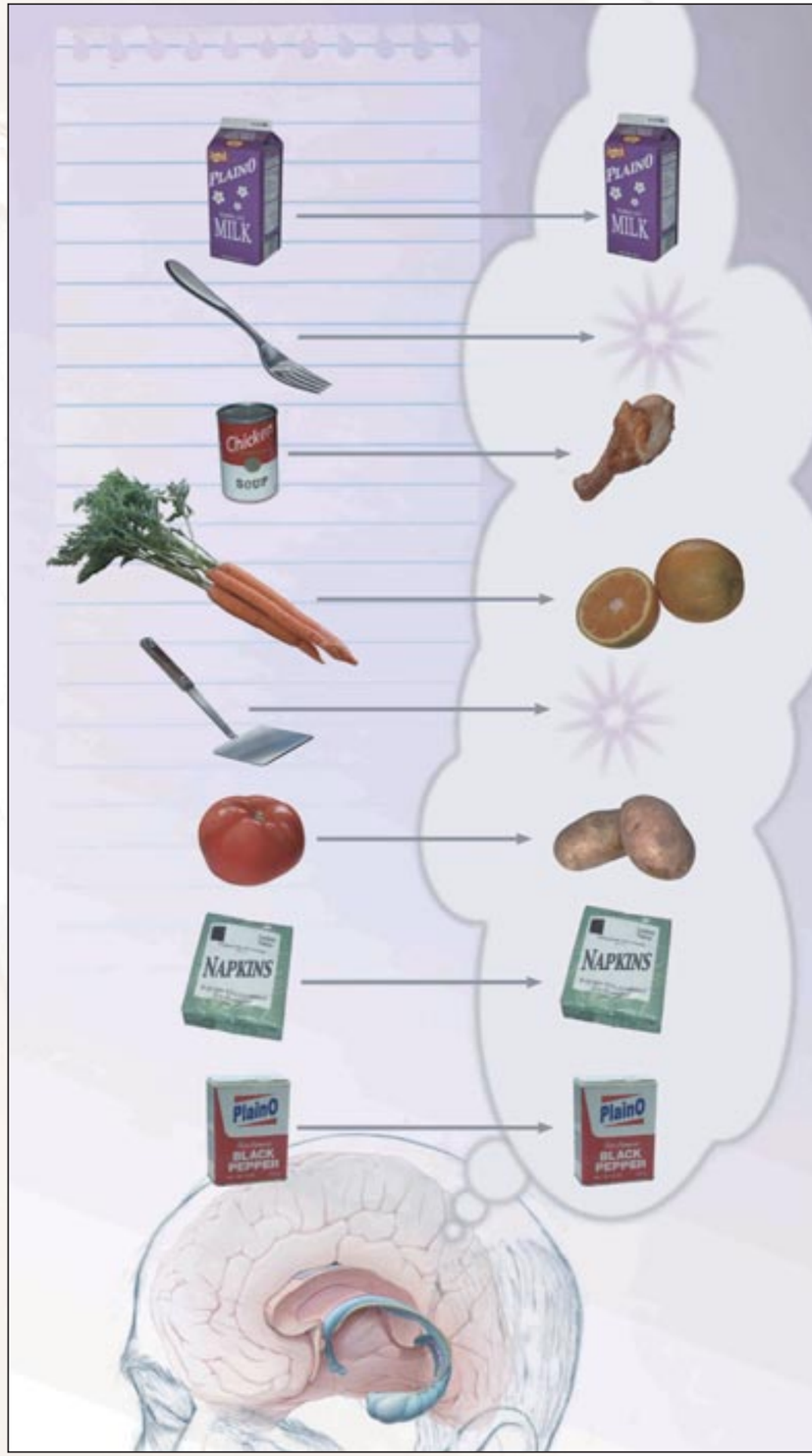
Memory lives in the nerve cells, where it grows infinitely more complex and difficult to understand.

Dr. Thomas Südhof, director of the Center for Basic Neuroscience and an investigator in the Howard Hughes Medical Institute at UT Southwestern, has spent his career exploring the communication between neurons and how they release chemical signals to each other. A remodeling of the neurons and the connections between them seems to be related to the process of memory, Südhof said.

How we remember

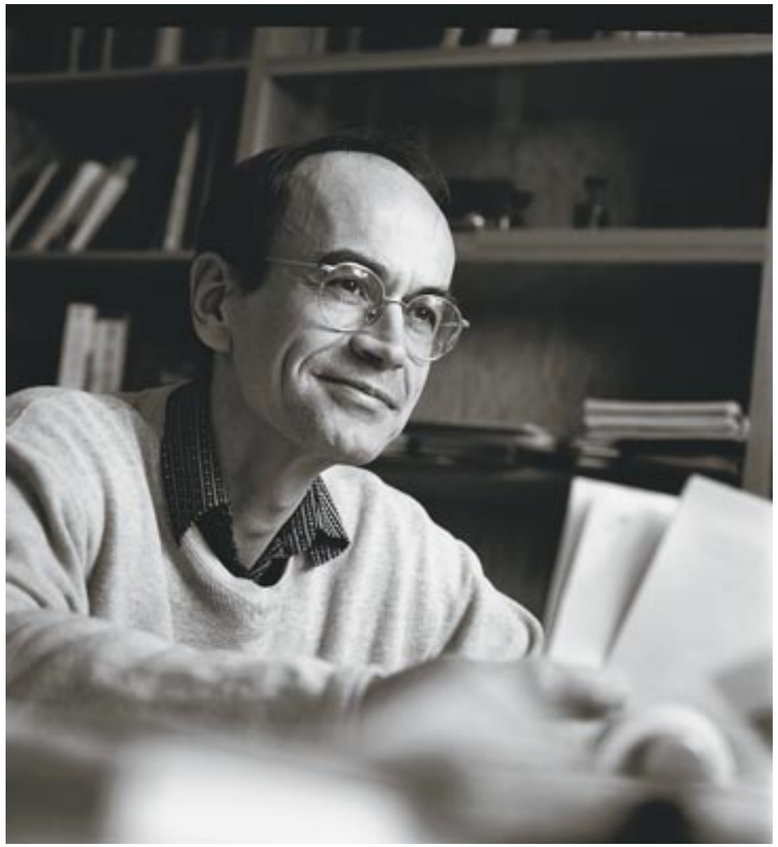
In this example of a memory task, a shopping list of items is presented for encoding and memorization. Some items are recalled with good accuracy (milk, napkins, pepper). Sometimes we may "draw a blank" and forget things completely (fork, spatula). Other responses may reflect faulty recollections or "near-misses" that bear some relationship to the target items (chicken soup – chicken leg) or belong to the same general category (carrots – oranges) or specific category (tomato - potatoes).

