THE DANA FOUNDATION'S

BRAINWORK

The Neuroscience Newsletter

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News FROM THE FRONTIER

••• **The crucial chemistry of sleep.** A research team at the University of Michigan, led by neurology professor Sid Gilman, has identified two missteps in the neurochemical pathways of the brain that appear to lead to sleep disorders. The study subjects were people with a neurodegenerative disease known as multiple system atrophy; although extremely rare, this condition does include two types of sleep disruption that occur on their own in millions of Americans.

One study focused on REM sleep behavior disorder, which causes people to thrash about, talk, stand up, or even strike their partner, all without waking. Gilman and his collaborators used PET imaging to find quantitative visual evidence of a neurochemical deficit that researchers in this field had suspected for some time: a shortage of nerve cells producing the neurotransmitter dopamine in the striatum, a brain area involved in the control of movement. The second study used SPECT, a slightly different imaging technique, and revealed a scarcity of neurons containing another neurotransmitter,

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IMAGES THAT LAST

The Amygdala and Emotional Memory

BY ANN MACDONALD

Why is it that most people recall much of what they were doing on the morning of September 11, 2001, but many would be hard-pressed to remember what they had for breakfast last Wednesday?

"A common myth is that memory is like a video camera, and that people record events as they happen and then play them back later," says Daniel Schacter, a psychologist at Harvard University and author of *The Seven Sins of Memory.*

Or as memoirist Patricia Hampl writes in *I Could Tell You Stories,* "I am forced to admit that memory is not a warehouse of finished stories, not a gallery of framed pictures."

Emotional memories, the type that are so vivid they feel as if they have been seared into the brain, are particularly complicated. Research into how these memories are generated and stored continues to yield surprises—some of which are forcing scientists to rethink fundamental concepts of how the brain works.

A Garage Breakthrough

Many recent insights into emotional memory are based on the pioneering research of neurobiologist James McGaugh at the University of California, Irvine. Working in a laboratory in his garage as a graduate student in the 1950s, McGaugh conducted a series of experiments that would eventually challenge much accepted wisdom about memory.

McGaugh wanted to determine how learning is transformed into long-term memory and whether drugs could interfere with the process. When he injected rats with a stimulant immediately after they learned something, the animals were better able to repeat the task later on. If he waited several hours, the stimulant injection had no effect.

The findings demonstrated not only that memory could be enhanced, but also that it takes a certain amount of time for the brain to place new information into long-term storage. Thanks to work by McGaugh and others, it is

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The amygdala, a part of the brain that helps form emotions, may also help shape the strong emotional memories that often seem seared in our brains.

(MEMORY, continued from page 1)

now accepted that any type of long-term memory involves a basic three-step process: acquisition of information, consolidation into neural circuits for storage, and retrieval by several parts of the brain working together.

Stress and Selectivity

A key question remains: Why are emotional memories so vivid? In research that continues today, McGaugh and colleagues have shown that the amygdala, the almond-shaped area of the brain that helps generate emotion, may also contribute to the development of particularly vivid memories by modulating the way that those memories are stored. The theory is that the activated amygdala interacts with norepinephrine and other stress hormones—the same hormones involved in the heart-pounding fight-or-flight response—to strengthen neural connections that produce emotional memories.

There may be an adaptive reason that the amygdala is involved, says neuroscientist Elizabeth Phelps of New York University: "One of the critical functions of the amygdala is to separate the significant from the mundane."

The brain discards most short-term memories quickly because there is no reason to save them longer than a few minutes or hours. People will look up a phone number and remember it long enough to dial the phone, for instance. Emotional memories, which consist of feelings as well as facts, tend to involve events of long-term importance.

But Phelps cautions that emotional memories are not always as accurate as people believe. "You do remember emotional events better, but not necessarily every detail of what happened," she says, citing a study now underway about people's memories of September 11th. "What we're finding is that people's memory for September 11th is better than for what happened a week ago," Phelps says, "but the idea that people remember every little detail is misguided."

Mars and Venus?

In findings that surprised scientists—but probably only confirm what the average man or woman has long suspected—other researchers have uncovered significant gender differences when it comes to emotional memory. Neuroscientist Larry Cahill at the University of California, Irvine, and colleagues found that the amygdala is activated in both men and women watching highly emotional film clips, and that this activation corresponds with better recall three weeks later. But men activate the right side of the amygdala, while women activate the left side. Other researchers using different brain imaging techniques have confirmed the finding.

