No protective effect on cancer from long-term vitamin E or vitamin C supplementation

The Physicians' Health Study II is a large-scale, long-term, randomized clinical trial that included 14,641 physicians who were at least 50 years old at enrollment. These physicians were given 400 IU of vitamin E every other day or its placebo, or 500 mg of vitamin C daily or its placebo.

Researchers followed these patients for up to 10 years for the development of cancer with high rates of completion of annual questionnaires, and the confirmation of reported cancer endpoints.

Analyses indicate that randomization to vitamin E did not have a significant effect on prostate cancer. This lack of effect for vitamin E also extended to total cancer. Vitamin C had a similar lack of effect on total cancer.

"After nearly 10 years of supplementation with either vitamin E or vitamin C, we found no evidence supporting the use of either supplement in the prevention of cancer," said Howard D. Sesso, Sc.D., M.P.H., an assistant professor of medicine at Brigham and Women's Hospital. "While vitamin E and C supplement use did not produce any protective benefits, they also did not cause any harm," he added.

Previous laboratory research and observational studies in which people who reported eating a diet rich in vitamins E and C were found to have a lower risk of cancer, had suggested that taking these vitamins as individual supplements may offer some protective benefits.

Study co-author and principal investigator J. Michael Gaziano, M.D., M.P.H., associate professor of medicine at Brigham and Women's Hospital and VA Boston, adds, "Individual vitamin supplements such as vitamin E and C do not appear to provide the same potential advantages as vitamins included as part of a healthy, balanced diet."

Finally, Sesso said that these results provide clinically meaningful new information. "Our results represent one of only a few clinical trials that have tested this idea. The final component of the Physicians' Health Study II, testing daily multivitamin supplementation, remains ongoing."

'Super-aged' brains reveal first secrets of sharp memory in old age

CHICAGO --- Maybe you have an 85-year-old grandfather who still whips through the newspaper crossword puzzle every morning or a 94-year-old aunt who never forgets a name or a face. They don't seem to suffer the ravages of memory that beset most people as they age.

Researchers at Northwestern University's Feinberg School of Medicine wondered if the brains of the elderly with still laser sharp memory -- called "super aged" -- were somehow different than everyone else's. So, instead of the usual approach in which scientists explore what goes wrong in a brain when older people lose their memory, they investigated what goes right in an aging brain that stays nimble.

Now they have a preliminary answer. Scientists examined the brains of five deceased people considered super aged because of their high performance on memory tests when they were more than 80 years old and compared them to the brains of elderly, non-demented individuals. Researchers found the super aged brains had many fewer fiber-like tangles than the brains of those who had aged normally. The tangles consist of a protein called tau that accumulates inside brain cells and is thought to eventually kill the cells. Tangles are found in moderate numbers in the brains of elderly and increase substantially in the brains of Alzheimer's disease patients.

"This new finding in super aged brains is very exciting," said Changiz Geula, principal investigator of the study and a research professor of neurology at the Cognitive Neurology and Alzheimer's Disease Center at Northwestern's Feinberg School. "It was always assumed that the accumulation of these tangles is a progressive phenomenon through the aging process. But we are seeing that some individuals are immune to tangle formation and that the presence of these tangles seems to influence cognitive performance." Individuals who have few tangles perform at superior levels, while those who have more tangles appear to be normal for their age, Geula noted.

Geula will present his findings Sunday, November 16, at the Society for Neuroscience annual meeting in Washington, D.C.

The number of plaques in the brains of the super aged was similar to that in the brains of the normally aging group. The plaque is an aggregation of protein called amyloid that becomes deposited outside the brain cell and disrupts communication between neurons. Like tangles, plaques also are found in modest numbers in the brains of aged individuals and show a dramatic increase in number in Alzheimer's disease.

Geula said the lower number of tangles in the super aged appears to be the critical difference in maintaining memory skills.

Some of the super aged in the study performed memory tasks at the level of people who were about 50 years old. For example, after being told a story, they were able to remember it immediately after and still accurately recall its details 30 minutes later. They also remembered a list of 15 words and recalled these words equally well when tested after 30 minutes.

