

BRAINWORK

The Neuroscience Newsletter

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News

FROM THE FRONTIER

••• **New experiences throw neurons into reverse.** The sleeping brain is known to replay the day's events; recordings taken from the brain cells of busy rats show that neurons active in a given behavior—exploring a new maze, for example—fire in the same sequence after the rat goes to sleep.

According to a new study, the brain also “rehearses” its neurons while awake—only it does so backwards.

David Foster and Matthew Wilson of the Massachusetts Institute of Technology used electrodes to record the hippocampal neurons of rats doing laps in a run that had food treats at each end. In their findings, scheduled for publication in a March issue of *Nature*, individual “place” cells fired in response to being in a specific part of the run.

But when the rat ate its food and rested for a moment, the same neurons fired in the opposite sequence. This reverse replay was more pronounced when the rat was in a new apparatus. In a separate test, when the rat was placed at the end of the run without having done the lap, the reverse pattern did not appear, suggesting that it only reflects the animal's actual experience.

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Dissecting Dyslexia

BY THOMAS S. MAY

Children who do not learn to read fluently by age 10 or 11 are often thought to be lacking in intelligence or motivation. In most cases, however, they are neither stupid nor lazy. They have dyslexia, a learning disability that makes it very difficult for them to understand written language, despite having a normal—or higher-than-normal—IQ. Depending on the diagnostic criteria used, dyslexia affects 5 to 17 percent of people in the United States.

Recent studies suggest that the reading difficulties people with dyslexia experience are caused by “faulty wiring” in certain areas of the brain, and there are indications that this

faulty wiring is due, at least in part, to identifiable genetic defects or variations. Early screening for such variations would make it possible to provide timely and appropriate remedial training, some experts suggest, allowing children with dyslexia to overcome their disability and learn to read at an acceptable level.

Dyslexia Gene Identified

Scientists have known for decades that genetics plays a very important role in dyslexia, with estimates of heritability ranging from about 40 to 70 percent. Over the years, several candidate genes have emerged as possible contributors to dyslexia, but only recently have

researchers been able to establish a strong link between one specific gene and this common learning disability.

In a study published in the November 22, 2005, issue of the *Proceedings of the National Academy of Sciences*, a research team led by Jeffrey Gruen, an associate professor at Yale School of Medicine, found several lines of

(Continued on page 2)



Researchers have uncovered a gene, *DCDC2*, that is strongly linked with dyslexia. Other studies indicate differences in brain structure and function, while still others suggest that training can help “rewire” the brain's reading circuit.

(DYSLEXIA, continued from page 1)

evidence indicating that reading ability is influenced by a gene called DCDC2, which is located on chromosome 6.

By studying 153 families with children who are dyslexic, the investigators were able to identify unique genetic patterns, or variations, within the DCDC2 gene that were strongly associated with dyslexia. One of the most interesting findings was the discovery of a deletion (a missing stretch of DNA) in DCDC2, which strongly correlated with severe reading disability.

In order to further investigate the role of DCDC2 in dyslexia, the researchers analyzed postmortem brain tissue samples and found that the DCDC2 gene is highly active in areas of the temporal cortex that are thought to be involved in reading.

The scientists also performed an experiment using 14-day-old rat embryos, some of which were injected with a substance that inhibits the expression of DCDC2. The rat embryos were then allowed to grow

inside their mothers for another four days, after which their brains were removed for analysis. The investigators found that, while the control animals' brains developed normally and showed typical "neuronal migration," this migration was arrested in the brains of animals with reduced DCDC2 expression.

These results indicate that the DCDC2 gene plays a role in the development of dyslexia, Gruen says. He adds, however, that other genes are probably involved as well: "It's very likely that dyslexia is caused by a mixture of some DCDC2 alleles, as well as mixtures of alleles from some other genes."

Different Brain Regions Used

Neuroimaging studies of children and adults with dyslexia consistently show that the underlying genetic variations that appear to be present in many of these individuals are manifested in observable differences in brain structure and function.

