THE DANA FOUNDATION'S

BRAINWORK

The Neuroscience Newsletter

Vol. 13 No. 6

November-December 2003

News FROM THE FRONTIER

••• **Antidepressants may fend off stroke-induced damage.** Studies show that after a stroke, depressed patients are between three and eight times more likely to die. But a short course of treatment with antidepressants within six months of a stroke has life-saving benefits for as long as nine years—whether or not the subjects were depressed.

In a study published in the October issue of the *American Journal of Psychiatry*, 104 patients were randomly assigned to receive fluoxetine (Prozac), placebo, or nortriptyline, another type of antidepressant, for 12 weeks. At the nine-year follow-up, 68 percent of patients given antidepressants were still alive, compared to only 36 percent of the placebo-treated group.

Treating depression makes patients more likely to comply with treatment regimens and take better care of themselves. But antidepressant therapy may do more than improve mood and behavior. Because only half of the patients treated actually suffered from depression—yet the increase in survival times applied equally to the depressed and nondepressed groups—and because

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New Vistas in Addiction Treatment:

Easier Access, Greater Choice of Medications

BY THOMAS S. MAY

Addiction to alcohol and other drugs is undoubtedly one of the biggest health problems worldwide. In the United States alone, almost 12 million people are addicted to or "dependent on" various substances (excluding tobacco), according to recent government statistics. Even though most of those affected by substance abuse or dependence are aware of the harmful consequences of their behavior, very few receive medical treatment for their condition. This is partly because most people—including many physicians—view addiction not as a medical disorder but as a character flaw or a sign of moral weakness.

But another important reason for most addicts' failure to get treatment is the lack of availability of effective medications. A survey of almost 1,400 substance abuse specialists has found, for example, that they very rarely prescribe either of the two drugs currently available in the United States for treating alcoholism. This is mainly because the doctors don't think these drugs are very effective—an opinion that is backed up by a large number of studies, according to the authors of the survey.

However, this situation is about to change, some experts say, as more and more medications are found to be effective for treating substance use disorders. In addition, there is a trend for moving the diagnosis and treatment of addictive disorders from specialized treatment centers to the doctor's office, where patients could receive these services in much greater numbers.

New Weapons in 'Battle Against the Bottle'

The most effective medication that is currently available in the United States for the treatment of alcohol dependence is a drug called naltrexone, according to Charles O'Brien, an addiction expert at the University of Pennsylvania. Naltrexone reduces the

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Acamprosate, ondansetron, and topiramate hold promise for treating alcoholism, and topiramate also has been studied as a treatment for cocaine addiction. Meanwhile, a recent study found buprenorphine to be effective in treating heroin addiction.

(ADDICTION, continued from page 1)

craving for alcohol by blocking the activity of opioid receptors, which in turn inhibits the release of dopamine inside the brain's "reward system," O'Brien explains.

Although naltrexone can help some alcoholics, it does not work for everyone, and even when it does, it is only moderately effective. Some studies indicate that its effectiveness might be boosted by combining it with some other medications, such as acamprosate, which has already been approved for treating alcoholism in Europe, Latin America, and Australia.

"Because acamprosate acts on a different neurochemical target than naltrexone, its corresponding effect on craving is thought to be distinct," O'Brien notes. "Rather than blocking the opioid receptors that help confer the neurochemical 'reward' associated with alcohol consumption," acamprosate modulates receptor activity of another neurotransmitter, glutamate-NMDA, and it appears to reduce the intensity of craving after drinking cessation. "Since the two medications work on completely different receptor systems, there is reason to believe that their results might be additive," O'Brien contends.