Geula said new research will focus on what makes cells in super aged brains more resistant to tangle formation. "We want to see what protects the brains of these individuals against the ravages that cause memory loss," he said. " Understanding the specific genetic and molecular characteristics of the brains that makes them resistant, someday may lead to the ability to protect average brains from memory loss. "

Geula's research is part of a larger super aging study at Northwestern's Cognitive Neurology and Alzheimer's Disease Center (CNADC). The study's goal is to identify high functioning individuals over 80 and investigate what factors are important to maintain this ability into old age. A number of super aged individuals have been identified and are being followed up annually with tests of cognitive abilities. Recruitment continues for the study.

Other Feinberg School collaborators on the study are Marsel Mesulam, M.D., CNADC director and the Ruth and Evelyn Dunbar Professor of Psychiatry and Behavioral Sciences; Sandra Weintraub, professor of psychiatry and behavioral sciences; Emily Rogalski, research assistant professor of medicine.

Scripps research scientists discover new cause of fatal brain injury from acute viral meningitis

In a November 16 advance, online publication of the journal Nature, the researchers say their discovery revamps common beliefs about how such potentially lethal infections may be ravaging the brain and suggests the possibility of new treatments. "This is a paradigm shift in how we think about some forms of meningitis and possibly other infections," says the study's lead investigator, Dorian B. McGavern, Ph.D., an associate professor in the Department of Immunology at Scripps Research. "What we thought were the killers are actually immune cells that recruit other accessory cells that then drive the disease. If we can find ways to block recruitment of the cells that actually do the damage into the brain, we may be able to limit the impact of the virus."

Meningitis occurs when the membrane (the meninges) that covers and protects the spinal cord and brain become inflamed, usually due to a bacterial or viral infection. The condition is considered a medical emergency because it can lead to an inflammatory response that results in brain swelling, seizures, blood clotting, epilepsy, or other complications, sometimes resulting in death. Many viruses can cause meningitis.

In this study, investigators looked at what happens in the brain of mice exposed to lymphocytic choriomeningitis virus (LCMV), a virus that can also infect humans, but which does not cause a lot of damage on its own. Instead, the virus pushes an immune response that, in itself, is damaging because it results in "leaky" blood vessels in the meninges at the blood-brain border.

"We use this mild virus because all the damage produced in the brain is caused by the immune system," McGavern says. "While other viruses are more pathologic, they all produce an immune response."

The researchers developed a unique way to "watch" what happens in the brain of mice infected with LCMV by tagging immune cells known as cytotoxic T lymphocytes (CTLs) - also known as killer T cells - with proteins that shine a fluorescent green. These cells, which the researchers knew reacted to LCMV, are the immune system fighters previously thought to be responsible for battling the virus and damaging the brain in the process.

When the researchers injected the tagged killer T cells into the mice, followed one day later with a dose of the virus, then a dye to visualize blood vessels, the scientist found that they could use two-photon microscopy to see what was happening 300-400 microns below the surface of the skull in the brain. Sure enough, the scientists could see blood vessels breaking down as meningitis developed and progressed, but the tagged killer T cells did not appear to be the direct cause of the vascular damage. "We thought the disease depended on these killer T cells, but they didn't seem to be associated with any of the damage we were seeing," McGavern says.

The researchers then tagged other populations of immune cells: monocytes, which usually clean up and repair damage, and neutrophils, which may help with antiviral immunity. To their surprise, the scientists saw that these cells flooded the brain after LCMV infection, and were associated with significant damage to blood vessels in the brain's membrane. "The vessels just start exploding," McGavern says. "This tells us that killer T cells recruit monocytes and neutrophils that actually produce the pathology we see with meningitis. What we thought were the cells responsible actually only recruit accomplices who commit the crime."

The researchers don't know exactly why monocytes and neutrophils are called to sites of infection by killer T cells, or how they produce such damage in meningitis. They theorize that the breakdown of blood vessels may be the result of these cells' attempts to move quickly out of the blood system into tissue within the confined space of the brain. Now, however, the scientists do have a new avenue to explore for possible treatments for the deadly disease.

Co-authors of the paper, "Myelomonocytic cell recruitment causes fatal CNS vascular injury during acute viral meningitis," include Silvia S. Kang from Scripps Research, and Jiyun V. Kim and Michael L. Dustin, from the New York University School of Medicine. The study was funded by grants from the National Institutes of Health, The Burroughs Wellcome Fund, and the Dana Foundation.