"Most of the available evidence points to the fact that the way the brains of children with dyslexia are wired is different from the typical brain organization in children who never experience difficulties in learning to read," says Panagiotis Simos, an associate professor at the University of Crete in Greece. Simos, in collaboration with scientists at the University of Texas Health Sciences Center at Houston, recently has conducted a series of studies that looked at brain activation patterns of children with dyslexia during various reading tasks.

Using magnetic source imaging (MSI), a technique that records tiny magnetic impulses generated by the electrical activity of neurons inside the brain, the researchers found that the brain circuit that children with dyslexia used when they attempted to read did not include an area (located in the left temporal lobe) that is typically used by nondyslexic readers. Children with dyslexia instead used the corresponding region in the right hemisphere, as well as certain areas in the frontal lobes, which are not normally used during reading.

These findings were in line with several previous studies that employed positron emission tomography (PET) or functional magnetic resonance imaging (fMRI) to compare brain activity between dyslexic and nondyslexic readers. But because MSI (also known as magnetoencephalography, or MEG,) can record not only the spatial arrangement of brain activity but its timing pattern as well, Simos and colleagues were also able to detect—in real time—very fast changes taking place in neuronal activity during the performance of various reading tasks.

When the investigators analyzed these "spatiotemporal activation" profiles of children with dyslexia, they found that even when these subjects used the same brain regions that non-impaired readers typically use, the time it took for different areas to become activated, as well as the order in which they became active, was markedly different between the two groups. However, the results of their latest study indicate that, with appropriate training, these differences can be minimized or, in some cases, completely eliminated.

Intensive Intervention

In their most recent study, Simos and colleagues gave 15 children with dyslexia, ages 8 and 9, 16 weeks of intensive training aimed at improving reading skills. Phonological awareness, the awareness of speech sounds, was taught for two hours per day during the first eight weeks. The second half of the program emphasized recognition of words, comprehension, and fluency for one hour per day.

The researchers compared the pattern of brain activation during reading tasks before and after the intervention and found that the intensive training resulted in increased activity in a region that is normally used by nondyslexic people. They also saw that the timing of the activity in the temporal and frontal cortices shifted to a pattern similar to the one seen in nonimpaired readers.

Tests of reading performance before and after the 16-week program showed that this apparent normalization of

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brain activity was accompanied by significant improvements in word recognition and decoding, as well as fluency and comprehension.

Simos says these results show that even if the brains of children with dyslexia are functionally and/or anatomically different from those of other children, these differences do not prohibit the retraining or “rewiring” of the brain circuit for reading. He

(using fMRI) in a group of adults with dyslexia while they were performing reading-related tasks. The investigators also tested a matched group of nondyslexic adults and found that, compared to these control subjects, individuals with dyslexia exhibited less activity in certain areas of the left side of their brains.

Half of the subjects who had the disorder were then given an eight-

Man's Best Friend: Genes Connect Dogs and Humans

BY SCOTT P. EDWARDS

Man's best friend just got a little closer to his master. In December 2005, a team of scientists announced in the journal *Nature* that they had sequenced the entire genome of the domesticated dog. Their report has important implications for the understanding of human genetic diseases, as well as gene-related personality and behavioral traits in humans.

“Humans and dogs have the same gene set,” says Kerstin Lindblad-Toh of Harvard's Broad Institute and the Massachusetts Institute of Technology, who led the dog genome project. “In fact, every gene in the dog genome is the same as it is in the human genome, with similar function.”

Scientists mapped the complete human genome—the entire set of 23 pairs of chromosomes and the nearly 25,000 genes they contain—in 2003, providing a greater understanding of genetic diseases and insight into human evolution. Lindblad-Toh's dog genome project sequenced, or determined the order of, the more than 2 billion chemical pairs that make up canine DNA, the molecular basis of heredity. Lindblad-Toh said it took about two years to map the dog genome, which scientists had partially decoded in the past, compared with more than a dozen years to map the human genome.