The anti-nausea medication ondansetron also appears to be useful for treating alcohol dependence in so-called "early-onset" alcoholics, who become dependent on alcohol before age 25 and are thought to have a strong biological predisposition to become alcoholics. In a clinical trial that involved 321 subjects and was published in the journal *Psychopharmacology* last year, Bankole Johnson of the University of Texas at San Antonio and colleagues found that early-onset alcoholics who had been treated with ondansetron plus behavioral counseling for a period of 12 weeks experienced significantly reduced craving and drank considerably less alcohol during that time than those who had received behavioral treatment and placebo. Ondansetron exerts its anti-craving effect "by ameliorating some serotonergic abnormality" in early-onset alcoholics, the authors suggest.

More recently, the same team of researchers reported in *The Lancet* that 12 weeks of treatment with the anticonvulsant drug topiramate reduced heavy drinking and increased days of abstinence in a group of 150 alcoholics by about 25 percent. "At the end of the 12 weeks, patients on topiramate reduced their drinking, their craving, and their quality of life improved significantly, when compared to [those treated with] placebo," said Nassima Ait-Daoud, one of the researchers involved in the study.

The scientists hypothesize that topiramate may combat craving by inhibiting alcohol-induced release of dopamine in the midbrain. According to Bankole Johnson, the study's lead investigator, "topiramate's properties could make it an attractive candidate for co-treatment with other specific medications for treating either early-onset or late-onset alcoholism." George Koob, director of the psychopharmacology division at the Scripps Research Institute, also thinks that successful treatment approaches will probably involve a combination of several medications (or one medication with a number of different ingredients) that "hit several molecular targets."

This diagram shows in red the binding sites and pathways of opiate drugs such as buprenorphine.

Topiramate may also be effective for cocaine addiction, according to a study presented in Florida earlier this year at the annual meeting of the College on Problems of Drug Dependence. Researchers from the University of Pennsylvania School of Medicine and Philadelphia Veterans Affairs Medical Center, Philadelphia, enrolled 40 cocaine-dependent individuals in the double-blind, placebo-controlled trial, which lasted 14 weeks. Half were given increasing doses of topiramate (up to a maximum of 200 mg/day), while the other half received placebo.

An analysis of urine samples showed that, after a one-week period of abstinence, most subjects in the placebo group gradually resumed their cocaine use over the course of the study. However, most patients treated with topiramate remained largely drug-free throughout the 14 weeks. The investigators therefore concluded that topiramate "may hold promise for relapse prevention in cocaine dependent patients."

BRAINWORK

The Neuroscience Newsletter

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Office-based Treatment

The number of prescription drugs that can be used to combat substance dependence continues to grow for other drugs of abuse as well. For example, in a recent study published in *The New England Journal of Medicine*, Paul J. Fudala of the University of Pennsylvania School of Medicine and colleagues found that the pain medication buprenorphine (alone or in combination with naloxone), administered in a doctor's office, was safe and effective in the treatment of heroin addiction.

In the past, heroin addiction could only be treated at specialized addiction treatment facilities, primarily using methadone, a synthetic form of heroin. However, access to such facilities is rather limited, and typically only a small minority of addicts get appropriate treatment, according to H. Westley Clark, director of the Center for Substance Abuse Treatment, Substance Abuse and Mental Health Services Administration, Department of Health and Human Services. "There are only about 1,200 regulated opioid-treatment programs nationwide, and six states have no such programs," he writes in a related editorial.

Buprenorphine is an opiate-receptor agonist (i.e., it enhances the effects of opiates), and it is used in many countries for the treatment of moderate to severe pain. Because it is a partial agonist, buprenorphine is not as dangerous as methadone, says Markus Heilig, a professor of psychiatry at Sweden's Karolinska Institute who has studied the effects of both medications. "Methadone is a full agonist, so if a person takes an overdose, they will get respiratory depression and they will die. The toxicity of buprenorphine is much lower, so if you increase the dose, you will reach a plateau, and no respiratory depression will occur," he explains.