A big bunch of tomatoes?

Why do poppies and sunflowers grow as a single flower per stalk while each stem of a tomato plant has several branches, each carrying flowers? In a new study, published in this week's issue of the open access journal PLoS Biology, Dr. Zachary Lippman and colleagues identify a genetic mechanism that determines the pattern of flower growth in the Solanaceae (nightshade) family of plants that includes tomato, potato, pepper, eggplant, tobacco, petunia, and deadly nightshades. Manipulation of the identified pathway can turn the well known tomato vine into a highly branched structure with hundreds of flower-bearing shoots, and may thereby result in increased crop yields.

While the development of individual flowers is well understood, the molecular mechanisms that determine the architecture of inflorescences - flower-bearing shoots - are not. The way that inflorescences branch determines the number and distribution of flowers; in peppers (capsicum) inflorescences do not branch, so flowers are singular; in tomatoes, inflorescence branching is repetitive and regular, forming a zigzagged vine The tomato mutants anantha (an) and compound inflorescence (s) have long been known to produce large numbers of branches and flowers, and the new work elucidates the underlying genetics.

Dr. Lippman, and a team of researchers drawn from three institutions in Israel, investigated inflorescence branching by studying these mutant tomato plants. They identified the genes responsible: the anantha (AN) and compound inflorescence (S) genes. S is a member of the well known homeobox gene family, which plays a crucial regulatory role in patterning both animals and plants. Lippman et al. have shown that manipulation of these genes in tomato plants can dramatically alter the architecture and number of inflorescences, and that altered activity of AN in pepper plants can stimulate branching. Variation in S also explains the branching variation seen in domestically grown tomato strains.

The two genes work in sequence to regulate the timing of development of a branch and a flower – so, for example, slowing down the pathway that makes a flower allows for additional branches to grow. While this study by Lippman et al. focuses on variations in particular nightshades, the insight leads to a new understanding of how many plants, such as trees, control their potential to branch.

Citation: Lippman ZB, Cohen O, Alvarez JP, Abu-Abied M, Pekker I, et al. (2008) The making of a compound inflorescence in tomato and related nightshades. PLoS Biol 6(11): e288. doi:10.1371/journal.pbio.0060288
http://biology.plosjournals.org/perlserv/?request=get-document&doi=10.1371/journal.pbio.0060288

Forests may play overlooked role in regulating climate

DURHAM, N.H. -- In a study to be published next week in the Proceedings of the National Academy of Sciences, scientists led by a team at the University of New Hampshire show that forests may influence the Earth's climate in important ways that have not previously been recognized.

When sunlight reaches the Earth's surface it can either be absorbed and converted to heat or reflected back to outer space, where it doesn't influence the Earth's temperature. Scott Ollinger, a professor at the UNH Institute for the Study of Earth, Oceans, and Space and the department of Natural Resources and the Environment, and colleagues have discovered that, of the total amount of sunlight that falls on forests, the fraction that gets reflected back to space is directly related to levels of nitrogen in their foliage.

While scientists have long known that nitrogen-rich foliage is more efficient at pulling carbon dioxide out of the atmosphere, this new discovery suggests that nitrogen plays an important additional role in the Earth's climate system that has never before been considered. Specifically, trees with high levels of foliar nitrogen have a two-fold effect on climate by simultaneously absorbing more CO2 and reflecting more solar radiation than their low-nitrogen counterparts.

Ollinger and UNH colleagues Andrew Richardson, Mary Martin, Dave Hollinger, Steve Frolking, and others, stumbled upon the discovery while poring over six years worth of data they collected from research sites across North America. The study involved a novel combination of NASA satellite- and aircraft-based instruments, along with meteorological towers from the AmeriFlux network and leaf-level measurements to analyze various aspects of forest canopies. When Ollinger noticed that the overall reflectivity of forest canopies (also known as albedo) rose and fell in conjunction with leaf nitrogen, he had a eureka moment.