"This is the kind of finding that science sometimes gives you, where you don't know what it means but you can't ignore it," Cahill says. In subsequent research, he combined his initial findings with a longstanding hypothesis that the right hemisphere of the brain tends to process "big picture" aspects of events, while the left hemisphere processes details. Hence the amygdala activated on the right would strengthen "big picture" memory while left-side response would enhance the storage of details.

To test this idea, volunteers took a drug that inhibits the amygdala's ability to enhance emotional memory. After this pharmaceutical version of a "knockout" experiment, men could not remember the gist of an emotionally disturbing story, but could recall particular details; in women, it was just the opposite. These results provide additional support for a gender dichotomy in emotional memory, and imply that—when the amygdala is functioning normally—men may recall more of the big picture about an emotional event, while women remember more details.

Another team of researchers found that men and women may employ different encoding processes to store emotional memories. Pyschologist Turhan Canli at the State University of New York, Stony Brook, and colleagues used a brain imaging technique to study volunteers as they first looked at a series of pictures and during a memory test three weeks later. When viewing emotional images, men activated more brain areas than the women, in a circuit that involved the right amygdala. Women activated a smaller network involving the left amygdala, but showed greater overlap between brain areas involved in ongoing emotional processing and memory—what the authors call "co-localization" of the evaluative and encoding processes. The authors speculate that such co-localization in women may provide a neural mechanism that explains why women tend to have stronger emotional memories than men.

Although research in this area continues, these early results have profound implications. "The assumption has been that the sex of our subjects doesn't matter," Cahill says. "That's wrong. Sex may well matter, and matter a whole lot, about how the brain works." Among other things, this concept could affect the way that clinicians treat disorders such as post-traumatic stress disorder and depression, which

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The Neuroscience Newsletter

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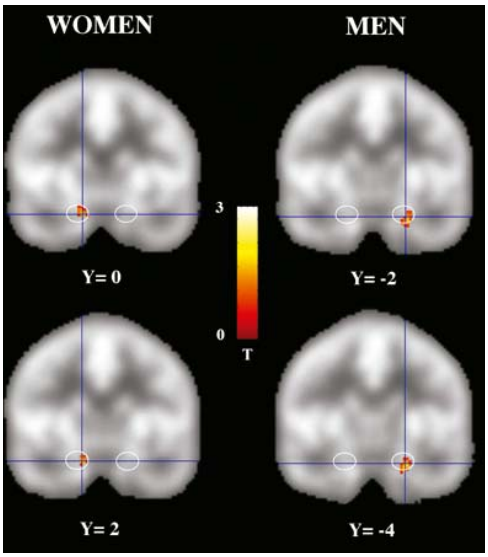

Activity of the amygdala on the left side of the brain relates to memory for emotional material in women. In men, however, memory for the same emotional material relates to activity of the amygdala on the right side of the brain.

affect more women than men.

Cahill emphasizes that this is not a scientific version of the pop psychology book *Men are from Mars, Women are from Venus.* "The brains of men and women on average are not processing emotional information in the same way," Cahill says. "There is still a lot of individual variation," as there is for height and muscle strength.

Age and Mood

Still other researchers have found that there may be age-related differences when it comes to emotional memory. A team led by Susan Turk Charles, also at the University of California, Irvine, recently reported that older people are more likely than young people to remember positive images. In one study, participants were divided into three age groups (18 to 29, 41 to 53, and 65 to 80). Everyone looked at a series of positive, negative, and neutral images. Middle-aged and older adults were able to recall a greater proportion of the positive images, while young people were more likely to remember the negative ones. These results were confirmed in a second study that ruled depression out as a contributing factor.

Psychological studies indicate that people tend to focus on the positive as they age because they are more aware of having a limited time left to live, but the authors also note that there may be a physiological difference at work. In related research, one of the authors found that in older people, the amygdala is activated equally by positive and negative images, while in young adults it responds more to negative images. The authors conclude that older adults may encode less information about negative information in the first place, which in turn would affect later recall.

Mood also matters when it comes to emotional memory. "There is a memory bias that goes on in depression," says Wayne Drevets of the Mood and Anxiety Disorders Program at the National Institute of Mental Health. Not only do depressed people tend to see even neutral events as negative, they also tend to dwell on sad thoughts.

