THE DANA FOUNDATION'S

BRAINWORK

The Neuroscience Newsletter

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News FROM THE FRONTIER

••• Vicious cycle between stress and aggression. The father of psychology, William James, suggested that emotions don't exist as separate entities; the feelings of racing pulse and fast breathing can be described as love or fear, depending on whether you've glimpsed a lover or a burglar. In studying aggression, researchers have had the same difficulty separating the "symptoms" from the context.

Now a report in the October issue of *Behavioral Neuroscience* shows that, in rats at least, aggression is an intrinsic mechanism and not merely the animal's response to being in a fight. The researchers put each test rat in a cage with an opponent rat and stimulated electrodes implanted in an area of the hypothalamus known to be involved in aggression. Blood tests before and after stimulation showed a sharp rise in two hormones central to the fight-or-flight response: adrenocorticotropic hormone and corticosterone.

Next the researchers stimulated the rats' brains without a challenger rat present—and found virtually identical activation of stress hormones even though

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The Hidden Cost of War:

PTSD and the Combat Veteran

BY BRENDA PATOINE

While the nation debates the war in Iraq in terms of lives, dollars, methods, and purposes, another problem lies largely between the lines of the news reports filed from the battleground: the psychological costs of combat on the men and women of the armed forces.

It's no secret that war traumatizes many of its warriors. References to symptoms that we might now categorize as anxiety or mood disorders go back nearly as far as written history: Homer is said to have described them among Trojan War protagonists in *The Iliad*. In more recent years, they have been given monikers such as shell shock, combat fatigue, soldier's heart, or post-Vietnam syndrome.

The first rigorous studies of post-combat psychiatric disorders, conducted in Vietnam veterans 10 to 20 years after active duty, found that a quarter of women and 30 percent of men had suffered from post-traumatic stress disorder (PTSD) at some point in their lives. Later studies of soldiers returning from the Gulf War and Somalia reported prevalence rates from 8 to 16 percent.

A report in the July *New England Journal of Medicine* is the latest to examine mental health in combat veterans, and the first to do so while the battle still rages. Charles R. Hoge, M.D., and colleagues at the Walter Reed Army Institute of Research found that 18 percent of Army recruits and 20 percent of Marines, who were interviewed anonymously three to four months after their return from combat duty in Iraq, met the current diagnostic criteria for post-traumatic stress disorder. When major depression and generalized anxiety disorder were included, the proportion of Army soldiers and Marines affected rose to just under 30 percent. The rates among Afghanistan war veterans were somewhat lower

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In the past decade, researchers started using brain-imaging studies to examine what happens in the brains of people with post-traumatic stress disorder, both combat veterans and survivors of other trauma.

(PTSD, continued from page 1)

(11.5 percent overall), consistent with lower rates of combat experiences.

(The prevalence of PTSD among the general population is between 3 and 4 percent, and clinically diagnosable PTSD has affected about 10 percent of the population at some point in their lives.)

Because the onset of PTSD may occur many years after trauma, it is unlikely that these early findings capture the full extent of the problem. The study's co-author, Lt. Col. Carl A. Castro, Ph.D., the acting chair of psychiatry and behavioral sciences at Walter Reed, suggests that the results were not extraordinary. "There really was no surprising or shocking finding," he says. "The value of our study is that we put numbers on things that we thought we already knew." These benchmark statistics will enable researchers to evaluate the effectiveness of prevention and early-intervention programs.

BRAINWORK

The Neuroscience Newsletter

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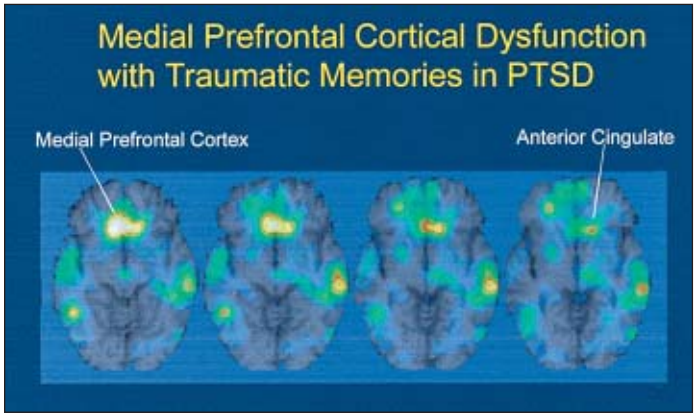
Such programs aim to quell PTSD symptoms before they become chronic, which can make treatment far more difficult, and avert a future mental health crisis among veterans. In addition to symptoms ranging from nightmares and flashbacks to relationship problems and "hyperarousal" that may cause explosive irritability, researchers have linked PTSD to a significantly increased risk of "suicidality," which includes suicidal thoughts and attempts as well as completed suicides. When PTSD co-occurs with other depression, substance abuse, or other psychiatric conditions—as it often does in veterans—the suicide risk increases (see sidebar, next page).