"Bits and pieces of evidence for this have been around for years but nobody put them together before because it's a question we hadn't even thought to ask," Ollinger says. "Scientists have long been aware of the importance of albedo, but no one suspected that the albedo of forests might be influenced by nitrogen. And because most of the effect is in the infra-red region of the sun's spectrum, beyond that which human eyes can detect, the pattern isn't immediately obvious."

The newly discovered link between foliar nitrogen and canopy albedo adds an interesting new twist to the understanding of the climate system and raises intriguing questions about the underlying nature of ecosystem–climate interactions.

Changes in climate, air pollution, land use, and species composition can all influence nitrogen levels in foliage, and all of these may be part of a climate feedback mechanism that climate models have not yet examined. Future research planned by the team will involve examining the underlying causes for why the relationship exists and working with climate modelers to determine how the nitrogen-albedo mechanism will influence predictions of climate change.

Indigo ointment may help treat patients with psoriasis

An ointment made from indigo naturalis, a dark blue plant-based powder used in traditional Chinese medicine, appears effective in treating plaque-type psoriasis, according to a report in the November issue of Archives of Dermatology, one of the JAMA/Archives journals.

Psoriasis is a chronic skin disease for which no cure exists, only therapies that bring it into remission, according to background information in the article. "Traditional Chinese medicine is one of the most frequently chosen alternative therapies in China and Taiwan, and psoriasis has been treated for centuries with topical and oral herbal preparations," the authors write. "Indigo naturalis is one of the Chinese herbal remedies that has been reported to exhibit potential antipsoriatic efficacy. However, long-term systemic use has been occasionally associated with irritation of the gastrointestinal tract and adverse hepatic [liver] effects."

Yin-Ku Lin, M.D., of Chang Gung Memorial Hospital and Chang Gung University, Taoyuan, Taiwan, and colleagues conducted a randomized trial of an ointment containing indigo naturalis in 42 patients with treatment-resistant psoriasis. Participants enrolled in the study between May 2004 and April 2005 and applied the indigo naturalis ointment to a psoriatic plaque on one side of their body (usually on the arm, elbow, leg or knee) and then a non-medicated ointment to a parallel plaque on the other side of their body. The researchers assessed and photographed patients' skin plaques at the beginning of the study and again after two, four, six, eight, 10 and 12 weeks.

After 12 weeks of treatment, the plaques treated with indigo naturalis ointment showed significant improvement in scaling, erythema (redness) and induration (hardening) when compared with the plaques treated with non-medicated ointment. "Weighting the sum of scaling, erythema and induration scores by the lesion area and comparing between the start and end of the study, the indigo naturalis ointment–treated lesions showed an 81 percent improvement, whereas the vehicle [non-medicated] ointment–treated lesions showed a 26 percent improvement," the authors write.

Of the 34 patients who completed the study, none experienced worsening psoriasis in the areas treated with indigo naturalis, while the treated plaques were completely or nearly completely cleared for 25 of them (74 percent). None experienced serious adverse effects. Four patients reported itching after applying the indigo naturalis ointment, but only for a couple of days at the start of treatment.

"In conclusion, we present a randomized controlled trial showing the use of topical indigo naturalis ointment for the treatment of chronic plaque psoriasis to be both safe and effective," the authors write. "Future research for a more potent extraction from this crude herb that can provide better absorption and convenience would help improve patient compliance with the treatment regimen. However, much more research will be necessary to clarify the pharmacology of indigo naturalis."

(Arch Dermatol. 2008;144[11]:1457-1464. Available pre-embargo to the media at www.jamamedia.org.)

Editor's Note: This study was supported by a grant from Chang Gung Memorial Hospital. Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

Time, surgery appear to reduce episodes of dizziness in patients with Ménière's disease

Episodes of dizziness tend to become less frequent over time in patients with Ménière's disease, a condition characterized by vertigo, hearing loss and ringing in the ears, according to a report in the November issue of Archives of Otolaryngology–Head & Neck Surgery, one of the JAMA/Archives journals. A second report finds that a surgical procedure to drain fluid from the inner ear appears to reduce vertigo in three-fourths of patients with the condition.

Several studies have outlined how hearing loss and tinnitus (ringing in the ears) progress over time in patients with Ménière's disease, according to background information in the article. "Hearing loss increases during follow-up until it reaches a moderate or severe level, and, similarly, tinnitus becomes constant, causing a decrease in the health-related quality of life in many individuals," the authors write. "However, the time course of episodes of vertigo [dizziness] is less clear, even though the primary goal of treatment is to decrease the frequency and duration of these episodes."