The Evolution of the Domestic Dog

Canis familiaris, the domestic dog, is a direct descendent of the gray wolf of East Asia and traces its roots back nearly 15,000 years (dogs themselves go back even farther, possibly 100,000 years). DNA studies show that the first domestic dogs in North America traveled with humans when humans

Although it may be easier to “rewire” the brains of children, Eden's research shows that there is plasticity in the adult brain, too.

admits, however, that some children with the disorder may not be able to become good (or even average) readers, despite extensive training.

“Our recent work has shown that children whose brain circuit for reading rewires in such a way as to become very similar to the brains of nonimpaired readers are those who show the greatest benefits from remedial instruction,” he says. “Children who continue to use compensatory brain circuits do not generally respond well to intervention.”

What About Adults?

Although some people become dyslexic during their adult years (as a result of a stroke, for instance), in most cases dyslexia is a developmental (i.e., childhood) disorder. Yet the majority of people with dyslexia are adults who have had it since childhood, points out Guinevere Eden, a neuroscientist at Georgetown University in Washington.

“One of the assumptions early on in neuroscience research, based on animal work, was that plasticity occurred only in the young brain,” she says. Although it may be easier to “rewire” the brains of children, Eden's research shows that there is plasticity in the adult brain, too.

In a study published in October 2004 in *Neuron*, Eden's research team looked at brain activation patterns

week, intensive (three hours per day) training program aimed at reinforcing the relationship between sounds and printed letters and words.

A comparison of fMRI recordings done before and after the intervention showed that the training sessions resulted in increased activity in the left hemisphere (in the same region the control subjects used), and in the right hemisphere as well, indicating the use of compensatory mechanisms by subjects with dyslexia. Tests also showed that the intervention program resulted in significant improvements in phonological awareness and paragraph reading accuracy.

Eden says these data suggest that remedial training can be beneficial for adults with dyslexia, too, although improvements in phonological awareness and reading accuracy do not necessarily translate into improvements in reading speed and/or comprehension.

“But once you have improved phonological awareness and reading accuracy, you can start working on fluency,” she says. “And once you bring up fluency, you probably improve comprehension.” ■

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(MAN'S BEST FRIEND, continued from page 3)

migrated from Asia about 12,000 years ago.

In recent centuries, says Lindblad-Toh, humans selectively bred dogs to achieve a variety of physical outcomes including size, shape, and coat color, as well as skills at herding, hunting, and obedience. Because of this selective breeding, there are more than 400 distinct domestic dog breeds throughout the world today.

One offshoot of this breeding, Lindblad-Toh and her colleagues wrote in *Nature*, is that dogs show a "high prevalence of specific diseases, including cancers, blindness, heart disease, cataracts, epilepsy, hip dysplasia and deafness." Most of these diseases are also seen in dogs' human companions, with similar clinical manifestations.

Closer to Us than Chimpanzees

Dogs may be considered "man's best friend" because they have lived so closely for such a long period of time. This closeness, scientists have found, has altered dogs' cognitive abilities such that they share many personality and behavioral traits with humans.

Anthropologist Brian Hare of the Max Planck Institute for Evolutionary Anthropology in Germany has reported that domesticated dogs are better at reading human communication signals, such as glances or pointing, than chimpanzees, which have long been thought to be closer to humans than any other primate.

