

INSIDE VIEW



ISSN # 1065-7320

Issue 10.1
Winter 2001

A QUARTERLY NEWSLETTER DEDICATED TO TRAUMATIC BRAIN INJURY ISSUES
PUBLISHED BY THE CENTRE FOR NEURO SKILLS

Blood to Brain: Converting Stem Cells to Neurons

For years, researchers studying stem cells have been intrigued by the possibility that these cells might be used to treat brain diseases. Recent studies have suggested that neural stem cells transplanted into the brain can migrate throughout the brain and develop into other types of cells. Now, two new studies show that bone marrow cells transplanted into mice can migrate into the brain and develop into cells that appear to be neurons. The studies suggest that bone marrow may be a readily available source of neural cells with potential for treating such neurological disorders as Parkinson's disease and traumatic brain injury.

While previous research has shown that bone marrow cells can develop into neuron-like cells in culture, the new studies are the first to show that this process can also happen in living animals. The two studies reached the same conclusion despite many differences in how the studies were performed. The results are reported in the December issue of *Science*.

"These are extraordinarily important studies, carefully done, with clear implications for brain disorders and for basic developmental biology," says Gerald D. Fischbach, M.D., director of the National Institute of Neurological Disorders and Stroke (NINDS).

In the first study, NINDS investigator Éva Mezey, M.D., Ph.D., and colleagues injected bone marrow cells from normal

male mice into newborn female mice that had no white blood cells of their own. Using marrow from male mice allowed the researchers to use the Y chromosomes in the transplanted cells as a marker to distinguish them from native cells. At different time intervals, the researchers examined cells from the brains of seven mice that had received the transplants and compared them to littermates that had not received the transplants. By 4 months after the transplants, they found a significant number of neuronal cells in several brain regions, including the cortex, the hypothalamus, and the striatum, that were descendants of the transplanted cells. This suggests that stem cells from elsewhere in the body can enter the brain and differentiate into neuronal cells, says Dr. Mezey.

In the second study, Helen Blau, Ph.D., and colleagues from Stanford University injected bone marrow from adult mice that express a marker called green fluorescent protein (GFP) into adult mice that had been irradiated to eliminate their bone marrow. They found that bone marrow-derived cells migrated into several regions of the brain, including the olfactory bulb, the cortex, the hippocampus, and the cerebellum. Some of the marrow-derived neuronal cells also grew long fibers and produced a protein that indicates cell activity. These results suggest that the marrow-derived neurons not only

entered the brain but also responded to their environment and began to function like the native ones.

These studies suggest that bone marrow, which is an easily available source of cells, could be used as a source of neurons to replace those damaged or lost in neurological disorders, the researchers say. It might also be possible to genetically engineer the cells in ways that would help them survive or work in beneficial ways. The fact that even bone marrow from adult mice generated neuronal cells shows an unexpected amount of flexibility in older cells and suggests that patients with brain disorders could be treated with their own cells, says Dr. Blau. Bone marrow cells taken from a patient's own body would not be rejected by the body's immune system.

Continued on next page

this issue

Converting Stem Cells to Neurons . . .	1
Creatine Protects Against TBI . . .	2
Pets Reduce Stress of Caregivers . . .	3
TBI and Alzheimer's Link	4
Brain Changes During Learning . . .	5
Public Awareness of TBI	5
Pacemaker Reduces Seizures	6
2001 Conference Schedule	7

Continued from previous page

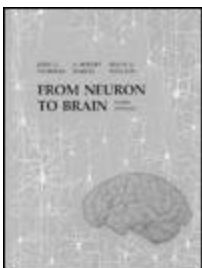
While the results are very promising, researchers need to answer many remaining questions before marrow-derived neural cell therapies can be tested in humans. A key question is what growth factors and other signals prompt the bone marrow cells to develop into specific types of neurons. If researchers can describe how the normal process of cell differentiation works, they may be able to reproduce it in patients with disorders such as brain injury or Parkinson's disease where neurons are not normally replaced. Researchers might also be able to discover factors that help cells enter the brain or connect with other cells. "We need much more data, but I think it's a pretty encouraging start," says Dr. Mezey.