These PET scans show brain activation patterns in combat veterans with PTSD during exposure to combat-related slides and sounds. There is decreased function in regions of the medial prefrontal cortex, including the anterior cingulate.

Is Combat PTSD Different?

Is there something about the war experience that makes combat-related PTSD unique? The answer is controversial, says Matthew J. Friedman, M.D., Ph.D., executive director of the Department of Veterans Affairs' National Center for PTSD, who wrote an editorial accompanying the *NEJM* report. "There are reasons to think that it might be [different], particularly because a combatant, as compared to a rape or a 9/11 victim, is also participating in perpetrating violence," says Friedman.

More than 90 percent of the Iraq war veterans in the study said they had been shot at, attacked, or ambushed, or had seen dead bodies or human remains. Nearly as many had shot and/or killed an enemy combatant (see chart, next page, for more statistics).

Brain-imaging studies have found similar brain changes whether PTSD was triggered by combat, childhood abuse, or sexual assault. "In terms of the neurobiology, we don't really see any differences," says J. Douglas Bremner, Ph.D., an Emory University mental health researcher who was among the first to examine what PTSD looks like in the brain.

"I think the jury is still out, but I have to say that right now the preponderance of evidence would suggest that once you cross that threshold into PTSD, [how you crossed it] is not as important as the fact that you crossed it," says Friedman. "Until proven otherwise, PTSD is PTSD."

Tracing PTSD Circuitry

Despite its existence probably since warriors first battled, PTSD has been recognized as a brain-based disorder only in the past decade. Scientists are now trying to understand what turns a traumatically stressful event into a psychiatric illness that may become chronic.

Beginning in the mid 1990s, brain-imaging studies were employed to trace the neural circuitry underlying PTSD in combat veterans as well as survivors of other trauma. A landmark study led by Bremner, then at the VA's National Center for PTSD, used magnetic resonance imaging (MRI) to look for differences in the volume of the hippocampus. Animal research has shown that the hippocampus could be damaged by stress hormones released during the "fear response," a primal reaction to imminent danger that originates in the neighboring amygdala.

Through its connections to other brain areas, the amygdala sets off a series of physiological changes, all of which evolved to help us survive threats in our environment (think saber-toothed tigers). The hippocam-

VETERANS' EXPERIENCES

Anonymous interviews with Army and Marine veterans of the Iraq war revealed that vast majorities had the following experiences.

	Army veterans	Marine veterans
Was attacked or ambushed	89 percent	95 percent
Was shot at	93 percent	97 percent
Saw dead bodies or human remains	95 percent	94 percent
Knew someone who was killed or seriously hurt	86 percent	87 percent
Shot or directed fire at the enemy	77 percent	87 percent
Saw injured women or children whom they were unable to help	69 percent	83 percent

Source: *New England Journal of Medicine*

pus, best known for its role in learning and memory, is believed also to be involved in turning off the fear response.

True to his hypothesis, Bremner found smaller hippocampal volume in veterans with PTSD, then replicated the finding in adult survivors of childhood abuse. Many studies later, a picture has emerged of a PTSD neural circuitry involving the amygdala, hippocampus, and the higher-thinking medial prefrontal cortex.

The most consistent finding from about 15 published imaging studies, Bremner says, is decreased function in the medial prefrontal cortex and anterior cingulate. These adjacent areas in the middle of the brain's frontal lobe are essential to "putting the brakes on the fear response," he says. "We can see that the higher brain areas are not kicking in to turn off the more primitive brain areas like the amygdala, so the amygdala seems to be over-responsive." With no brakes, the stress response floods the system with potent hormones and sets off a damaging cascade that feeds back on itself.