Herminio Perez-Garrigues, M.D., Ph.D., of Hospital Universitario La Fe, Valencia, Spain, and colleagues studied 510 individuals from eight hospitals who met criteria for definitive Ménière's disease between 1999 and 2006. The patients were given conservative care and followed through 2006 to evaluate the frequency and duration of vertigo through the course of the disease.

"Ménière's disease affects both sexes and both ears equally, with onset generally in the fourth decade of life," the authors write. "The number of episodes of vertigo is greater in the first few years of the disease. Although episodes of vertigo that last longer than six hours are less frequent than shorter episodes, they occur with similar frequency throughout the natural course of the disease."

The percentage of patients with no episodes of vertigo increases as the disease progresses, and 70 percent of patients who did not have vertigo during any one year also did not have any episodes in the following year. "In contrast, the likelihood that patients who had episodes of vertigo continued to have them was slightly greater than 50 percent," the authors write.

"This may mean that the activity of the etiologic factor causing the episodes persists for a few months and then ceases to be active," they continue. "However, the problem remains latent until this or another factor again alters inner-ear function. Logically, the evolution of Ménière's disease depends on certain unknown variables such as etiology and personal characteristics. After analyzing our results, we believe it would be interesting to study whether patients can be classified into groups with the same evolutionary process and to investigate the variable or variables that might define such groups."

In another study, Stephen J. Wetmore, M.D., of West Virginia University School of Medicine, Morgantown, reports on the results of endolymphatic sac surgery for patients with Ménière's disease who did not respond to more conservative therapies, such as low-sodium diets or diuretic medications. The surgery involves inserting a shunt into the endolymphatic sac in the inner ear and draining the fluid inside to relieve symptoms. Between 1989 and 2006, 51 patients underwent this surgery for the first time and 16 underwent revision surgery for recurring disease.

After 24 months, the surgery improved major spells of vertigo in 77 percent of patients undergoing the procedure for the first time and 65 percent of patients undergoing revision surgery. For those having revision surgery, results appeared better in patients who developed recurrent symptoms more than two years after than procedure than among those who failed treatment earlier.

"Endolymphatic sac surgery seems to be beneficial in regard to decreasing or eliminating major dizzy spells in those patients who continue to have frequent and severe dizzy spells despite maximal medical therapy," Dr. Wetmore concludes. "For those patients who initially do well after sac surgery but who experience recurrence of symptoms later, revision surgery is often beneficial. The longer the interval between primary endolymphatic sac surgery and the revision procedure, the more likely it is that the patient will obtain a beneficial response from the revision surgery."

(Arch Otolaryngol Head Neck Surg. 2008;134[11]: 1149-1154, 1144-1148. Available pre-embargo to the media at www.jamamedia.org.)

Editor's Note: Please see the articles for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

Cooling the brain prevents cell death in young mice exposed to anesthesia

By Jim Dryden

Nov. 17, 2008 - New research from Washington University School of Medicine in St. Louis suggests cooling the brain may prevent the death of nerve cells that has been observed in infant mice exposed to anesthesia. The effects of anesthesia on human infants and young children have been debated among neuroscientists, but growing evidence suggests exposure to anesthetic drugs during brain development may contribute to behavioral and developmental delays.

The same researchers previously had reported that when young rodents were exposed to alcohol, anesthetics or anticonvulsants, large numbers of their brain cells died through a process known as neuroapoptosis. This latest work suggests such damage may be preventable.

The new findings are reported today at Neuroscience 2008, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

"Cooling the brain seems to be quite effective in suppressing nerve cell death after an infant animal has been exposed to an anesthetic drug," says John W. Olney, M.D., the study's senior investigator and the John P. Feighner Professor of Neuropsychopharmacology. "We don't yet know whether this cooling only temporarily suppresses or whether it permanently prevents this brain damage from occurring. We're currently working to clarify that."

Olney's research team previously had demonstrated that a small dose of anesthetic drugs, enough to lightly anesthetize an infant mouse for about one hour, was sufficient to trigger neuroapoptosis. "It has been widely assumed that the benefits of anesthesia can be achieved without adverse consequences," Olney says. "But that assumption has been called into question in recent years by work from our laboratory and others around the world."