The amygdala may be involved in both instances. Drevets and others have done research showing that people with certain types of depression have an overactive amygdala, even at rest; the more severe the depression, the more active the amygdala. Furthermore, Gregory Siegle of the University of Pittsburgh reported that in healthy people, negative words briefly activate the amygdala. In depressed people, the words boost amygdala activity much longer.

"Siegle's work shows that the amygdala may play a role in persistence," Drevets says. "One hypothesis is that this persistence of a negative state may be what is going on in the brains of people who ruminate about sad things."

Phelps at NYU has done other research showing that real and imagined fears activate different parts of the amygdala—a finding that has implications for anxiety disorders. Clearly many questions remain. "We're just beginning to tease all this apart," says Cahill.

Ann MacDonald writes about science and medicine from Wakefield, R.I.

New Mouse Model Narrows Search for Schizophrenia Genes

BY MAIA SZALAVITZ

Schizophrenia, a psychiatric disorder marked by hallucinations, disordered thoughts and social isolation, is caused by a yet-to-be-deciphered mix of genetic and environmental factors. But researchers have recently discovered some intriguing new clues that help explain some of the genetic risks for the disorder, which affects 2.2 million Americans.

Maria Karayiorgou, M.D., director of the Human Neurogenetics Lab at Rockefeller University is looking for susceptibility genes in people with schizophrenia and their families and then determining what those genes do in the brain.

Last year, she and her colleagues published two papers in the *Proceedings of the National Academy of Sciences* (*PNAS*) on a gene linked to schizophrenia located on chromosome 22. They had previously developed a mouse that lacked this gene. This mouse could be the first animal model of schizophrenia because it has a key defect in sensory processing that is typical of the disease in humans.

In June, *PNAS* published two more papers: one detailing a second mouse model of the disease generated by deleting a different gene, and Karayiorgou's group's accompanying paper, which showed that this new gene was also associated with schizophrenia risk in humans.

Birgit Funke, Ph.D., Instructor of Medicine at Harvard Medical School, points out that schizophrenia is both common and debilitating. "Given its frequency, it is important that we learn to understand what the predisposing factors are," she says, adding that such knowledge could lead to the development of new ways of treating, or even possibly preventing, schizophrenia.

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(SCHIZOPHRENIA, continued from page 3)

Mouse models are particularly helpful because they can be used both to study the brain pathways affected by particular genes and to test new drugs in ways that would be impossible in humans. Karayiorgou's mouse has already helped researchers understand how one gene and its product may be involved in some cases of schizophrenia.

A Dramatic Link

The story begins in the mid 1990s, when Karayiorgou found evidence in humans that a gene on chromosome 22 was linked to increased risk for schizophrenia. She examined DNA samples from patients and their families and determined which genes were unusually common in affected people and close relatives.

Then, she says, "We became aware of a syndrome associated with the q11 region of chromosome 22." This syndrome has been given various names, including velo-cardio-facial syndrome and DiGeorge syndrome. Affected babies often have cleft palate, other distinct facial malformations, heart defects, and language and coordination problems. They also tend to have psychiatric problems, which worsen as they age. The individual manifestations vary, but everyone with the disorder is missing a particular section of the q11 region of that chromosome, so it is now called 22q11 deletion syndrome.

What fascinated Karayiorgou and her colleagues was that there had been case reports suggesting that some people with 22q11 deletion become psychotic. "We put two and two together," she says, and decided to see if these patients were actually diagnosable as having schizophrenia. If they were, that would implicate 22q11 as a real "region of interest" and would help researchers delineate more precisely which genes on chromosome 22 might cause the disease.

When they studied people with 22q11 deletion, they found that a remarkable 20 to 30 percent met diagnostic criteria for schizophrenia. "That's a dramatic enrichment of risk from 1 percent in the general population," says Karayiorgou. In fact, it is the highest risk factor for the condition so far discovered, outside of being the identical twin of someone with schizophrenia or the child of two schizophrenic parents.

Karayiorgou then studied large samples of schizophrenic patients, to determine how many had the deletion. Only 2 percent did, but that still made it the genetic problem most strongly linked with the disease so far. "The genetic etiology of schizophrenia is complex," explains Funke. "Only a fraction of the risk can be attributed to genes." Studies of identical twins reveal as much: Only 40 percent share the condition, which means something in the environment is also critical to its development. "The genetic risk is not attributable to one gene alone," Funke continues. "Therefore, each gene will only be responsible for a small fraction of the risk."