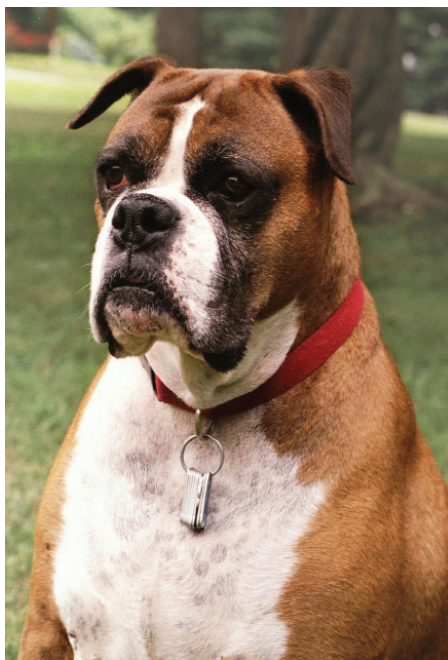
In a presentation to the American Association for the Advancement of Science in 2004, Hare reported findings from his research on a subspecies of wild dogs from New Guinea that were once domesticated but have lived without significant human contact for thousands of years. Hare's study involved concealing food under one of two cups and having a human gesture toward the cup covering the food.

Few of the wild dogs approached the food cup more than half the time, as statistical analysis would suggest; however, almost all of the domesticated dogs in the study found the food after following the human's gesture. Hare says that these findings show that

constant human contact over the years has led domesticated dogs to acquire the ability to read human communication signals, much the way a young child does.

"This is where co-evolution comes in," Lindblad-Toh says. "We have the same gene sets, we live together, and we respond to the same types of cues, visual and otherwise. This helps us learn about important gene functions over time."

Lindblad-Toh says that further evidence of dog-human co-evolution



A boxer named Tasha was chosen from more than 60 breeds for the sequencing of the dog genome because boxers have relatively little genetic variation. Because dogs and humans have co-evolved, the dog genome could lead to clues about human diseases.

comes from studies of dogs, mice, and humans that show how specific brain genes have evolved more quickly in both dogs and humans, but not in mice. These studies, she says, show a good correlation in the genetic evolution of the two species.

Victoria Wobber, a Max Planck researcher who collaborates with Hare on canine genetic research, says one of the most important points in Lindblad-Toh's paper is the finding that the rate of genetic change in the brain is similar in dogs and humans, suggesting that both species have

evolved their functionally innovative behaviors quite quickly.

"This demonstrates that humans are not unique in their rapid rate of genetic change, and that another species evolved at a similarly fast rate and could have experienced just as drastic behavioral changes," Wobber says.

The Human Brain Connection

The dog genome may tell us as much about humans as it does about dogs. Lindblad-Toh says the potential benefits of this knowledge include insights into disease mechanisms, which may lead to therapies to treat both species. Dogs and humans share similar brain diseases, including epilepsy, narcolepsy, and brain tumors, as well as such behavioral disorders as obsessive-compulsive disorder and hyperaggressiveness.

Lindblad-Toh and her team identified nearly 2.5 million genetic differences among breeds of dogs. These small genetic changes or variations that occur in DNA are called single nucleotide polymorphisms, or SNPs. They do not produce physical changes, but scientists believe they may predispose dogs—or people—to disease and may even influence their response to drugs.

Using these SNPs, the scientists created haplotype blocks—sites of closely located SNPs that are inherited in blocks—which are almost 100 times larger in dog populations than they are in humans.

"The haplotype structure in dogs is more advantageous for finding disease genes [than it is in humans]," Lindblad-Toh says. "Because these building blocks are very big in dogs, it's easier to find these disease genes in dogs."

Because the gene set in dogs and humans is so similar, once a disease gene is identified in a dog, the corresponding gene in humans should be easy to identify.

"The genetic contributions to many common diseases appear to be easier to uncover in dogs," says Lindblad-Toh. "This is a significant step forward in understanding the roots of genetic disease in both dogs and humans."

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Stroke Rekindles Researchers' Attention

BY BRENDA PATOINE

Stroke research is heating up again, fanned by promising results from large-scale clinical trials for a new drug under investigation for acute stroke. The results are generating excitement in a field that has been strangely quiet in recent years, following a long series of disappointments that seemed to scare off pharmaceutical investment and put a damper on the search for therapies that might make a dent in stroke's devastating toll.