Any persistent saturation with stress hormones, whether from chronic stress in the environment or from an internally generated memory, takes a toll on the brain. High levels of glucocorticoids, for example, are known to damage the hippocampus. Too much norepinephrine can "take your brain off-line by causing frontal lobe dysfunction," Bremner says.

Stigma is Critical Barrier to Care

Two drugs (Paxil and Zoloft) are FDA-approved for PTSD, and two psychologic therapies (prolonged exposure therapy and cognitive processing therapy) are considered effective. The problem is to ensure that people who need treatment get it.

Fear of being stigmatized emerged as a major factor in whether veterans got the care they needed. Those who met the criteria for a mental disorder were twice as likely as others to report concerns about stigmatization. More than half cite harm to one's career, being seen as weak or untrustworthy, or being treated differently by leadership as barriers to seeking care. Those with the most severe symptoms were the least likely to take advantage of health services.

"The impact of stigma was in precisely the wrong direction," Friedman says. "The people who were most stigmatized were the ones who were most in need of treatment."

Friedman says the stigmatization a soldier fears is "on a continuum with what is happening in civilian culture," but can be uniquely problematic in a military culture, where someone with a psychiatric disorder "is perceived in some military circles as not having 'the right stuff.'"

The stigma of mental illness is "embedded into our larger culture," says Castro. "You don't change culture overnight; it's a long-term process. But one of the ways we think we can begin addressing this is by, number one, talking about it in an open forum. You can begin to destigmatize it by discussing it and trying to bring it to the forefront."

"If we can get these folks in, we've got a lot to offer in terms of treatment," says Friedman. "And hopefully, we can abort the career of chronicity that has happened to many of the Vietnam veterans, in whom PTSD is many decades old."

Brenda Patoine is a freelance science and medical writer based in LaGrangeville, N.Y.

VETERANS AND SUICIDE RISK

Whether the types of trauma combat veterans encounter makes them especially vulnerable to suicide is a question with no simple answer. "I don't think there's accurate data on it," says Charles Marmar, M.D., a psychiatrist at the University of California, San Francisco and mental health expert with the San Francisco VA Medical Center. "My gut feeling is that suicide rates in combat PTSD are probably more like the suicide rates in other forms of chronic PTSD affecting young people."

In combat, young, vulnerable people are subjected to multiple different kinds of trauma, he says, and it often involves "a background of constant danger punctuated by very extreme traumatic stress during actual combat incidents."

Another question is whether the nature of the war being fought influences PTSD or suicide risk among veterans. "Many wars are more similar than they are different in terms of the actual experience of combat," says Marmar. "What matters is how long you were under life threat, how repeatedly and how directly, and what you witnessed."

The geopolitical context of the war, and whether it is popular or unpopular, "may not have much to do with who develops acute PTSD, but it may have more to do with subsequent recovery," Marmar says. World War II was "the good war," he says, whereas Vietnam was very unpopular: "There is evidence from Vietnam that the negative homecoming adversely affected the recovery. Under unfavorable political conditions you have a greater rate of chronicity."

—B.P.

Mitochondria Play Life-and-Death Role

BY SCOTT P. EDWARDS

Consider the mitochondria. Found throughout the body, these organelles are considered cellular "power plants" because their primary purpose is to manufacture adenosine triphosphate (ATP), an energy source for many life processes. In the central nervous system, mitochondria provide energy for synaptic firing.

Mitochondria, which are usually rod-shaped but can be round, depending on the cell type, also play a critical role in apoptosis, or programmed cell death, and in cell proliferation. Thus, as Duke geneticist Margaret Pericak-Vance says, "Mitochondria are involved in the life and the death of a cell."

In the process of producing energy, mitochondria also make oxygen free radicals, a group of reactive atoms that can damage cells, proteins, and DNA by altering their chemical structure. Mitochondria, says Giovanni Manfredi of Cornell University's Weill Medical College, come equipped with a "scavenger" system that blocks the proliferation of these damaging free radicals.

A certain percentage of free radicals, however, escape this scavenging system and can damage DNA, proteins, and neurons. When neurons in a normal, healthy brain are affected by free radicals, mitochondria program cells to die. But this protective mechanism can fail, leading to neurodegeneration—the death of neural cells—which can cause a variety of diseases.