Although it is much safer than methadone, buprenorphine can still be abused, Heilig notes, "if addicts chase the euphoria and inject it, instead of taking it by mouth." Therefore, another drug, naloxone, is sometimes added to the preparation to counteract the effects of buprenorphine and "to prevent addicts from getting a kick out of it," should they try to inject the medication, he says. "Naloxone is not absorbed if you take it orally, so as long as people take their combination the way they're supposed to, then naloxone is just irrelevant."

Buprenorphine may also be effective for alcohol dependence, Heilig says: "It looks very promising in animal experiments, but the data are just not in yet from human studies." What is important, however, is that the idea of treating addictions with pharmacological agents has now become widely accepted, Heilig contends. "I don't think we're going to cure addiction from one day to another," he says. "What's going to happen is we're going to find some drugs that will fit some patients and other drugs that will fit others. That's the way most fields in medicine have developed, and this development has now started in the field of addictive disorders."

Thomas S. May is a science and medical writer based in Toronto, Canada.

Beating Chronic Pain

BY HAKON HEIMER

For most of human history, pain treatment has been akin to painting your house by training a fire hose on it from across the street. If your blast is strong enough, you will cover much of the house with paint. But there will be unpleasant side effects—paint on your windows and roof—and you'll completely miss the back wall.

Until recently, the fire hose of pain pharmacology was filled primarily with drugs such as Aspirin for mild pain and opium-based compounds for more serious cases. For the pain of injuries or infections, these drugs were sufficient. For the back wall—chronic pain—they have been mostly ineffective.

The causes of chronic pain are many and varied. Most pain patients suffer from rheumatological disorders such as arthritis, and recent drugs called Cox2 inhibitors have provided a

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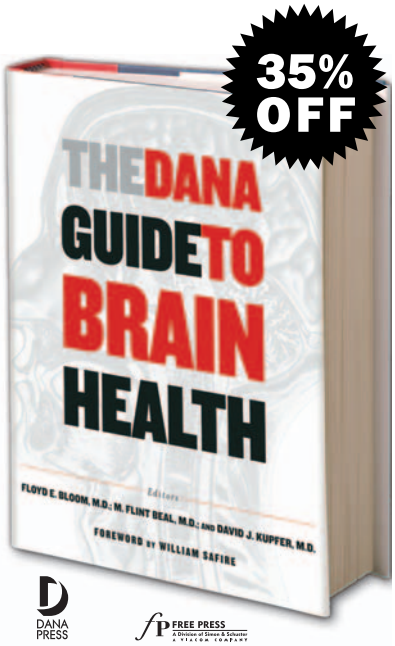

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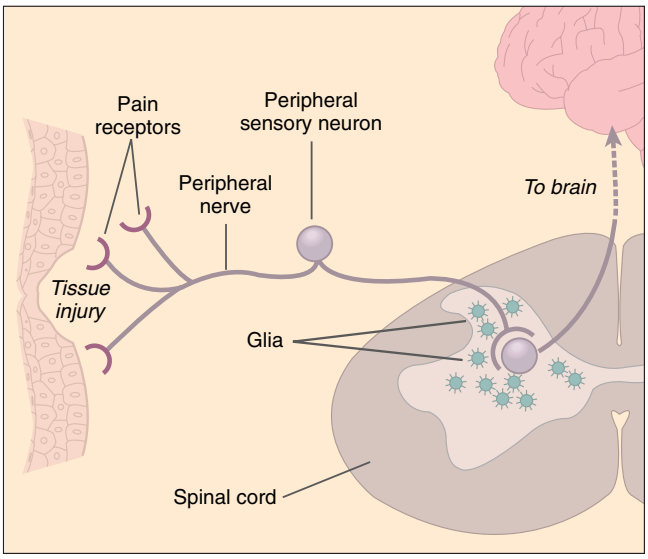
reasonable, and relatively safe, level of relief for this group.

The situation is very different for people whose pain is caused by nerve damage, termed neuropathic pain. The causes range from physical nerve injuries to diabetes to AIDS. Their numbers are smaller—but still in the hundreds of thousands—and their pain is typically severe. "With neuropathic pain, patients have persistent pain, and the current standard of treatment is not great," says Clifford Woolf, of Massachusetts General Hospital. "Almost all the therapies are associated with significant side effects."