Since the studies used whole bone marrow, it is important to determine which population of bone marrow cells develop into neurons, the researchers say. Other questions for future studies include whether marrow-derived neurons function like normal neurons and if they can make appropriate connections with other cells. The findings in Science should speed the pace of research to answer these and other important questions, the researchers say. However, they believe it will be several more years before the results reported in these studies will lead to effective therapies.

Related Literature

From Neuron to Brain

By John G. Nicholls



Amazon Rating
★★★★★

Hardcover
\$76.95

To order go to:

www.neuroskills.com/booksneuro.shtml

Creatine Protects Against Traumatic Brain Injury

Creatine, a food supplement frequently used by professional and amateur athletes, may prevent brain damage following traumatic brain injury, according to a new research study led by Stephen Scheff, Ph.D., professor, University of Kentucky Sanders-Brown Center on Aging and UK College of Medicine Department of Anatomy and Neurobiology.

Creatine is one of a class of molecules called amino acids. Creatine is produced naturally in the body in the liver, kidney and pancreas and is used as a way to store energy.

Many athletes now use creatine as a dietary supplement to increase muscle mass, strength, and the recovery time of muscles between bursts of activity. Each year about 7 million people in North America experience traumatic brain injuries (TBI) caused by motor vehicle accidents, falls, assaults and sports-related activities. Estimated costs to treat these injuries range from \$20 billion to \$48 billion each year.

According to the Centers for Disease Control and Prevention, about 300,000 TBIs occur each year due to sports or recreational activities. Athletes, especially those participating in sports that are likely to involve blows to the head such as football, hockey, wrestling, skiing, baseball and boxing, often experience TBIs. Most of these TBIs are concussions. These concussions can result in subdural hematomas (bleeding under a membrane surrounding the brain), loss of cognitive function or even death.

TBI causes both primary and secondary damage. The primary damage occurs at the time of injury as a result of the trauma. Secondary damage

Continued on next page

Inside View

Publisher
CENTRE FOR NEURO SKILLS

Executive Editor and Design
Craig S. Persel

Managing Editor
Mary E. Slater

Publications Office
17120 Advantage Pointe
Bakersfield, California 93306
661.873.0313 (phone/fax)
insideview@neuroskills.com

Subscriptions
\$12 annual US & Canada
\$24 annual foreign
Call 1-800-922-4994

CENTRE FOR NEURO SKILLS

President
Mark J. Ashley

CNS - Bakersfield
2658 Mt. Vernon Avenue
Bakersfield, California 93306
661.872.3408 or 800.922.4994
661.872.5150 (fax)
bakersfield@neuroskills.com

CNS - Los Angeles
16542 Ventura Blvd. Suite 500
Encino, California 91436
818.783.3800 or 800-992-6752
818.783.8412 (fax)
losangeles@neuroskills.com

Admissions Department
Stacy Persel
Britt Squires
Cherryl Bider Small

CNS - Texas
3501 N. McArthur Boulevard
Building 200
Irving, Texas 75062
972.580.8500 or 800.554.5448
972.255.3162 (fax)
texas@neuroskills.com

Admissions Department
Rocky Brogden
Mitzi King

World Wide Web
www.neuroskills.com

Continued from previous page

develops following the injury and can occur as long as days after the initial trauma.

The cause of the secondary injury is not well understood, but appears to be associated with disruption of the regulation of calcium levels in brain cells following injury. Regulation of calcium levels is crucial to mitochondrial function and to proper adenosine triphosphate (ATP) synthesis and use. ATP is a molecule that is present in all living cells and operates as the energy source for the majority of the chemical reactions which take place in cells.

Scheff's research team demonstrated that brain damage in mice was reduced 21 percent and 36 percent when creatine was administered three and five days before the TBI respectively.

The data also show that in rats fed a diet supplemented with creatine for four weeks before TBI, brain damage was reduced 50 percent when compared to rats fed a regular diet.

"Our data show that creatine supplementation protects against secondary damage associated with TBI by inhibiting the calcium-induced activation of a protein in the mitochondrial membrane, which preserves proper function of the mitochondria. The damage also is reduced because creatine acts to maintain appropriate amounts of ATP in brain cells," Scheff said.