Karayiorgou reasoned that people who had damage to the 22q11 region, not just those who are missing it entirely, might also be at risk for schizophrenia and that studying this theory might allow researchers to home in on which gene or genes in the area might be most important.

Chemical Connections

Her group did a systematic screen of all the nearby genes in patients with schizophrenia who did not have the deletion. "We identified two regions of association," she says, recounting the research published in her 2002 *PNAS* papers. One was a gene for PRODH, an enzyme that breaks down a protein called proline.

While its function is not fully understood, in the brain proline appears to be involved in the synthesis of the neurotransmitters glutamate and GABA. Proline may also act as a neurotransmitter itself in glutamate neurons. Because prior research suggests that glutamate is important in schizophrenia, this connection seems plausible. Understanding the connections between proline and glutamate might allow interventions in that system.

Karayiorgou's lab developed a mouse in which the gene for PRODH was deleted. The PRODH "knockout" mice showed the same impairments as humans with schizophrenia in tasks involving what researchers call sensorimotor gating, a process that involves filtering information from the senses—and information within the brain—for its relevance and usefulness to current activities.

More recently, Susumu Tonegawa and his colleagues at the Massachusetts Institute of Technology developed a mouse that is similarly defective in sensorimotor gating—and that shows additional difficulties with organized behavior, working memory, and social interaction. For example, while normal mice curl up together to sleep, these mice sleep alone. And while normal mice build a neat nest, the new mice scatter nesting material around their cages. In human schizophrenia, social isolation is typical, as are disorganized thoughts and behavior.

Tonegawa's mice are missing a gene for another chemical used by the brain, calcineurin, which is thought to have effects inside neurons that may influence the way they react to glutamate and dopamine signals. Like glutamate, dopamine is a neurotransmitter previously linked to schizophrenia. Effective antipsychotic drugs seem to affect either one or both of these brain chemicals.

Karayiorgou has already linked one gene associated with calcineurin processing, PPP3CC, to schizophrenia risk. However, there are numerous genes associated with the calcineurin pathway, many of which have not yet been studied. Says Tonegawa, "The amazing thing is that most of these genes fall into [regions already known to be] schizophrenia-susceptibility [areas]." In fact, one is in the chromosome 22q11 region.

Karayiorgou and Tonegawa are continuing to follow up these leads, which offer new insight into how genes can increase susceptibility to schizophrenia and which may yield new medications and genetic therapies for people with schizophrenia and those with 22q11 deletions or mutations.

Maia Szalavitz is a freelance science writer from New York, N.Y.

Fishing in a Murky Pond:

Seeking the Role of Hormone Replacement Therapy in Neuron Health

BY RABIYA S. TUMA

In July 2002, researchers drew front page headlines when they stopped the Women's Health Initiative study prematurely. They closed the study, which was designed to determine the long-term effects of hormone replacement therapy in post-menopausal women, when they detected a slight increase in breast cancer in the women who were taking combined estrogen-progesterone therapy as opposed to those on the placebo.

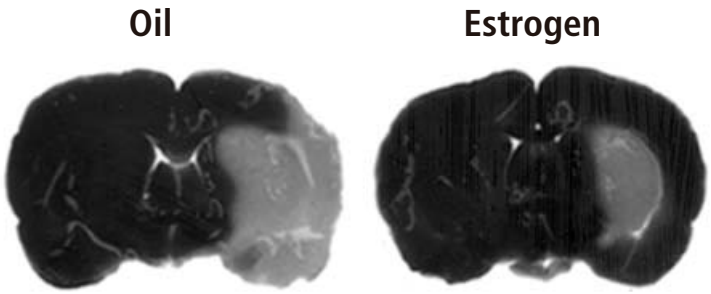
However, hormones don't just affect reproductive tissues; they also have a large effect on brain function. But just what role estrogen or estrogen-progesterone combinations have with neurons is still a matter of debate.

Based on animal, cell, and molecular studies, neuroscientists conclude that estrogen is necessary for normal neuron function and that the hormone can actually mitigate damage from injuries such as stroke. For example, when Phyllis Wise and colleagues at the University of California at Davis remove ovaries from rats, the animals no longer produce estrogen—similar in some ways to a postmenopausal woman. The researchers then supplement half of the animals with normal amounts of estrogen; the control animals do not get estrogen. When Wise's team then induces a stroke in the animals, the rats that have estrogen in their systems sustain less damage than those that lack the hormone.