The chronic pain of neuropathy arises in the nerve pathways that detect pain (nociception). Scientists are targeting different molecular sites along this pathway in the search for effective therapies.

New Approaches to Pain

Hope for effective therapies for neuropathic pain comes from recent shifts in pain research—away from classifying chronic pain by its causes, and away from an emphasis on delivering drugs to the the central nervous system (CNS), where they are most likely to cause side effects.

The new focus is on understanding the molecular mechanisms of pain, particularly in the "peripheral" nerves that conduct sensations into the CNS. The key players are the sensory neurons, whose fibers extend out to organs such as the skin, where they detect sensations including touch, temperature, and pain. The sensory neurons pass these signals along to neurons in the spinal cord, which relay the information to the brain.

Neuropathic pain arises when physical damage or inflammation cause the neurons in the periphery and cord to become jammed in the "on" setting, sending pain signals in the absence of any real stimulus. In some cases this becomes chronic pain; in others, hypersensitivity (allodynia), where a light touch on the skin can induce severe pain.

A Focus on Receptors

Pain research was invigorated when David Julius and his colleagues at the University of California, San Francisco, reported the discovery of the first receptor molecule sensitive to pain in 1997. The presence of receptor molecules on the ends of nerve fibers that detect pressure, temperature, or chemicals had long been just an article of faith. Subsequent research has shown that the vanilloid receptor discovered by Julius's group responds to heat and to capsaicin, the chemical that gives chili peppers their burn.

Since then, researchers have identified a number of other receptors that sense heat or cold or respond to capsaicin. A recent highlight was the discovery of a noxious cold receptor, reported in the March 21 issue of *Cell*. A research team led by Ardem Patapoutian of the Scripps Institute in La Jolla, California, has determined, at least in mice and rats, that a receptor termed ANKTM1 detects temperatures low enough to be painful. Receptors for touch or pressure remain elusive, however.

The value of these receptors is that they control activity in the peripheral nerves, and researchers may be able to design receptor-targeted drugs that can turn off the chronic pain signals in neuropathy.

In addition to sensory receptors, there is great interest in receptors that respond to endocannabinoids. These potent pain relievers are the body's own version of the psychoactive ingredients in marijuana. "The holy grail in cannabinoid research is to find a way to avoid the psychoactive effects," says Woolf, of Massachusetts General Hospital. Unfortunately, most evidence to date suggests that the receptor that produces the main analgesic effect, the CB_1 receptor, also produces the euphoria.

Recent research led by Philip Malan of the University of Arizona, published in the *Proceedings of the National Academy of Sciences*, offers evidence that another cannabinoid receptor, CB_2, may also contribute to pain relief. The researchers designed a cannabinoid-like drug that selectively activates only CB_2 receptors and reported that the compound could reduce pain in an animal model of allodynia.

Daniele Piomelli, of the University of California, Irvine, finds the results encouraging: "The novelty in this study is that they show a frank anti-allodynic effect. It's a validation of the concept." But he adds that it remains to be seen whether activating CB_2 receptors is sufficient to address severe pain in humans, or whether drugs must also target CB_1.

Venturing Back into the CNS

Not all the action in pain research is in the periphery. A new line of inquiry points back into the spinal cord, toward the neuron's less glamorous cousin, the glial cell. Until recently, glia appeared to play a limited role in the nervous system, primarily serving up nutritive molecules to the neurons. Scientists now recognize that glia are active players in processes such as inflammation and pain.

A research group led by Linda Watkins of the University of Colorado reported in the February 1 *Journal of Neuroscience* that they could eliminate the allodynic pain of inflammatory neuropathy in an animal model by injecting the spinal cord with a compound that interferes with the metabolism of glial cells.