Neuroanatomically, the process of encoding and retrieving such recently presented information is dependent upon memory systems in the temporal lobes of the brain, primarily involving the hippocampus.



“It is amazing that you can remember things that happened decades ago. Fundamentally, everything that happens in the brain happens because cells communicate with each other, but that is only the beginning.”

—Dr. Thomas Südhof



“In many ways, memory is a tremendous challenge,” Südhof said. “The nature of memory storage is unclear. It is amazing that you can remember things that happened decades ago. Fundamentally, everything that happens in the brain happens because cells communicate with each other, but that is only the beginning.”

Cell communication is complex, since one neuron may constantly talk to 1,000 or 10,000 other neurons.

“Memories are not like something you write down on paper,” said Südhof, who holds the Loyd B. Sands Distinguished Chair in Neuroscience and the Gill Distinguished Chair in Neuroscience Research. “The brain is constantly losing neurons, but memories are not lost when this happens. Ensembles of neurons, almost like a circuit, hold the memories.”

One advantage in the study of memory is that it is relatively easy to measure, Südhof said. Show 10 different people 10 different things; ask them to recall them 10 minutes later; and you’ve measured memory.

But with synapses — or connections between nerve cells — millions of times more numerous than the number of genes in the human genome, the web of brain function remains an enormous challenge for researchers, Südhof said.

Much of the ongoing work at UT Southwestern concerns the nature of cell communication and what role it plays in memory. For example, Dr. Joachim Herz does research on the biochemistry of cellular receptors that are involved in the transport of cholesterol and other molecules in the brain. His work has shown how disturbances in cholesterol can play a role in diseases like Alzheimer’s. In the brain, cholesterol interacts with proteins, altering the chemical communication between neurons. For instance, the creation of the “Ab” protein, which plays a pivotal role in the development of Alzheimer’s disease and gives rise to amyloid plaques in Alzheimer’s-affected brains, is reduced under low-cholesterol conditions and increased when cholesterol is high.

“As medicine has gotten more advanced and people are living longer and longer, research into how the brain works has grown more important,” said Herz, professor of molecular genetics. “We’ve extended the life span, but that’s no good if your brain gives out.”

Herz’s continued research focuses on how these key chemical pathways work and what happens to them when cellular communication breaks down. With a clearer understanding of this process, Herz, holder of the Thomas O. Hicks Family Distinguished Chair in Alzheimer’s Disease Research, hopes to uncover Alzheimer’s disease treatments that attack the disease process at the most fundamental level.

He believes Alzheimer’s disease will be conquered in the next two decades.

“What goes wrong within a cell?” he asks. “What does it mean? Exactly what are the proteins in cells doing? We have a lot of exciting scientific work ahead of us.” ✣

Memory and Emotion

How emotions work

on the brain’s memory is a complex question of integrated circuitry, cell communication and structural changes in the neurons of the brain.

“We still don’t understand what makes long-term memory, and I’ll defy anyone who says the opposite,” said Dr. Eric Nestler. “It’s something like a pinball machine, with protein X bouncing off of protein Y and hitting protein Z. But it’s a biochemical cascade of these interactions infinitely more complex than a pinball machine.”

Nestler should know. His 30-year career has focused primarily on the biochemical mechanisms of addiction. While scientists may not yet understand how memories are made, the chairman of psychiatry says it’s obvious memory affects addiction.

“Cocaine addicts used to tell people that those old antidrug billboards with the mirror, white powder and razor blade were one of the most potent triggers for them,” said Nestler, holder of the Lou and Ellen McGinley Distinguished Chair in Psychiatric Research. “They would avoid driving on highways just to avoid seeing the billboards and bringing back a powerful wave of craving.

“For a former addict, their most powerful memories are of highs and lows. Their memories are as intense as for a person suffering from post-traumatic stress disorder after war or a rape victim reliving the rape again and again. The memory of the high is just that powerful and all-consuming.”

Visual and emotional cues are part of what makes memory so complicated. The way we remember multiplication tables is different than how we remember the way we felt on our first date. The way we remember not to do something is different than how we remember to do something. As our knowledge of the brain grows more sophisticated, researchers are beginning to see that emotions help channel and organize our memories, Nestler said.

“We will always remember what day the airplanes crashed into the World Trade Center,” he said. “We have a strong emotional trigger for that day.”

What is it about memory that makes us so afraid to lose it? The answer, doctors say, is really quite simple.

We are our memories.

“Memory is us,” Nestler said. “If you don’t have memory, you don’t have yourself. You’re a different person if you have different memories.” ✣