Significantly, treating the animals after the stroke with physiological levels of estrogen does not mitigate the damage that already was sustained, says Wise. This finding implies that for the hormone to protect neurons it must be in the system prior to the injury or trauma.

Unfortunately the clarity of the animal and molecular studies becomes clouded when one looks at clinical human studies of the effects of hormones on brain function and health. When asked to evaluate the value of hormone replacement therapy (HRT) on cognitive function in post-menopausal women, neuroscientists point to two recent studies as being the most informative. The studies, however, have nearly contradictory results.

In the first study, called the Cache County study because researchers followed nearly 3500 healthy adults in Cache County, Utah, for ten years, the researchers found that 10 or more years of hormone therapy reduced a woman's risk of developing Alzheimer's disease by 59 percent relative to those who did not take hormones.



Regions of damage appear in white in these sequential brain sections from an animal that was not exposed to estrogen and one that was exposed.

"Current use of estrogen was not important," says Barbara Sherwin, a clinician and researcher at McGill University in Toronto, Canada, who was not affiliated with the study. "What was important was past use of greater than ten years."

The other recent study that Sherwin and others talk about is the Women's Health Initiative Memory Study (WHIMS), a substudy from the main Women's Health Initiative study. Researchers in charge of this study announced in May 2003 that women taking combined hormone therapy, estrogen- and progesterone-like hormones, have twice the risk of developing dementia of those who are not taking HRT.

So how could two studies come up with such conflicting results? Sherwin, who was an advisor to the WHIMS, said the contradictions are likely the result of several differences, two of which play a prime role, she believes.

First, the two studies are different in their very nature. The Women's Health Initiative study and the memory study that went with it were a randomized controlled trial, where the researchers put the women on hormone replacement therapy at the age of 65, well past the age at which most women hit menopause. The Cache County study, on the other hand, was an observational study, in which the researchers simply asked people to report their behavior over time. In this case, the women and their personal physicians decided whether the women would take HRT, and then they reported that to the researchers. Because most women who initiate HRT do so close to the time of menopause onset, most women in the Cache County study likely started treatment on average much earlier than those enrolled in the WHIMS. In fact, the results from the Cache County study imply that there is a window of opportunity for HRT to be efficacious; by the time the women in the WHIMS initiated treatment at 65 it was likely too late for HRT to demonstrate a protective affect because these women had been without their natural hormones for more than a decade already.

The second major distinction, Sherwin says, is that all of the women in the WHIMS study were on a single drug, Prempro, whereas those in Utah could have been on Prempro or other therapies, including some that are more like human hormones. This is important because Prempro is composed of hormone compounds that are somewhat different from natural human estrogen and progesterone.

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Numerous animal and cell studies indicated that neurons react differently to Prempro than to the natural human hormones.

So what's the right answer? Does hormone replacement therapy protect neurons? Sherwin says there is no one answer yet. "This is an individual decision and women need to sit down with their doctors and make their own choice—and re-evaluate it every year or so," said Sherwin.

However, it is becoming increasingly apparent from molecular and animal experiments that if clinical researchers can design the right drugs or drug regimens, then hormone therapy will help preserve neural function, and with minimal risk to other organ systems in the body. "The thing I am really impressed with is that low levels of estrogen replacement can be very efficacious in the area of protection," Wise said.

Rabiya S. Tuma is a science and medical writer in New York, N.Y.

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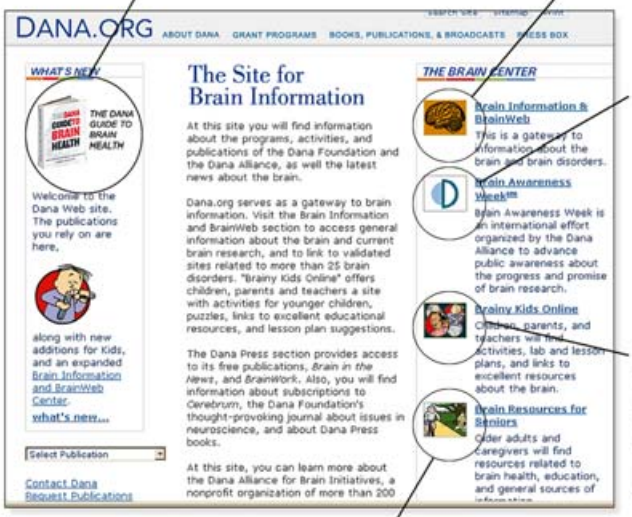

Brain Awareness Week℠
Brain Awareness Week is an international effort organized by the Dana Alliance to advance public awareness about the progress and promise of brain research.