In the August 14 issue of *Nature*, Kazuhide Inoue, of the National

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Our Brains Are Plastic—and That's Good News

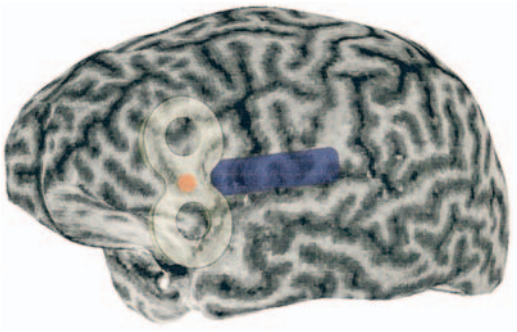
BY SANDRA J. ACKERMAN

The scene, set in a laboratory, looks simple enough: A person sits quietly in a chair, with electrodes attached to one arm and an electric coil fixed on his scalp. A brief current passes through the coil, and the subject's arm begins to twitch. Is this experiment designed to explore some new aspect of electricity, or to measure the cooperativeness of the typical research volunteer? Neither of the above—the point at issue here is just how plastic the brain can be.

In everyday conversation, describing something—or worse, someone—as "plastic" is hardly a compliment. In the brain, however, plasticity is not only natural but necessary: It is the ongoing ability to strengthen or weaken the connections among neurons, and even to develop new connections, in response to the constant stream of stimuli reaching the brain.

Neuroplasticity has long been known as the powerful engine that drives all kinds of learning in infancy and childhood, but the same force was recognized only recently in the mature brain: The brain's ability to rewire itself provides the physical basis for learning throughout the human lifespan. But this ability can serve another vital purpose as well: When driven by proper therapy and training, neuroplasticity can help the brain to recover from injury and to regain some degree of functioning in parts of the body whose control sites in the cerebral cortex have undergone considerable harm. Strokes, for example, often take a toll on the motor cortex, leaving damage that ranges from weakness or stiffness of the muscles to painful spasms or paralysis. In rehabilitation today, the deepening understanding of neuroplasticity leads to a focus on the "inside," targeting treatment and therapy to the motor cortex directly, as well as on the "outside," forcefully encouraging movement in the impaired limb or region of the body.

At the National Institute of Neurological Disorders and Stroke, neurologist Leonardo Cohen and his colleagues are exploring new ways to enhance the activity of the motor cortex by delivering carefully designed patterns of electrical signals. "We try to stimulate the motor cortex at a time when it is already primed by a preceding stimulus," says Cohen. In a recent study from his lab, healthy volunteers received a mild electrical stimulus to the median nerve of the right wrist, followed by a single pulse of transcranial magnetic stimulation delivered to the skull area that lies over the left motor cortex (the brain area that controls movement in the right half of the body). The researchers found that when stimulation of the median nerve preceded the stimulation of the motor cortex by precisely the right interval—25 milliseconds, a figure determined by the time it takes for a signal to travel from one brain site to another—the response from the motor cortex was stronger than average. A shorter interval between the two stimuli, such as 10 milliseconds, drew a response that was weaker than average. These results show that the same set of stimuli can produce two different effects, depending solely on the relative timing of the stimuli. The eventual success of a mode of rehabilitation rests on such fine details.



In this 3-D surface view of the brain, reconstructed from a magnetic resonance image, the magnetic coil (in the shape of a figure 8) used to stimulate specific brain areas is projected over the target area (here, the inferior prefrontal gyrus, indicated by the colored dot). Coil positioning is achieved by a frameless, MRI-guided, stereotactic system. The bluish, oblong object is part of the coil handle.