Stroke remains the No. 1 cause of long-term disability in the United States, and the third leading cause of death. It costs the country more than \$54 billion annually in health-care expenses alone, and untold billions in lost productivity. Yet, for the vast majority of people who suffer a stroke, there is little doctors can do.

"I've always been surprised at how relatively underweighed the need for a stroke treatment is in the public's eye," says Dennis Choi, head of neuroscience research for Merck & Co. Inc. "It just hasn't been seen as a priority for society to address aggressively."

A Legacy of Disappointment

In the 1990s, stroke research was on fire. Scores of so-called neuroprotective drugs, perhaps a hundred or more, were in development. Virtually every major pharmaceutical firm had a robust stroke program, and academic research centers were inundated with clinical trials testing drugs that seemed to hold promise for finally getting a handle on the problem of stroke. None made it to market.

With the exception of tissue plasminogen activator (tPA), the clot-dissolving agent approved for the treatment of acute stroke in 1996, there have been no breakthroughs in stroke care. Even tPA gets mixed reviews, and

everyone agrees that it is underutilized, thanks to a tight therapeutic window of three hours, serious risks of hemorrhage, and a health-care system that does not reliably get patients the right care at the right time. Compounding the problem is the fact that many stroke sufferers, whether because of ignorance or denial, do not seek urgent care.

This bleak landscape may finally be seeing some light. In February, the results of a second large clinical trial testing the efficacy of an investigational stroke drug known generically as NXY-059 were presented at the American Heart Association's annual stroke conference. Suddenly, stroke researchers are talking about neuroprotection again, and optimism is replacing the cynicism fueled by past failures.

Stanford's head of neurosurgery, Gary Steinberg, says the drug's clinical benefits are extremely encouraging: "It has the potential to open up a whole new era in stroke treatment."

AstraZeneca, which is testing NXY-059 under license from Renovis Inc., says its proposed mechanism of action is "free radical trapping." The idea is to neutralize the unstable molecules, released by dying neurons, that help fan a widening cascade of damage and nerve cell death after an ischemic stroke—the kind of stroke caused by a blood clot that restricts the flow of oxygen to the brain.

The fact that NXY-059 has so far survived the test of large-scale clinical trials may, however, have more to do with how the research landscape has changed than with how the drug works. After the widespread failures of the 1990s, industry and academia teamed up to figure out what went wrong and fix it. The result was the Stroke Therapy Academic Industry Roundtable, or STAIR. The group has since published a stringent set of guidelines for the development of stroke drugs.

Failure by Design?

The consensus was that a lot of the drugs that failed in the heyday of neuroprotectant development may have been good drugs, but the trials were not designed well. Outcome measures may have been too stringent to identify

subtle benefits in improving a patient's day-to-day functioning, and many trials simply were not large enough to have the statistical power necessary for drug approval. Moreover, drugs that showed promise in animal studies when given within two hours of an induced stroke were given up to 12 hours post-stroke in patients, so there was a disconnect between animal and human testing.

"We had some learning to do, and we had to go to school on how to do clinical trials and preclinical work that were complementary to one another," says Wade Smith, the director of neurovascular care at the University of California, San Francisco. NXY-059, Smith says, is one of the few drugs to have met all of the STAIR criteria, and its success so far is an indication of how productive the effort to improve drug development has been.

Perhaps more important, Smith and Steinberg say, any success story in neuroprotection can help restimulate interest in stroke research, which will eventually translate to better prognoses for the 700,000 or so people who suffer a stroke each year. "We see renewed interest already," Steinberg says.

Merck, for one, is back in the stroke game—for the third time, after two previous drugs failed in preclinical development. It has licensed a compound, ONO-2506, which was developed by Japan-based Ono Pharmaceuticals. ONO-2506 is said to block the activation of astrocytes, a type of non-neuronal glial cell in the brain. This mechanism may in turn help protect nerve cells from the cascade of toxicity following a stroke.