In this study, Olney found the anesthetic drugs isoflurane and ketamine increased neuroapoptosis in infant mice at normal or high temperatures. However, hypothermia during exposure to anesthesia blocked neuroapoptosis and also reduced the low level of neuroapoptosis that occurs normally during brain development. "Some cells fail to make the normal connections that they are supposed to make in order to become integrated into a neural network," he explains. "It's necessary for those cells to die and to be removed from the brain. Cooling the brain also suppresses that process."

If Olney's research team can demonstrate cooling the brain only delays that healthy process temporarily, but permanently prevents unhealthy neuroapoptosis due to anesthesia exposure, the technique may be useful someday in preventing cognitive and developmental problems in some children exposed to anesthesia during surgery.

Olney says it's tricky to demonstrate links between developmental deficits and exposure to anesthetic drugs because the type of deficit can vary depending upon the developmental age at which exposure occurs. Different parts of the brain develop at different times, so exposure during one period of development may have a very different effect than exposure earlier or later in brain development. "We believe there are certain early periods when the damage is not only more likely to be severe, but it's also likely to be more widespread throughout different regions of the brain," he says. "Naturally, if more of the brain is involved and damage to those regions is more severe, it's going to cause more pronounced neural and cognitive consequences."

Olney says it is likely that the protective effects of hypothermia can be achieved either by cooling the entire body or by applying a cooling helmet to the head. In addition, Olney has demonstrated in other research that it may be possible to prevent neuroapoptosis by treating mice with other drugs. He recently reported that the drug lithium may provide similar protection against damage from anesthesia.

Creeley CE, Straiko MMW, Cattano D, Olney JW. Hypothermia prevents spontaneous and anesthesia-induced neuroapoptosis in the infant mouse brain. Abstract for Neuroscience 2008. Presented on Nov. 17, 2008.

Olney has a patent application pending on methods for protecting the developing brain, but it is not related to the hypothermia research. Funding from the National Institutes of Health supported this research.

Drug therapy for premature infants destroys brain cells in mice

By Jim Dryden

Nov. 17, 2008 -- A class of drugs that are used in premature infants to treat chronic lung damage can cause damage in the brain. New research at Washington University School of Medicine in St. Louis suggests the drugs may cause cognitive and motor-control problems even when they are given before birth.

The researchers have identified the cells damaged by the drugs, called glucocorticoids, as well as the time window during which brain injury can occur. They say it may be possible to avoid damage to brain cells and still aid the development of premature lungs if synthetic forms of the drugs can be replaced with hormones made naturally in the body.

The researchers reported their findings today at Neuroscience 2008, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

Studying the effects of the drugs in mice, the investigators found that the synthetic glucocorticoids dexamethasone and betamethasone, commonly prescribed to spur the development of premature lungs, cause damage in the brain's cerebellum, the structure that controls movement, as well as other functions.

Brain cells in the mice died following glucocorticoid treatment when the drugs were given between four and 10 days after birth. The corresponding window in human infants would be approximately 20 weeks of gestation to six weeks following birth. That's also the time span in which these drugs are given to pregnant women at risk for preterm birth or to prematurely born infants who are having problems breathing.

"The cells that are damaged are called neural progenitor cells, which are responsible for producing new neurons," says first author Kevin K. Noguchi, Ph.D., a scientist in the Department of Psychiatry. "So you can imagine that if you kill the cells responsible for producing new neurons, you can cause severe neurodevelopmental deficits."

That's exactly what the researchers found when they studied adolescent mice that had been treated with glucocorticoids during infancy. A single exposure to glucocorticoid drugs permanently decreased the number of neurons in the cerebellum of the mouse brain.

In the past, the steroid drugs were given to low-birthweight infants after they were born, but studies determined that exposure to the drugs following birth could lead to cognitive problems and neuromotor deficits, particularly difficulty with balance and coordination. In 2002, the American Academy of Pediatrics recommended post-natal glucocorticoid use be stopped unless used in clinical trials, but the drugs still are given frequently to mothers at risk for preterm birth.