Another way to bolster the activity of the motor cortex is to administer a drug, amphetamine, in combination with the sensory stimuli. At the Institute for Neuroinformatics at Ruhr-University in Bochum, Germany, Hubert Dinse, together with Martin Tegenthoff of the Department of Neurology, recently directed a study that tested the effectiveness of tactile stimulation, with and without amphetamine, in increasing subjects' sensory acuity—that is, their ability to distinguish among several stimuli that are delivered within a small area. The subjects received tactile stimuli to a 1 cm patch of skin on one hand, which excited many neurons at once, in a technique called "coactivation." After three hours of coactivation, the subjects showed measurable gains in sensory acuity in this patch of skin. When they were given amphetamine along with the coactivation, they showed even greater gains; however, amphetamine given without the coactivation produced no change at all.

As Dinse and his colleagues see it, reorganization in the sensory cortex of the brain is what underlies the gains in sensory acuity, and the reorganization itself is triggered by the information (the signals coming from the skin receptors) delivered to the target neurons. Amphetamine enhances this effect because it helps the synapses to transmit information more efficiently. However, as Dinse points out, "It's important to note that just taking the drug by itself has no effect on the synapses' efficiency. You have to be learning something, and then the drug enhances the learning."

The Ruhr-University team has also obtained good results using repetitive transcranial magnetic stimulation (rTMS) in place of amphetamine. The relative merits of single-pulse TMS, rTMS, and amphetamine await further study. But one principle is already clear: Recruiting the power of neuroplasticity has the potential to take a patient of brain injury or stroke a long way toward recovery.

Sandra J. Ackerman is a science writer based in Durham, N.C.

Neuroscientist Couples Engage Hearts, Minds

BY ANN MACDONALD

Sally and Bennett Shaywitz, co-directors of the Yale Center for the Study of Learning and Attention, are internationally recognized for their work on the brain, particularly for their research on dyslexia. But a nametag, not research, initially brought the two together.

Sally was a medical student at the Albert Einstein College of Medicine, where Bennett was just starting his medical training in pediatrics. The medical school hosted a party for new residents, and Sally dropped by.

"I saw a man wearing a nametag with an unusual last name," Sally recalls. "I walked over and said, 'How do you pronounce that name?' Little did I know that it was soon going to be mine."

They married two months later. "I've always believed that you should do what your heart tells you," says Sally. "Don't analyze it to death." There may be something to that philosophy: Recently the couple celebrated their 40th anniversary.

Likes Attract

While no official statistics exist about the number of neuroscientist couples, the editors of *BrainWork* easily identified about 15 of them. This seems to confirm a report this summer in the *Proceedings of the National Academy of Sciences*, which found that likes—not opposites—attract: People seek partners similar to themselves.

Gerhard Sonnert, a Harvard sociologist of science, stumbled onto the phenomenon of scientist couples with his colleague Gerald Holton. The two set out to compare male and female career trajectories; their findings were published in *Who Succeeds in Science: The Gender Dimension*. Sonnert and Holton interviewed hundreds of scientists. One area they investigated was the impact of marriage and family on career. They were surprised to find that many scientists in the study—especially women—were married to other scientists.

"Over 62 percent of the married women scientists had a spouse with a doctorate, but fewer than 20 percent of the men did," Sonnert says. "It's not that the men were marrying down, but that there were fewer women scientists to begin with."

From left, Dr. Bennett A. Shaywitz, Dr. Adam J. Shaywitz, Dr. David A. Shaywitz, Dr. Jonathan E. Shaywitz and Dr. Sally E. Shaywitz pose at Adam Shaywitz's graduation from Harvard Medical School in 2002. Two of the three sons have done advanced study in neuroscience.

Another surprise was that most scientist couples were happy with their choices. "We thought they would come up with negative things, like being held back professionally or having an added strain on the marriage," Sonnert says. The chief downside reported was the challenge of trying to find a job in the same geographic location. Mainly the response was positive. "People we talked to said there is a level of understanding and support that you get from a scientist-spouse that you wouldn't get from someone else," Sonnert says. "Another scientist understands the demanding work schedule and can function as a sounding board for ideas."