A North American clinical trial of the drug was discontinued in May 2005 for lack of efficacy, but Merck apparently has not given up on it yet. Choi suggested the study's failure to demonstrate efficacy was related to trial design issues—a problem all too familiar to researchers involved in the previous round of failures. ■

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Immune Cells in Spinal Cord Cause Neuropathic Pain

BY RABIYA S. TUMA

Nearly one-fifth of us will experience neuropathic pain during our lifetimes, with exaggerated pain sensations or pain in response to a stimulus that is not normally painful, such as a light touch. Now, researchers report that overly active immune cells in the spinal cord may be to blame.

Yves De Koninck at Laval University and Michael Salter at The Hospital for Sick Children in Toronto and colleagues have linked two earlier observations together to map of at least one route to neuropathic pain. The new data may suggest novel ways to treat the problem.

Normal pain is triggered by a stimulus somewhere in the body. The signal then passes through the spinal cord, where initial processing occurs, and travels to the brain, where it is perceived as pain. Any disruption along the way can lead to neuropathic pain, including abnormal processing of information from nonpainful stimuli.

In 2003, De Koninck's team identified a key mechanism in the spinal cord that leads to neuropathic pain. In healthy people, some spinal cord neurons dampen pain signals, allowing individuals to tolerate intense stimuli at times, such as when a woman is giving birth or during a fight. During neuropathic pain, this inhibitory mechanism goes awry and actually amplifies the pain signal.

Normally, when a pain signal arrives from sensory nerves, it stimulates both relay neurons and inhibitory neurons in the spinal cord. The inhibitory neurons release a neurotransmitter called gamma-aminobutyric acid, or GABA, which also acts on the relay neurons. If the amount of GABA released by the inhibitory neuron is large enough, it will cause the interior of the relay neuron to become negatively charged and

unresponsive to the signal from the sensory neuron. When that happens the pain signal will be stopped in its tracks, or at least decreased in strength.

However, in order for this local repression to work, the concentration of negatively charged chloride ions inside resting relay neurons must be much lower than the concentration outside them, a process that relies on a chloride pump. During neuropathic pain, this pump stops working.

Also in 2003, Salter's group showed that microglia, which are central nervous system immune cells, play a role in neuropathic pain. After injury, microglia express a new receptor, called P2X4, on their surface. When the researchers prevented P2X4 receptors from being activated by ATP, a nucleotide that can act as a signaling molecule, they blocked hypersensitivity to normally nonpainful stimuli in rat models.

In the current study, which was published in the December 15, 2005, issue of *Nature*, De Koninck and colleagues report that the chloride pump and microglia are two parts of the same pathway that lead to neuropathic pain.

Salter and De Koninck found that when ATP binds to the P2X4 receptor

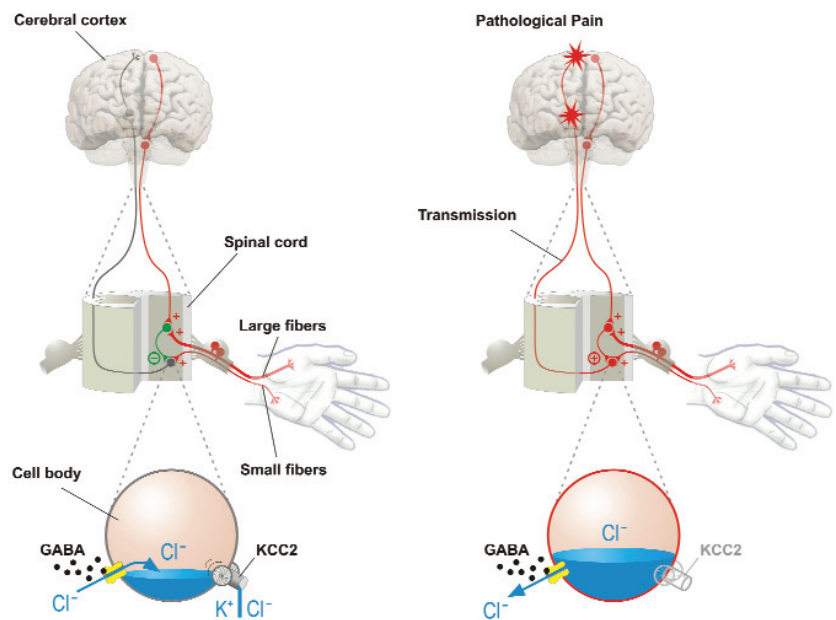
on microglia, it starts a cascade of events. ATP activates the microglia, causing them to release a small peptide called brain-derived neurotrophic factor, or BDNF. BDNF then binds to a protein on the surface of relay neurons in the spinal cord, which causes the chloride ion pump to stop working. What would have been an inhibitory response becomes an amplifying one.