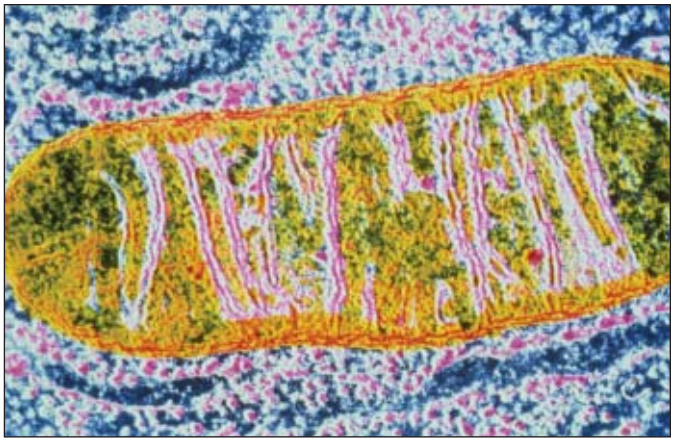
"Neurons require a lot of energy," says Manfredi. "Because they are so long-lived, neurons are subjected to cumulative damage from free radicals."

Mitochondria also regenerate, says Pericak-Vance, to make more mitochondrial DNA (mtDNA), the DNA that is located within the mitochondria itself rather than in a cell's nucleus. If there are problems with this replication, direct oxygen species (free radicals) from normal cellular respiration attack the DNA and cause it to mutate.

"This mutation happens all the time," Pericak-Vance says. "But, cells can't handle too many mutated genes. These mutated genes cause low energy production, cell death and disease." The brain, she adds, has a low threshold in terms of how much mutated mtDNA its cells can effectively manage before they begin to die off.

Mitochondria and Neurodegenerative Diseases

Mitochondrial dysfunction and mutations in mtDNA have been implicated in a number of neurodegenerative diseases, including Alzheimer's, Parkinson's, and Huntington's diseases and amyotrophic lateral sclerosis (ALS).



Mitochondria such as this one drive cellular chemical reactions. In the central nervous system they provide the energy behind synaptic firing; their dysfunction may play a role in diseases.

Researchers have found mitochondrial defects in the neurons of Parkinson's patients. The accumulation of oxygen free radicals is also thought to contribute to the disease, which may explain why disease risk increases with age (giving free radicals more time to accumulate and cause damage) and why there appears to be no hereditary cause.

Several studies have suggested that mitochondrial metabolism disturbances and mtDNA abnormalities may contribute to the progression of Alzheimer's disease (AD) pathology. Other studies have found that AD brains show a high rate of oxygen consumption and oxidative stress, as well as altered antioxidant defenses, suggesting that free radical proliferation may play a role in the pathogenesis of the disease as well.

In addition, mitochondrial scavengers are found less frequently in AD brains, and the ones that are present cannot handle the large amount of free radicals that have escaped, says Joelle van der Walt of the Duke Center for Human Genetics.

Research published in the July 20 *Proceedings of the National Academy of Sciences* by Pinar Coskun, M. Flint Beal, and colleagues suggests that a significant factor in the development of late-stage, sporadic Alzheimer's may be the accumulation of mutations in somatic mtDNA control regions of the brain caused by free radical damage. Once they arise, these mutations become enriched in postmitotic brain cells, resulting in mitochondrial respiratory deficiency, increased free radical production, and loss of synaptic connections through apoptosis.

Manfredi focuses much of his work on ALS, specifically mutations in SOD1, an abundant protein in the brain and central nervous system. ALS involves the loss of motor neurons, and Manfredi says that about 20 percent of cases are caused by an SOD1 mutation.

"SOD1 scavenges free radicals," Manfredi says. "However, when it mutates, the protein acquires a new toxic function, which causes the neuronal degeneration common to ALS."

Finally, a defect in energy metabolism is thought to be a potential pathogenic mechanism of Hungtington's disease (HD), in which neural degeneration leads to uncontrolled movements. Mutant huntingtin, the protein that is known to be defective in HD, is believed to cause mitochondrial dysfunction because it blocks the activity of critical transcription factors that are involved in mitochondrial energy metabolism and mitochondrion-initiated apoptosis.

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No Effective Therapy

Manfredi says there is "no miracle therapy" to treat mitochondrial dysfunction. There are models that address the use of antioxidants to rid nonfunctioning mitochondria of free radicals, but the results have yet to yield effective therapies for humans. Van der Walt says clinical trials are under way to examine the effects of common antioxidants, such as vitamin E and beta-carotene, on neurodegenerative diseases.