"The cerebellum connects to other brain structures, so when granule cells in the cerebellum are lost, you also have detrimental effects on cognitive function in non-motor regions of the brain," says senior investigator Nuri B. Farber, M.D., associate professor of psychiatry. "Other researchers have found I.Q. declines in children who have received these drugs early in life, and our findings may help explain why."

But both Farber and Noguchi say therapy with these drugs may be essential for some children with immature lungs as a lifesaving measure. They believe, however, that it may be possible in the future to use different drugs to help the lungs mature without damaging brain cells.

"We're looking at differences between glucocorticoids that are made naturally in the body and hormones that are manufactured," says Noguchi. "The brain has some natural defenses against exposure to endogenous glucocorticoids but not the synthetic ones. So it may be possible to administer some of those natural hormones, which can help the lungs mature without putting the brain at risk."

It also may be possible to develop other drugs that would assist with lung development without killing cells in the cerebellum. But as they study those possibilities, the investigators say they want parents to know that the observed toxic effects of steroid drugs are not a problem for adults and older children. They estimate that by about three months of age, human infants no longer are at high risk for this damage.

"The toxic effects decline when the cerebellum finally finishes its development," Farber says. "These drugs are used for many different purposes, so there are other reasons why a baby might get prednisone or dexamethasone or another glucocorticoid, but our research in mice suggests once a human infant is a few months old, these drugs have fairly innocuous effects in the brain."

Noguchi, KK, Smith DJ, Swiney BS, Farber NB. Acute exposure to multiple corticosteroids can induce selective apoptotic cell death in the neural progenitor cells of the developing cerebellum of neonatal mice. Abstract, presented Nov. 17, 2008 at Neuroscience 2008. This research was supported by grants from the National Institutes of Health.

Researchers Find Link Between Nicotine Addiction And Autism

COLUMBUS, Ohio – Scientists have identified a relationship between two proteins in the brain that has links to both nicotine addiction and autism. The finding has led to speculation that existing drugs used to curb nicotine addiction might serve as the basis for potential therapies to alleviate the symptoms of autism.

The discovery identified a defining role for a protein made by the neurexin-1 gene, which is located in brain cells and assists in connecting neurons as part of the brain's chemical communication system. The neurexin-1 beta protein's job is to lure another protein, a specific type of nicotinic acetylcholine receptor, to the synapses, where the receptor then has a role in helping neurons communicate signals among themselves and to the rest of the body.

This function is important in autism because previous research has shown that people with autism have a shortage of these nicotinic receptors in their brains. Meanwhile, scientists also know that people who are addicted to nicotine have too many of these receptors in their brains.

"If we were to use drugs that mimic the actions of nicotine at an early time in human brain development, would we begin to help those and other circuits develop properly and thus significantly mitigate the deficits in autism? This is a novel way of thinking about how we might be able to use drugs to approach autism treatment," said Rene Anand, associate professor of pharmacology in Ohio State University's College of Medicine and principal investigator of the research. "It would not be a complete cure, but right now we know very little and have no drugs that tackle the primary causes of autism."

The drugs in question are known as cholinergic agents, which interact with the brain to counter nicotine addiction. Anand said the medications could be retailored for use in children in an effort to increase the level of neurexin-1 beta protein in the brains of people with autism.

More neurexin would in turn not only enhance the presence of nicotinic acetylcholine receptors, but also a host of other proteins that are important for the proper formation and maturation of synapses. Proper synapse function is critical to the nervous system's ability to connect to and control other systems of the body.

"Now that these associations have been made, we believe that nicotine in smokers' brains possibly increases the level of neurexin-1 and, as a consequence, helps bring more receptors to the synapses and makes those circuits highly efficient, reinforcing the addiction. In autism, we have the opposite problem. We have a lack of these receptors, and we speculate that neurexin levels are lower," he said.

Anand presented the research Monday (11/17) at the Society for Neuroscience meeting in Washington, D.C. in autistic individuals, thus increasing susceptibility to these devastating neurological disorders."

Autism symptoms include impaired social interaction, problems with verbal and nonverbal communication, and repetitive or severely limited activities and interests. An estimated three to six of every 1,000 children are diagnosed with autism, and boys are four times more likely than girls to have the disorder, according to the National Institute of Neurological Disorders and Stroke.