Significantly, the investigators found that if they blocked microglial activation or BDNF activity, they could reverse the problem in the spinal cords of rats. That could be a first step toward treating neuropathic pain in humans.

"Neuropathic pain is normally hard to treat," says Amy MacDermott, a professor at Columbia University who also works on pain signaling in the spinal cord. "But they have figured out enough of the pathway that they could reverse, at least temporarily, an existing condition."

Some of the BDNF released by the microglia may be involved in tissue repair, but a side effect of that is hypersensitivity, De Koninck says. "Everyone will develop hypersensitivity after an injury. That is a normal process. Our

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In neuropathic pain, right, negatively charged chloride ions (Cl⁻) inside neurons are more concentrated than ions outside them, resulting in a failure to limit the pain signal. Recent research shows that overactive immune cells called microglia play a role. Blocking microglia may offer treatment possibilities for neuropathic pain.

News

FROM THE FRONTIER

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In an early online edition of *Nature*, the authors explain that reverse replay lets the brain evaluate the steps leading to a central, anchoring event such as a food reward—unlike the pattern seen in sleep, when the brain merely goes over recent events. “Moreover, by converting single experiences into multiple reverse events ... awake replay represents efficient use of hard-won experience,” the authors write.

••• **Hunger hormone plays role in memory.** Feelings of hunger are triggered, in part, when the empty stomach releases a hormone called ghrelin (GRELL-in), which acts on neurons in the hypothalamus in a process called synaptic remodeling. The same process underlies learning and memory in other parts of the brain, leading researchers to study whether ghrelin contributes to these “higher” functions. In the March issue of *Nature Neuroscience*, Tamas Horvath of Yale University and colleagues identified ghrelin and its receptors in the hippocampus—a brain area in which synaptic remodeling brings about navigational memory and recall of place and context.

In rats treated with ghrelin, the investigators showed an increase in dendritic spines—points at which neurons make connections—as well as an increase in a cellular form of memory, called long-term potentiation, in the hippocampus. Ghrelin improved rats' performances on a memory-taxing maze test. It also boosted the memory of mice compared to “knockout” animals missing the ghrelin receptor and mice with a condition mimicking Alzheimer's disease.

The authors note that aging and obesity—both associated with low ghrelin levels—influence the progression of Alzheimer's disease. Horvath said the findings raise the hope that ghrelin supplementation can improve

memory in Alzheimer's and other dementias. The work also raises caution for therapies aimed at controlling appetite by inhibiting ghrelin, the study concludes.

••• **Diversions may affect memory.** A new study shows that age-related memory decline may begin sooner than was previously thought. But 40-somethings take note: countering it may be a matter of minimizing distractions.

Many researchers wonder if changes in memory involve multiple mechanisms. To investigate, Cheryl Grady and colleagues at the Rotman Research Institute at Baycrest, University of Toronto, used functional magnetic resonance imaging (fMRI) to measure brain activity in adults performing memory tasks. The findings were reported in the February issue of the *Journal of Cognitive Neuroscience*.