"This strongly suggests that athletes may be gaining a neuroprotective benefit inadvertently by chronically supplementing their diet with creatine," Scheff said.

Pet Dog Reduces Stress of Those Caring for a Brain-Injured Spouse

The latest findings on the ability of pet dogs to reduce cardiovascular stress in persons living high-stress lives -- in this case those caring for brain-injured spouses -- shows that dog owners experienced one-fifth the rise in blood pressure during stressful, care-giving activities compared to those without dogs.

Moreover, when participants without dogs acquired them six months into the study, their average blood pressure and heart rate during stress-producing situations dropped to match that of the initial group.

Karen Allen, Ph.D., research scientist in the University at Buffalo's Division of Clinical Pharmacology in the UB School of Medicine and Biomedical Sciences, conducted this and several earlier studies on the effects of owning a pet dog on cardiovascular reactivity. She presented results of her current research today (Oct. 19) at the annual meeting of the Society for Psychophysiological Research in San Diego.

"This study shows how the presence of a pet dog can diminish stress responses to real-life daily stress over which caregivers have no control," Allen stated. "It demonstrates a therapeutic role for pet dogs, especially for individuals with hypertension who live under conditions of great responsibility and stress."

Allen conducted the study over one year. It involved 60 volunteers, equally divided between men and women, who were assigned randomly to either an experimental or control group. All were caring for spouses with traumatic brain injury and were taking ACE inhibitors to control hypertension. ACE inhibitors have been shown to control blood pressure during normal daily activities, Allen noted, but not to be effective in holding down pressure during stressful situations. All participants also had to be willing to acquire a dog.

At the beginning of the study, all participants wore blood-pressure monitors for 48 hours and kept diaries of their activities. Data on blood pressure and heart rate were captured during the first day when participants were caring for their spouses. These data were labeled natural stressors. On the second day, cardiovascular readings were taken while participants performed two activities used by researchers to simulate stressful situations - giving a speech, in this case on the problems of caring for a disabled spouse, and immersing one hand in ice water for two minutes (cold pressor test).

The experimental group then adopted dogs, and cardiovascular readings were taken from all participants again at six months under the same conditions. At this

point, the control group also adopted dogs, and readings were repeated once again after six months.

Results showed that before dogs entered the picture, all participants reacted similarly to natural and simulated stressful situations. "Interestingly, although the speech and cold pressor tasks elicited large increases in blood pressure and heart rate, natural spouse interaction produced even greater increases," Allen said. "Before pets, the speech task raised systolic blood pressure by 28 mmHg (millimeters of mercury), but spouse interaction raised systolic blood pressure by 52 mmHg."

After six months, those with dogs showed only a small rise in blood pressure when caring for their spouses, while blood pressure in the control group rose nearly 40 mmHg on average. After 12 months, when all participants had dogs, once again there was little difference between the groups, results showed.

"The findings of this study show that pets can help lower responses to everyday stress, even among individuals who take medication for their high blood pressure," Allen said. "Although medication reduces resting blood pressure, it appears a beloved pet influences how we react to stressful people and situations that we cannot change."

Serious Head Injuries Linked to Alzheimer's Disease

A new analysis of head injuries among World War II veterans links serious head injury in early adulthood with Alzheimer's disease (AD) in later life. The study, by researchers at Duke University and the National Institute on Aging (NIA), also suggests that the more severe the head injury, the greater the risk of developing AD.

For some time, scientists have been examining the association between head injury and AD. Studies in recent years have gone back and forth, some finding a relationship and others not. This new finding, by Brenda L. Plassman, Ph.D., of Duke University, Richard J. Havlik, M.D., M.P.H., of NIA, and colleagues is of great interest not only for its conclusions, but also for how the research was conducted.

By looking at documented evidence of head injury from medical records of the veterans, scientists were able to move away from information solely based on a participant's or family member's recall about injuries that may have occurred decades - in this case 50 years - earlier.

Havlik cautions that the new findings do not demonstrate a direct cause-and-effect relationship between head injury in early life and the development of dementia, but rather show an association between the two that needs to be studied further. "This study made a great effort to address some of the limitations of previous epidemiologic research in this area. We now need to hone in on what's behind these findings, especially what may be happening biologically," says Havlik.