Brainy Kids Online
Children, parents, and teachers will find activities, lab and lesson plans, and links to excellent resources about the brain.

New! **Brain Resources for Seniors**
Older adults and caregivers will find resources related to brain health, education, and general sources of information.

New Neurons in the Adult Brain:

Dogma Overturned or Open Debate?

BY BRENDA PATOINE

It has been four years since a report in *Science* asserted that new neurons were continuously born in the neocortex of adult monkeys, an area that in humans is the site of the highest cognitive functions. The paper stunned the scientific community and generated front-page news declaring that centuries-old neuroscience dogma had been overturned, since it had long been accepted that the generation of new neurons (neurogenesis) was, in mammals at least, limited to developmental periods. If monkeys—humans' closest cousins on the evolutionary tree—were continuously generating neurons in the cortex, it would force a reconsideration of virtually all of our current concepts about brain function and development. But has it?

Even in the midst of the excitement the 1999 report fueled, the cognoscenti of the field raised an eyebrow. Wait and see if it's replicated, experts cautioned, pointing out that the true test of science is if other researchers achieve the same results. In this case, numerous attempts by various groups have not been able to replicate the findings. In fact, at least four published papers (two in primates, two in rodents) have found the opposite result.

"Virtually every journalist writing about this subject has taken the tack that adult neurogenesis overturns entrenched dogmas, but few have delved into the methodological criteria that are required to be met in order to make this extraordinary claim—and were often not met," says Pasko Rakic, chairman of neurobiology at the Yale School of Medicine. As a result, he says, the public is left with the impression that our brains make new neurons throughout life, which is only part of the story. "In mammals, including humans, 99.9 percent of neurons are

not replaced spontaneously, as is painfully obvious to all those who suffer from brain injury or neurodegenerative diseases," Rakic says.

Accepted, with Caveats

Adult neurogenesis is "absolutely" accepted as a fact by neuroscientists, says Fred Gage, a neurobiologist at The Salk Institute, with the caveat that it's accepted in two regions: the dentate gyrus of the hippocampus, and the olfactory bulb, to which new neurons born in the subventricular zone migrate. "For those two regions, you will find agreement even among the most critical skeptics of global adult neurogenesis," he says.

Although there have been individual reports going back 30 years of neurogenesis occurring in a number of other brain regions, including visual cortex, frontal cortex, amygdala, striatum, and substantia nigra, "none of them have been replicated in a way that gives confidence," Gage says. In fact, he says, in each of these cases, published reports have contradicted the claims.

"The pendulum is beginning to swing back the other way," argues cell biologist Richard Nowakowski of Robert Wood Johnson Medical School, away from "enamored" acceptance of new neurogenesis claims and toward "appropriate skepticism," where methodologies are critically reviewed. Controversy surrounds the amount and type of stains used to "tag" dividing cells, and the methods used to identify and count neurons vs. other brain cells, among other issues.

The subtleties of complex methodological differences are generally lost on non-scientists. Moreover, there is a tendency to think of the brain as one unit, when in fact human brains comprise numerous specialized structures that have different evolutionary roots. The areas where neurogenesis is accepted, the hippocampus and the olfactory bulb, are two of the "oldest" regions in evolutionary terms, whereas the neocortex is one of the "newest" structures. Rakic posits that as one moves up the evolutionary scale, from fish to reptiles to birds to mammals

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acetylcholine, at sites in the brainstem that are involved in respiration. The results were published by *Neurology* in the July 8 issue.

Although both studies showed a correlation between the neurochemical deficits and the sleep disorders, they stopped short of establishing that the abnormal brain chemistry *caused* the disorders. Says Gilman, "We don't know yet if we will find this same effect in patients with other neurological diseases or in people who are otherwise neurologically well." He and his colleagues are moving ahead quickly to find out.