Converging Interests

Certainly that has been the case for Sally and Bennett Shaywitz. Although the two started out on parallel tracks (he was interested in consciousness and attention, while she focused on learning disabilities), their work has increasingly converged over the years. Recently they have collaborated extensively on the cause and treatment of dyslexia—research that is summarized in Sally's most recent book, *Overcoming Dyslexia*. "We feel lucky that we can share so much in common and can understand the issues and the questions we're dealing with, and really be supportive," Sally says.

Ellen Frank and David Kupfer, both at the University of Pittsburgh School of Medicine, echo this sentiment. The couple, who will celebrate their 30th anniversary next year, have long shared an interest in the cause and treatment of mood disorders. They have received international recognition—individually and jointly—for their contributions to neuroscience.

"One of the nice things is that we come at a problem from different perspectives," Kupfer says. "Ellen brings a psychotherapeutic approach, while I think more in terms of biology. So it's a nice fit."

Two heads are also better than one.

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NEUROSCIENTISTS IN THE FAMILY

Also among the 15 or so neuroscientist couples *BrainWork* identified are:

Carol Barbour and Sid Gilman
J. Richard Baringer and Jeanette Townsend
Joshua Bederson and Isabelle M. Germano
Floyd Bloom and Jody Corey-Bloom
Xandra O. Breakefield and David P. Corey
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the duration of treatment was quite short, the researchers believe the antidepressants may work on the brain directly during the crucial post-stroke period. "Antidepressants may protect the brain to produce long-lasting changes in the networks involved in the stress response," says study author Robert Robinson of the University of Iowa. "In addition, because 40 percent of stroke patients develop depressive disorder, even those who are not depressed initially, short-term antidepressant treatment might be a good idea for all stroke survivors."

•••Mapping the brain's "map" cells. Besides its essential role in memory, the hippocampus is a brain area that conveys our sense of space and place. Studies in animals suggest that hippocampal neurons are "dedicated" to remembering where things are. But though imaging studies of the human hippocampus show that this area is active in spatial tasks, it also seems to play a role in visual recognition.

In the September 11 issue of *Nature*, a team of researchers separated the functions of navigation versus image recognition. Working with a group of epilepsy patients who were undergoing "invasive monitoring" with intracranial electrodes in preparation for surgery, Michael Kahana of Brandeis University, Itzhak Fried of the University of California at Los Angeles, and colleagues asked the subjects to act as virtual taxi drivers. The mission: to pick up passengers on a computer screen and deliver them to selected shops in a virtual town.

The researchers, recording from electrodes already in place, tracked the firing rates of neurons in the hippocampus and surrounding areas. A substantial number of neurons in the hippocampus fired only in response to being in particular locations, regardless of what the subjects were looking at. Neurons in an adjacent area, the parahippocampal region, "recognized" images such as shopfronts. Unexpectedly, a few neurons throughout the brain proved even more specialized—some firing only when the subject was searching for a particular shop and some only when the subject looked at the sought-for shop. "To see the cellular responses that allow us to navigate is very exciting," Kahana says.

••• How HIV infects the brain. Besides crippling the immune system, the human immunodeficiency virus (HIV) also attacks the brain; more than 20 percent of AIDS patients suffer from dementia. Just how the virus damages the brain is a puzzle. Instead of infecting neurons directly, HIV touches off a cascade that somehow turns the brain's own defenses toxic.

In a report published online on September 21 by *Nature Neuroscience*, Christopher Power and colleagues at the University of Calgary and the University of British Columbia reveal a novel pathway through which HIV may wreak its havoc. Studies show that after infection with the virus, immune cells called macrophages and microglia release key enzymes, matrix metalloproteinases (MMPs). These "cleave" their target molecule, cutting through its DNA at a precise location. In the brains of mice, research indicated brain damage caused when HIV prompts the MMPs to cleave a chemokine, or signal used by immune cells. However, pretreating the mice with antibodies that neutralized the chemokine—or with Prinomastat, a drug that inhibits MMPs—prevented the damage.