"While we may not fully understand what's going on, as a practical matter, it may be one more reason to wear that bike helmet instead of keeping it in a closet," Havlik adds. Havlik cautions, however, that the findings from the veterans study may not be applied to today's common exposures to head injury, such as in sports, where helmets are used or where injuries may not be as serious as those examined among veterans who

were hospitalized for head trauma.

The researchers began the study by looking at military medical records of male Navy and Marine World War II veterans who were hospitalized during their period of service with a diagnosis of head injury or an unrelated condition. The use of records instead of recall, the scientists said, allowed them to avoid the problem of "recall error," with which, they estimated, probably fewer than 70 percent of people with a true head injury in prior studies would have recalled their injuries many years later.

. . . the more severe the head injury, the greater risk of developing Alzheimer's Disease.

A specially trained team evaluated the records according to agreed-upon criteria for defining head injury and its severity. (Mild injury involved loss of consciousness or post-traumatic amnesia for less than 30 minutes with no skull fracture, moderate involved loss of consciousness or post-traumatic amnesia for more than 30 minutes but less than 24 hours, and/or a skull fracture, and severe injury was loss of consciousness or post-traumatic amnesia for 24 or more hours.) Veterans were located in 1996-1997 and most contacted agreed to participate in the study. Eventually, 548 veterans who had suffered a head injury and 1,228 veterans without a history of head injury, who comprised the control group for the study, took part.

Using a three-stage screening and assessment process, including home visits in some cases, the scientists then identified the aged veterans with dementia. They also determined whether the veterans had Alzheimer's disease specifically or another type of dementia.

The researchers then compared the number of veterans with AD or other dementias in the group who had suffered

a head injury to those in the group with no head injury. The risk of AD and dementia was increased about two-fold among all those with moderate head injury. And risk increased with the severity of the injury. Those with head injuries categorized as severe - who had been hospitalized and who remained unconscious or amnesic for 24 hours or more - had a four-fold greater risk.

Why head injury may be involved in AD and dementia is still unknown. The researchers, in one attempt to help address that question, also looked for a possible interaction effect between head injury and genetic factors associated with AD. Among study participants, they looked at apolipoprotein E, or APOE, an important gene in AD. APOE has various forms, or alleles, and its e4 allele has been associated with increased risk of AD. The scientists wanted to see if increased risk of AD associated with head injury was only present in those men with an APOE e4 allele. The analysis did not find a statistically significant interaction.

The analyses also looked at other factors that possibly could influence the development of dementia among the veterans, including education, positive family history of dementia, and a history of alcohol or tobacco use, but none was involved in the association between head injury and dementia found in this study.

Plassman and her colleagues note more generally that the findings are consistent with current thinking on the etiology, or course, of AD. The increased risk of dementia, some 50 years after the head injuries had occurred, is one more indication that AD is a chronic disease that unfolds over many decades, she points out. "Understanding how head injury and other AD risk factors begin their destructive work early in life may ultimately lead to finding ways to interrupt the disease process early on," says Plassman.

Study Describes Brain Changes During Learning

A new study by brain scientists at Brown University provides evidence that learning engages a brain process called long-term potentiation (LTP), which in turn strengthens synapses in the cerebral cortex.

The study provides the strongest evidence to date to support the 25-year-old hypothesis, generally accepted by neuroscientists, that learning uses LTP to produce changes in the connections (synapses) between brain cells (neurons) that are necessary to acquire and store new information, said lead author Mengia-Seraina Rioult-Pedotti.

Neuroscientists also theorize that higher forms of learning occur in the cerebral cortex. Evidence from the study supports that theory.

In the study, published in the October issue of *Science*, Brown University researchers taught rats to reach into a hole in a box to grasp food pellets, a new motor skill for the animals. After five days, the rats were tested.

The researchers found that not only had the animals' behavior changed through the learning of a new skill, but that their brains had also changed. Associated with that learning, the strength of synaptic connections between neurons in the motor cortex had increased through a process consistent with the use of LTP.

"Importantly, the overall range of synaptic modification - the maximum possible increase or decrease in strength - had not changed," said Rioult-Pedotti, a neuroscience investigator. "Using this synaptic modification range as a reference allowed our group to eliminate a weakness of earlier work," she said.