Researchers at Harvard Medical School recently showed that neurotoxins commonly associated with Parkinson's disease (malonate, 3-NP, and MTPT) caused significantly less damage to the brain cells of animals treated with coenzyme Q10, a potent free radical scavenger. In his laboratory at Cornell, Manfredi is studying mitochondrial dysfunction in cellular models of Huntington's disease and developing therapeutic approaches that target the expression of mutant huntingtin. A breakthrough, however, has been elusive.

"Most of the models of mitochondrial dysfunction and the strategies to treat it are not very encouraging," Manfredi says.

The Chicken or the Egg

There is strong evidence that mitochondrial dysfunction plays a critical role in the pathogenesis of neurodegenerative diseases. However, there are different schools of thought as to why and when this dysfunction occurs.

"What makes this whole issue controversial is the chicken-or-the-egg question: which came first?" Manfredi says. "Most of these neurodegenerative diseases are chronic and often caught at an advanced stage. At that point, it's hard to tell if the mitochondrial dysfunction came prior to the onset of the disease or if it started later in the disease progression."

For most of the "big" disorders with no genetic foundation, he says, mitochondrial dysfunction may be a cause, but almost certainly not the only one.

Scott P. Edwards is a freelance medical writer based in Holliston, Mass.

Influenza and the Vulnerable Brain:

Untangling the Complex Causes of Schizophrenia

BY HAKON HEIMER

Genes are the biggest influence on the risk of developing schizophrenia. This has been made most clear by studies of twins, which have shown that the chances of developing the devastating psychiatric disorder are almost 50 percent if a twin's identical sibling has the disorder (compared to 1 percent for the general population). But the 50 percent of identical twins who do not fall victim to their siblings' disease indicates that something in the environment needs to interact with vulnerable genes.

"Environment," in this case, begins as soon as the fertilized egg begins to divide. Epidemiological studies have linked various early environmental factors to increased risk of schizophrenia. "The two pre- or perinatal risk factors that have the most compelling epidemiological support are obstetric complications that lead to decreased oxygen to the baby and prenatal exposure to viruses, notably influenza and rubella," says Matcheri S. Keshavan of the Western Psychiatric Institute and Clinic and the University of Pittsburgh School of Medicine.

The influenza link was first shown in a study in Finland. Researchers found that children born after a 1957 influenza epidemic—most of whom were in the womb at the time many of their mothers were exposed to the flu virus—had a higher risk of developing schizophrenia. Some, but not all, subsequent studies have also found this to be true.

Blood Reveals Who Got Flu

An epidemiological study published in the August 2004 issue of the *Archives of General Psychiatry* overcomes some of the limitations of the earlier studies, especially uncertainty about which women were actually exposed to flu as opposed to merely being pregnant during a flu season. The research team, led by Alan S. Brown and Ezra S. Susser of Columbia University, was able to positively identify which mothers in their study had been exposed to influenza because they had access to blood samples taken from the women during pregnancy.

The samples came from women who participated in the Child Health and Development Study, conducted between 1959 and 1966 in Alameda County, California. Brown and colleagues found that the risk of developing schizophrenia was tripled among offspring whose mother had contracted a flu virus during the first half of pregnancy. There was no increased risk when mothers contracted flu during the second half of pregnancy.

"Although we can't rule out a direct effect of influenza virus on the fetus, we think it is more likely related to the maternal immune response to the infection," Brown says. "This includes the release of maternal antibodies or cytokines, which cross the placenta and could damage the fetal brain in a way that increases the vulnerability to schizophrenia."

Antibodies and cytokines are molecules employed by the immune system to identify and fight off foreign molecules, including viruses. Animal research has shown that elevated levels of maternal cytokines can damage the fetal brain, and an earlier study by the Columbia researchers had found evidence of elevated interleukin-8, a

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"Even a single pathway such as the flu can teach us a lot about how schizophrenia might be caused."

(INFLUENZA, continued from page 5)
cytokine that signals an inflammatory response to infection, among pregnant mothers whose children went on develop schizophrenia.

Brown and his colleagues note, however, that other factors associated with influenza in the mother—including fever, reduced oxygen in the blood, and even over-the-counter flu medicines—could also have a negative impact on fetal development.