The groups—people in their 20s, 40s, and over 65—answered questions about words and pictures, such as whether they were of living or nonliving things or appeared in upper- or lower-case letters. Next, in the memory phase, participants selected from a list the words and pictures they had seen.

Ideally, brain activity increases in areas involved in the task itself and decreases in those devoted to unrelated things, such as monitoring one's internal state or planning dinner. Those in their 20s showed this pattern—probably explaining young people's ability to study, watch TV, and chat with friends all at once, Grady says.

But an imbalance appeared in the middle-age group, with activity continuing in the “non-task-related” parts of the brain. Such activity was more pronounced in participants over 65.

“Our study shows that the brain changes seen in older adults begin gradually, in the 40s and 50s, and has implications not just for memory but for focus,” Grady concludes. “Once we're past that magic age where multi-tasking is no problem, we might want to step back, turn off the distractions, and concentrate on what we're doing.”

••• **Diabetes may change the brain.** Diabetes is known to damage nerves in the arms and legs, sometimes leading to the painful condition known as diabetic neuropathy or the need to amputate limbs. Research since the 1960s has suggested the disease may also affect the brain itself; for example, people with diabetes are twice as likely as the general population to develop depression.

To find out whether the depression is a “psychological” response to the illness or results from structural brain changes, Alan Jacobson and colleagues at the Joslin Diabetes Center and Harvard Medical School, Boston, examined levels of gray matter—brain tissue rich in cell bodies, which constitutes key areas such as the cerebral cortex and the movement centers known as the basal ganglia.

The team used voxel-based morphometry, which creates detailed, three-dimensional representations of magnetic resonance imaging (MRI) scans. Reporting in the February issue of the journal *Diabetes*, the researchers found that diabetes patients had decreased levels of gray matter density in areas of the brain responsible for memory, language processing, and attention, compared with healthy controls. The decreases were more prevalent in patients with wide fluctuations of blood sugar, particularly in those with many episodes of low blood sugar resulting in unconsciousness.

Although cognitive tests revealed few differences between diabetes patients and controls, “it's possible that the structural changes we observed signal future cognitive problems,” says study author Perry Renshaw of McLean Hospital in Belmont, Mass. Future studies will use MRI to help measure any cognitive and emotional changes, with the goal of treating and preventing depression in diabetic patients.

“News” was written by Elizabeth Norton Lasley, a freelance science writer in Woodbury, Conn. She can be reached at elasley@erols.com.

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Benefits of the Dog Genome

Lindblad-Toh and other scientists consider the mapping of the dog genome to be only the “tip of the iceberg” in terms of understanding the genetic link between dogs and humans.

Armed with this new knowledge, researchers can now find traits and disease genes in dogs and translate them to human genes; better understand the on/off signals in human genes that determine how neuronal connections are made; and learn about the wiring of the two species’ brains to determine if there are similarities.

“The dog genome gives us the basic tools to look in detail at the brain,” says Lindblad-Toh. “This is a parts list that helps us understand how genes, including brain genes, have evolved and function.” ■

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pain system is designed to sensitize itself, because it forces you to protect yourself. But after tissue repair, there are a certain number of people where the system doesn’t reset.”

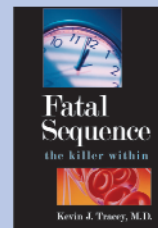
The major question now—and one the group is working on—is why pain hypersensitivity becomes chronic in some people after an injury heals, while pain processing returns to a normal, pre-injury state in others. ■

Rabiya S. Tuma is a science and medical writer in Berkeley, Calif. She can be reached at Rabiya@nasw.org.

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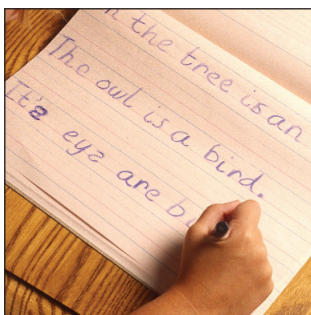


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