"These findings point to a novel mechanism of cell death," Power says. Prinomastat and other MMP inhibitors are already in phase 3 clinical trials for the treatment of cancer because malignant cells produce MMPs to help them invade surrounding tissue. Such drugs may also be tested for AIDS dementia and diseases involving neuronal death, such as Alzheimer's and Parkinson's disease.

••• Prompt intervention in MS is both doable and crucial. Multiple sclerosis (MS) strikes in young adulthood and often follows an unpredictable course. Early signs, such as dizziness and fatigue, do not always lead to the motor, visual, and cognitive disabilities that characterize the disorder. But reports this fall point to the possibility of early diagnosis and the value of early treatment.

In the September 9 *Neurology*, Elliot Frohman and colleagues at the University of Texas Southwestern Medical School, Dallas, released a set of diagnosis guidelines based on their survey of all available scientific studies. Their conclusion: In many cases, a single MRI of the brain and spinal cord can predict whether someone will develop the disease. MS results when the immune system mistakenly attacks the nervous system, producing visible damage, called lesions. The new guidelines note that a patient with three or more lesions in specific areas has a more than 80 percent chance of developing MS within the next seven to ten years—allowing for quick intervention.

Meanwhile, findings presented at the September 17 meeting of the European Committee for Treatment and Research in MS (ECTRIMS) show that treatment with the drug Avonex within a month after onset of symptoms delays new symptoms by more than two years. The study followed 203 patients, half of whom received Avonex immediately after showing initial symptoms and half who began treatment after the second attack. Thirty-five percent fewer patients in the first group went on to develop clinically distinct MS, and promptly treated patients had a 43 percent reduction in the number of relapses. Even more promising, patients who began treatment immediately were more likely to be symptom-free four to five years after the first symptoms—suggesting that "immediate, early intervention may prevent the development of disability over five years," according to R. Philip Kinkel at Beth Israel Deaconess Medical Center, Boston.

"News" is written by Elizabeth Norton Lasley, a freelance science writer in Woodbury, Conn.

(PAIN, continued from page 4)

Institute of Health Sciences in Tokyo, and colleagues reported that a receptor called P2X4, found in spinal cord glia, is critical for pain. Two separate strategies—blocking the receptor with drugs and reducing the number of receptors—reduced allodynic pain in experimental models of neuropathic pain.

Even if glia are found to play a critical role in neuropathic pain, the challenge of delivering drugs safely into the spinal cord remains. "Despite being in the CNS, glia could still be an attractive target for really intractable pain, such as late-stage cancer pain or pain syndromes that last for an entire lifetime," says David Julius.

Genomic research will soon present many more candidate molecules for roles in neuropathic pain. Researchers welcome this added complexity because it represents opportunities to design specific therapies for different patients with unique pain problems.

Hakon Heimer is a science and medical writer in Providence, R.I.

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"We sometimes jumpstart each other's thinking process," Kupfer says. "We come up with something together that we wouldn't have come up with individually."

Challenges and Inspiration

There can be challenges, however. "Because we work together, people sometimes assume that one always knows what the other does," Sally Shaywitz says. "Someone will tell me something that I didn't know, and the person will say, 'But I told your husband.' I have to explain that we don't debrief each other."

When the offspring of a neuroscientist elect to pursue a career in the field, more vexing problems can arise. One young neuroscientist contacted for this article, whose father is a well-known neuroscientist, declined to be interviewed because she is just getting started in her career. In an e-mail message, she explained that she wants the focus to be on her own research, not on her family connections.

Frank experienced an especially painful event when she applied for tenure. The academic promotion committee asked that she detail the nature of her independent contributions to each of the 75 papers she co-authored with her husband.

Frank won tenure, but the incident still rankles. Yet she is inspired by the example set by her aunt and uncle, who are both accomplished photographers. "What I learned from them is how wonderful marriage can be when two people are passionate about the same profession."

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

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