••• **Protectors of the hippocampus.** Short-term memory, certain modes of learning, and connections to emotional brain areas are just part of the task list of the hippocampus, a brain region located deep in the cerebral cortex. Small but powerful, the hippocampus sends out and receives signals from virtually every part of the brain. Recently, several brain illnesses such as major depression have been found to damage the hippocampus, causing it to shrink and lose volume. But a new paper in the August *American Journal of Psychiatry* suggests that millions of people with depression have been protecting themselves against hippocampal damage without even knowing it, simply by taking their medicine.

In interviews with 38 women who had had multiple episodes of clinical depression, psychiatrist Yvette Sheline, of the Washington University School of Medicine, and her collaborators ascertained the total number of days on which each woman had experienced depression, and the number of days of depression on which they had not received treatment (i.e., antidepressants). The scientists then took an MRI scan of each subject's brain. The scans showed that the longer depression went untreated, the greater the toll on the hippocampus—up to an average 10 percent loss of volume, enough to impair normal functioning.

Earlier studies had painstakingly established that the shrinkage did not involve the death of great numbers of neurons or their supporting cells. According to Sheline, "The evidence points to the loss not of cells but of the substance between cells," specifically the dendritic fibers that are vital to the work of signal transmission from one nerve cell to another. It's not yet known whether antidepressant medication can help the brain to rebuild some of these lost fibers, but the study brings out a new reason for people with depression to seek treatment as early as possible.

••• **New genes for the treatment of epilepsy.** Although a number of new anti-epileptic drugs have proved beneficial, many people with epilepsy have not yet found an effective treatment. One promising line of investigation is a new use of gene therapy, as reported by Thomas McCown and his collaborators at the Gene Therapy Center of the University of North Carolina School of Medicine. Their paper, published in the August issue of *Nature Medicine,* presents the results from gene therapy trials in rat models of epilepsy.

Earlier work showed that the neuropeptide galanin could suppress the irregular nerve signals in the brain that lead to seizures; however, the galanin was ineffective if it simply was produced within neurons and never secreted out beyond the cell walls. To avoid this roadblock, the UNC researchers used not only the gene for making galanin but also a gene that would cause neurons to secrete the galanin out into the intercellular space.

"Neither the galanin-expressing sequence nor the secretory sequence is enough by itself," says McCown, but the two together succeeded in decreasing the frequency of seizures in the animal model. As a bonus, when seizures did occur, the brain areas that had been treated with gene therapy

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(NEUROGENESIS, continued from page 7)

and finally to humans, the degree of neurogenesis dwindles. While it made evolutionary sense for birds or fish to have a constant supply of new neurons, if neurons were routinely replaced in the human cortex, we would lose the memories and learnings of a lifetime of experience, he says.

The debate over where, why, and how neurogenesis occurs is not likely to end any time soon, but nearly everyone agrees that a better understanding of the processes involved could pave the way for novel therapies for brain disorders. Gage says a "dominant theme now" among researchers in this field is to determine what it is about the so-called neurogenic areas that makes them special, and how the phenomenon might be harnessed to induce neural self-repair.

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lost far fewer neurons than untreated areas. McCown and his colleagues are hoping their demonstration of long-term seizure attenuation will lead to the development of additional gene therapies for epilepsy and other neurological disorders.

Patricia S. Goldman-Rakic, 1937-2003

The Dana Alliance for Brain Initiatives notes with sadness the death of Patricia S. Goldman-Rakic, professor of neuroscience at Yale University, on July 31. A founding DABI member in 1993, Dr. Goldman-Rakic also served a term as president of the Society for Neuroscience, from 1989 to 1990, and was elected to the National Academy of Sciences in 1990. Her research achievements, ranging over four decades, included the first explorations of the frontal lobe, or "executive center," of the brain; the identification of specific cells in the prefrontal cortex that are responsible for short-term memory; and the association between certain deficits of short-term memory and the thought disorders that are commonly seen in schizophrenia. Dr. Goldman-Rakic is survived by her husband, Pasko Rakic, M.D., Ph.D., also a neuroscientist at Yale; and a sister, Dr. Ruth Rappaport. Calling Dr. Goldman-Rakic "one of the most distinguished neuroscientists of her generation," Yale president Richard C. Levin said, "We grieve her tragic loss in the knowledge that her important contributions will live on."

"News" is written by Sandra J. Ackerman, a science writer based in Durham, N.C.

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