In previous studies, the researchers showed that synapses were modifiable through the LTP process when those synapses were activated artificially by electrical impulses. "However, it was not known whether LTP was actually used to modify synapses when learning takes place in the living brain," Rioult-Pedotti said.

"The link between LTP, synaptic modification and learning was tentative," said senior author John Donoghue, professor of neuroscience. "This latest study provides strong evidence that learning itself engages LTP in the cerebral cortex as a way to strengthen synaptic connections."

The research also provides a model to study the relationship between learning and synaptic activity. For example, "the model may be used to study whether synaptic connections get stronger or weaker when you continue learning for long periods of time," Donoghue said. "Or, it gives us a model to test whether drugs or other therapeutic agents can be used to enhance LTP or learning."

Learning and memory are thought to occur through LTP. This is a system in which synapses become increasingly sensitive so that a steady level of pre-synaptic stimulation becomes converted into a larger post-synaptic output. LTP involves patterns of synaptic strengthening and weakening that can last for weeks.

The research further validates the assumptions of a theory proposed by other Brown researchers which says synapses are constantly modifying and that the LTP process is closely related to learning, said Rioult-Pedotti.

Rioult-Pedotti and Donoghue are continuing to examine the relationship between learning and LTP. In particular they are studying which cells and genes are involved in the learning process.

The researchers are also looking at the effect of different training programs on synaptic changes.

"We'd like to find what kind of training programs initiate or sustain changes in the cortical circuitry," Donoghue said. "Is there a brain basis for different kinds of learning? How could you learn something optimally?"

Poll Shows Public Awareness of Traumatic Brain Injury is Very Low Given Incidence

Brain injury occurs every 15 seconds and sends more than one million individuals to hospital emergency rooms each year. Surveillance data from the Centers for Disease Control and Prevention (CDC) reveals that there are more than 5.3 million Americans-- slightly more than two percent of the U.S. population--living with a disability as a result of a traumatic brain injury. Yet given this nationwide incidence, public awareness of brain injury--and the frequency with which it occurs--is very low, as the results of a recently conducted Harris Poll reflect.

"Brain injury occurs more frequently than breast cancer, AIDS, multiple sclerosis and spinal cord injury" remarked Allan I. Bergman, President and CEO of the Brain Injury Association (BIA). "It is quite incredible, then, to see how few people believe this is the case. We have quite a task ahead of us in helping raise awareness of brain injury."

Conducted by Harris Interactive, Inc., the poll surveyed a sample of 1,012 adults aged 18 or older regarding their awareness of brain and head injury. The poll found that one in three Americans say that they are not familiar with the term "brain injury." Given the number of individuals living with a brain injury, only one in twenty individuals surveyed (5%) said that they themselves had sustained a brain injury.

Individuals surveyed were asked whether they thought brain injury occurred more or less frequently than breast cancer, AIDS, multiple sclerosis and spinal cord injuries. The poll found that two out of three adults (66%) believe that brain injuries happen less frequently than breast cancer, and half believe they happen less frequently than AIDS. However, the poll did reveal that

Continued on next page

Continued from previous page

adults are as likely to believe that brain injuries occur more frequently than spinal cord injuries or multiple sclerosis as to believe that they happen less frequently than either of these injuries/illness.

“There has been the belief that sustaining a brain injury doomed you to life in a persistent vegetative state or coma,” said James McDeavitt, MD, BIA Chairperson and Medical Director of the Charlotte Institute of Rehabilitation. “The results of BIA's Harris Poll certainly prove this belief false, since the majority of those surveyed believe individuals sustaining a brain injury are capable of living 'normal' and productive lives. Hopefully this will help end some of the stigma surrounding brain injury, which leads individuals to deny they've sustained such an injury. Additionally, we certainly hope these results will lead to an increase in community living and support services provided to those who sustain brain injury, since the current level of service is quite low.”