Although the study would seem to support current recommendations that pregnant women should have flu shots, Brown has a word of caution: "If maternal antibodies turned out to be the factor that increased risk of schizophrenia, you may not want to cause a spike in antibodies during pregnancy, which you do when you give a flu vaccine."

Different Schizophrenia Paths

Researchers are quick to point out that genetic heritage is still the major risk factor for schizophrenia.

"That being said, even a single pathway such as the flu can teach us a lot about how schizophrenia might be caused," says Dolores Malaspina, also of Columbia. She notes that further research in animal models can indicate how influenza damages fetal brain development, which may, in turn, identify other physiological factors for epidemiologists to examine.

Research into environmental risk factors could thus help answer a fundamental question about schizophrenia: How many diseases is it really? Scientists agree that schizophrenia is no more than a catch-all category of disorders whose characteristic symptoms may include hallucinations, confused thought, and social withdrawal. People with schizophrenia also vary in responses to treatment, degree of cognitive impairment, and family history.

Malaspina believes that different minor risk factors may contribute to specific sets of symptoms. "I'm not suggesting there is one different type of schizophrenia for each different risk factor. Instead, there may be some final common pathways," she says.

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

Stem Cells as Information Databases

BY RABIYA S. TUMA

In August 2001, President Bush declared that federal funds could be used to research only those human embryonic stem cell lines that were already in existence. That restriction has slowed stem cell research, according to experts, but has not halted progress.

New, privately funded lines of embryonic stem cells continue to enter the public domain. Information from their study may help researchers develop therapies to repair, for example, damaged neurons or their surrounding tissue.

In the past year alone, about 100 newly derived embryonic stem cell lines have been developed with private money and placed in the public domain, says Leonard Zon, a Howard Hughes Medical Institute (HHMI) investigator and professor of pediatrics at Harvard Medical School in Boston.

Seventeen of the lines were developed by Zon's Harvard and HHMI colleague Doug Melton with funding from HHMI. Additionally, researchers in Chicago, Sweden, South Korea, and Singapore have created stem cell lines from embryos from in vitro fertilization clinics, left over after patients decided their families were complete.

The new lines improve access and diversity, says Zon, who is also president of the International Society for Stem Cell Research. But as yet no central storage bank exists to hold and register them all. Furthermore, U.S. researchers are still prevented from using federal grant monies to support research on these lines in any way.

To enable their scientists to work with the non-federally-approved lines, several research institutes, including Harvard University and the Salk Institute in La Jolla, Calif., have set up completely separate facilities. Money for these facilities has to come from private fundraising or foundations, and that supply is limited.

Fred Gage, professor of genetics at Salk, and his team use embryonic stem cells to study the early decisions a cell makes on its way to becoming a neuron. When they compare their findings to similar work from animal models, they find that, despite similarities, although many of the decision points are similar, the pathway in humans is not an exact replica of the mouse pathway. "It's important to keep up the work on human cells," Gage says.

Much of the publicity in the stem cell field has focused on using stem cells derived from either embryos or adult tissue as a source of transplant material to treat a variety of diseases. Gage says a more likely scenario is that researchers will use these stem cells to understand more about the life history and needs of a particular cell or tissue, and use that information to develop therapies to help damaged neurons, for example, or surrounding tissue repair themselves.

Ron McKay of the National Institute of Neurological Disorders and Stroke in Bethesda, Md., seconds that point. His team works on Parkinson's disease, a disorder in which the dopaminergic neurons are lost specifically from the substantia nigra, a region of the brain responsible for motor control.

The researchers are able to induce adult neural stem cells to divide in culture dishes and produce a large number

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News
FROM THE FRONTIER

(Continued from page 1)

no fight was going on. A vicious cycle appeared when the scientists experimentally raised levels of stress hormones; this activated the "fight center," decreasing the amount of electrical stimulation needed to provoke attack behavior.

The authors suggest that therapies to reduce the hair-trigger stress hormones often found with aggression "may be a novel approach to understand and control violent behavior."

••• **Blindness leads to more acute hearing.** Studying the ways in which blind individuals take advantage of sound cues, many scientists have focused on sounds that occur within arm's reach, allowing the person to validate impressions through touch.

In a study published in the October 5 issue of *Current Biology*, researchers at the University of Montreal examined whether the blind are equally adept at localizing sound farther away. The investigators worked with three groups: those who had been blind since before the age of 11, those whose blindness occurred after the age of about 16, and sighted subjects wearing blindfolds. Participants were asked to describe the locations of bursts of sound played through speakers.