One surprising result of the poll was that more than half of adults (56%) surveyed believe that when a person sustains a concussion, he or she sustains a brain injury. Concussions are the most common form of brain injury, yet recent media coverage of these injuries rarely, if ever, linked the term “concussion” with the term “brain injury.” This may explain, to some extent, the low number of individuals indicating that they had sustained a brain injury. Recent research of brain scans, conducted by the UCLA Brain Injury Research Center, illustrated the significant changes the brain experiences after sustaining even one concussion. Concussion is the most common form of brain injury, with an estimated one million people sustaining a concussion annually.

The Brain Injury Association (BIA) conducted the Harris Poll as part of a five-year, cooperative agreement with the Health Resources and Services Administration (HRSA), a branch of the United States Department of Health and Human Services. Public awareness campaigns emphasizing how frequently brain injuries occur, how easily they can be prevented and the rich potential for life following brain injury will be launched during this five-year period, and follow-up polls to measure the effectiveness of these campaigns will be undertaken in years three and five of the agreement.

“Brain injury is the leading cause of death and disability among America's youth,” McDeavitt said. “Almost all brain injuries--most often caused by motor vehicle crashes, falls, sporting accidents and violence--can be prevented. BIA is committed to increasing public awareness of this 'silent epidemic' significantly in the next few years, as well as emphasizing that those who sustain brain injuries are capable of living out their dreams.”

Brain Pacemaker Alleviates Seizures

Duke University Medical Center researchers have discovered a promising new way to alleviate epileptic seizures by stimulating a facial nerve that extends into the brain, disrupting the cycle of seizure activity. Their experiments in rats also involved testing the concept of a “brain pacemaker,” which could be reduced to a small device that could detect potential seizure activity and stimulate the nerve to prevent seizures in humans.

Their findings offer hope of greatly improved seizure control for the 10 percent to 50 percent of epileptic sufferers whose disorder is resistant to antiepileptic medication or surgery.

In the paper, Associate Professor of Neurobiology Miguel Nicolelis and colleagues Erika Fanselow and Ashlan Reid report that stimulating one of the two trigeminal nerves in rats given a seizure-producing drug could reduce those seizures up to 78 percent. Stimulation of both trigeminal nerves, which carry sensory information from either side of the jaw into the brain, proved even more effective.

“It has been long known that electrically stimulating cranial nerves such as the vagus nerve can have powerful effects in the cortex,” said Nicolelis. “And it was known that these effects include desynchronizing neurons that are firing together in synchrony - the highest level of such synchrony being a seizure.

“Such stimulation of the vagus nerve has proven somewhat useful in stopping seizures, and in fact is now used in patients,” Nicolelis said. “However, since the vagus nerve is so powerful, controlling the heart, lungs and other autonomic functions, such stimulation is relatively risky, perhaps disrupting heart function, for example.” According to Nicolelis, the powerful effects of vagus nerve stimulation also meant that only one vagus nerve, the one that does not affect the heart, could be stimulated in attempts to reduce seizures.

Thus, Nicolelis and his colleagues reasoned that the trigeminal cranial nerve -- which seemed more benign because it innervates only the face -- might prove a more effective route to preventing seizures.

The scientists tested their theory by treating rats with a seizure-producing drug and attempting to reduce or eliminate those seizures through trigeminal nerve stimulation.

“We found that such stimulation clearly relieved seizures, which was a big surprise because nobody had thought about it, even though the basic understanding that stimulating cranial nerves affected the brain has been available for 50 years,” Nicolelis said.

Continued on back page

Conferences and Symposiums

January

10
Twin Cities TBI Conference
 Eagen, MN
 Phone: 651-686-0405
 rdschuette@owobopte.org

February

22-23
23rd Annual Neuromuscular Symposium
 Dallas, TX
 Phone: 214-559-7830
 susani@ixnetcom.com

March

3-4
**Trauma 2001:
 The Australasian Trauma Society**
 Sydney, Australia
 Phone: 61-9956-8333
 contact@conferenceaction.com.au

22-23
Annual TBI Conference
 Detroit, MI
 Phone: 248-349-6030

22-23
BIA of Maryland Annual Conference
 Towson, MD
 Phone: 410-448-2924
 info@biamd.org

24-27
BIA Public Policy Conference
 Alexandria, VA
 Phone: 703-236-6000
 www.biausa.org

April

20-22
Society for Cognitive Rehabilitation
 Westminster, CO
 PamLaw1014@aol.com
 www.cognitive-rehab.org.uk

May

5-9
4th World Congress on Brain Injury
 Turin, Italy
 Phone: 39-011-53-00-66
 www.internationalbrain.org/programs/4wc/

June

6-9
Annual Case Management Conference
 Nashville, TN
 www.cmsa.org

17-21
17th World Congress of Neurology
 London, England
 Phone: 44-0181-743-3106
 won@concorde-uk.com

20-23
APTA Annual Conference
 Anaheim, CA
 www.apta.org

28-31
BIA Annual National Symposium
 Atlanta, GA
 Phone: 800-444-6443
 www.biausa.org

August

26-31
Joint Meeting of the International and American Societies of Neurochemistry
 Buenos Aires, Argentina
 conginte@congresos.com.ar

September

13-16
European Pediatric Neurology Congress
 Baden-Baden, Germany
 Phone: 49-551-398035
 hanefeld@mad.uni-goettingen.de

20-25
International Child Neurology Congress
 Beijing, China
 Phone: 66-010-66176450
 jiangyw@bj.col.com.cn

November

7-9
New Trends in Brain Injury Rehabilitation
 Oslo, Norway
 Phone: 49-551-398035
 http://suite.sunnaas.no/english/index.html

2002

June

12-15
Annual Case Management Conference
 Orlando, FL
 www.cmsa.org

INSIDE VIEW

NEWSLETTER

17120 ADVANTAGE POINTE
BAKERSFIELD, CALIFORNIA 93306
PHONE/FAX: 661.873.0313
EMAIL: INSIDEVIEW@NEUROSKILLS.COM
WEBSITE: WWW.NEUROSKILLS.COM

PRSR STD U.S. POSTAGE PAID SEATTLE, WA PERMIT NO. 588
--

Continued from page 6

The scientists' finding lends support to the theory that nerve stimulation reduces seizures by activating a non-specific "arousal" mechanism in the brain. Such non-specificity implies that any nerve reaching into the appropriate brain regions can be stimulated to disrupt synchrony.

The scientists also found that they could stimulate both trigeminal nerves using a lower current and yet achieving even greater seizure reduction. The ability to use lower voltages reduces the chance of nerve damage or pain from nerve stimulation, said Nicoletis.

"When we found that such trigeminal nerve stimulation was so successful, we believed that we could achieve even more effective seizure prevention, as well as reduce the risk of nerve damage, by stimulating only when a seizure appeared imminent," Nicoletis said. In contrast, he said, current vagus nerve stimulation in humans is manually operated, either on a fixed intermittent cycle, or by the patient who is having a seizure or feeling one coming on.

Thus, the neurobiologists, working with Duke biomedical engineers, developed and tested a system in the rats that would monitor their brain wave patterns via brain electrodes and automatically activate the trigeminal nerve stimulation only when the tell-tale patterns marking a seizure appeared.

The seizure-related system proved almost 40 times more effective at seizure reduction per second of stimulation than was periodic stimulation not related to seizure activity, the scientists said.

"These findings lead us to believe that we could develop a system that would work like the brain equivalent of a heart pacemaker to actually prevent seizures," Nicoletis said. "It could continuously monitor brain wave patterns, using non-invasive EEG electrodes on the person's scalp, in order to detect the well-known pathological signature of seizures from a few seconds to a minute before they start. Then, the system could stimulate the trigeminal nerves to prevent the seizures."

Microchip technology could allow the EEG detection and pattern-analysis circuitry to be reduced to a tiny size, said Nicoletis, and he and his biomedical engineering colleagues are now developing such microcircuitry. Also, he said, such pattern analysis could be highly sophisticated, using multiple methods, or algorithms, for recognizing pre-seizure brain wave patterns and "voting" on whether a seizure was imminent. Using such multiple methods could increase the accuracy of detection of pre-seizure activity, Nicoletis said.

"We have now demonstrated for the first time the concept of unsupervised seizure detection and seizure therapy systems in awake animals," he said. "And the level of seizure reduction we have achieved is above what the FDA has considered justifiable for the vagus nerve implant that is already in clinical use. Thus, we believe that the first clinical application of this technique could be possible in about five years."