When the sound was close to and directly in front of the subjects, all three groups performed equally well. When the sound was farther away, however (a distance of about 4 yards), both groups of blind individuals performed significantly better than the blindfolded controls. The researchers surmise that significant skills of compensation are possible even when blindness comes later in life.

Blind individuals can "invest significant neural and cognitive resources to develop strategies to cope with their handicap," the authors conclude.

••• **Custom-designed therapy "switches off" brain tumors**. A new therapy shows striking success against medulloblastoma, virtually eradicating the tumor and greatly prolonging survival.

Medulloblastoma occurs in children 10 and under; although 45 to 65 percent of patients survive, the treatments—surgery, chemotherapy, and radiation—have serious side effects. Previous research showed that a molecular pathway beginning with a protein dubbed Sonic Hedgehog (Shh) is crucial to the tumor's development and that a small molecule known as Hh-antag could switch off this pathway.

In the September 2004 issue of *Cancer Cell*, researchers from St. Jude Children's Research Hospital in Memphis gave Hh-antag to mice bred to carry both the tumor and the Shh "fingerprint." The treatment disrupted the tumor-causing chain of events.

"The treatment interrupts the specific molecular pathway that causes this type of cancer, so healthy brain tissue isn't damaged," says study author Tom Curran. "We believe that such precise interventions could spare children from the devastating effects of surgery, chemotherapy, and radiation."

••• **Counseling reduces stress and boosts immune system in cancer patients.** Regular psychological

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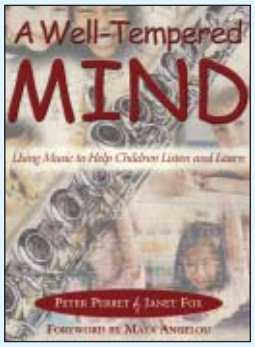

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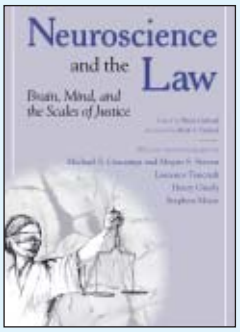

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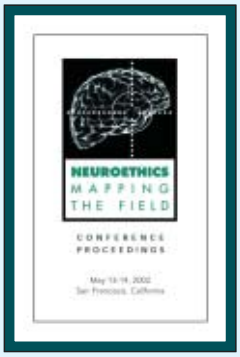

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(NEWS, continued from page 7)
counseling for breast cancer patients improves mood and quality of life in cancer patients, but whether these patients live longer is uncertain. Barbara Andersen and colleagues at the Ohio State University in Columbus have begun a long-term study to examine the survival question in breast-cancer patients. In an early report published in the September issue of the *Journal of Clinical Oncology*, the researchers found that, in support-group participants, some measures of immune system activity improved along with the patients' perceived quality of life.

Researchers assigned 227 women to one of two groups—one that received psychological intervention and one that received only an assessment. Researchers also took blood samples for immunity studies. "Intervention" patients met weekly to learn to reduce stress, improve support from friends and family, eat less fat and more fruits and vegetables, exercise regularly, and quit smoking. Not surprisingly, these patients showed more improvement on all fronts.

No difference was observed between groups in the number of immune cells measured in the blood. However, in the intervention group, key immune cells known as T-cells showed an improved ability to grow and divide when stimulated in a test tube.

"What the T-cell response means in terms of cancer progression isn't clear, but the effects tracked closely with psychological improvement," says study co-author William Carson, a molecular virologist at Ohio State.

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

Note to Readers: The expanded January-February issue of *BrainWork* will reach you later than regular issues to include complete coverage of the Oct. 23-27 Society for Neuroscience conference.

(STEM CELLS, continued from page 6)
of healthy, functional neurons. However, when they transplant these human neurons into rats, the dopaminergic neurons die at a much higher rate than other types of neurons.

This information may lead to new insight about why the dopaminergic neurons are so vulnerable in Parkinson's patients. McKay says a future treatment for Parkinson's disease is unlikely to involve transplantation of new neurons; rather, he thinks the knowledge researchers gain from studying neural stem cells, which naturally occur in the brains of adults, may enable them to find a way to activate these cells in patients to repair or replace the damaged neurons.

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