Anand and colleagues were studying drug abuse and addiction when they discovered the neurexin-1 beta protein's relationship to a certain type of nicotinic receptor. The timing of the discovery was key, as it built upon two other research groups' previous observations: The brains of people with autism and other neurological disorders that were examined after their death showed a 60-percent to 70-percent decrease in specific nicotinic receptors, and some patients with autism have mutations in the neurexin-1 gene that suggest the gene's improper functions could play a role in the disorder.

"These have all been 'association studies.' None has been able to prove what causes autism," Anand said. "And then we accidentally discovered that neurexin-1 and nicotinic receptors tangle. So we knew that there was a genetic link to the process leading to synapse formation, and we had nicotinic receptors that had disappeared in the brains of autistic patients. Our finding filled a gap by saying there is a physical and functional association between these two things occurring in the brain."

Neurexin has implications for tobacco addicts, as well, Anand said. Yet another group of researchers recently found that people with a mutation in the neurexin-1 gene were more likely to be smokers, meaning changes in the gene's functions that lead to excess levels of the nicotinic receptors might make people more susceptible to nicotine addiction.

"Our research reveals how changes in the functions of neurexin could affect the guidance of nicotinic acetylcholine receptors to their functional destinations in nerve cells, perhaps increasing receptors in tobacco addicts while decreasing them in autistic individuals, thus increasing susceptibility to these devastating neurological disorders," Anand said.

The finding also has implications for nicotine addiction because drugs known to alter neurexin's guidance of nicotinic receptors within nerve cells could be used to suppress tobacco addiction.

This work is partially funded by the National Institute on Drug Abuse, the National Alliance for Research on Schizophrenia and Depression, and by an OSU Medical Center Research Day Travel Award.

Coauthors of the study are Stephanie Amici and Susan McKay of Ohio State's Department of Pharmacology; Shi-Bin Cheng, Xiao-Qin Ren, Magdalen Treuil and Jay Rao of the Louisiana State University Health Sciences Center in New Orleans; and Jon Lindstrom of the University of Pennsylvania.

Prophesy of economic collapse 'coming true'

* 16:05 17 November 2008 **by Jeff Hecht**

Things may seem bad now - with fears of a world recession looming - but they could be set to get much worse.

A real-world analysis of a controversial prediction made 30 years ago concludes that economic growth cannot be sustained and we are on track for serious economic collapse this century.

In 1972, the seminal book Limits to Growth by a group called the Club of Rome claimed that exponential growth would eventually lead to economic and environmental collapse. The group used computer models that assessed the interaction of rising populations, pollution, industrial production, resource consumption and food production. Most economists rubbished the book and its recommendations have been ignored by governments, although a growing band of experts today continues to argue that we need to reshape our economy to become more sustainable.

Now Graham Turner at the Commonwealth Scientific and Industrial Research Organisation (CSIRO) in Australia has compared the book's predictions with data from the intervening years.

'Steady state economy'

Changes in industrial production, food production and pollution are all in line with the book's predictions of collapse in the 21st century, says Turner. According to the book, the path we have taken will cause decreasing resource availability and an escalating cost of extraction that triggers a slowdown of industry, which eventually results in economic collapse some time after 2020. "For the first 30 years of the model, the world has been tracking along an unsustainable trajectory," he says.

According to Herman Daly of the University of Maryland, Turner's results show that we "must get off the growth path of business as usual, and move to a steady state economy," stopping population growth, resource depletion, and pollution.

Yet Turner reckons his report [pdf format] shows that a sustainable economy is attainable. "We wouldn't have to go back to the caves," he says. *Journal reference: Global Environmental Change (vol 18, p397)*

Evolution of the visual system is key to abstract art

LIVERPOOL, UK – Famous works of abstract art achieve popularity by using shapes that resonate with the neural mechanisms in the brain linked to visual information, a psychologist at the University of Liverpool has discovered.

Humans make aesthetic judgements about shapes and forms quickly and easily, preferring certain shapes to others, even in the absence of any narrative. Dr Richard Latto, from the University's Psychology department,

has discovered that these shapes resonate with the processing properties of the human visual system, which is responsible for analysing what we have seen.

Dr Latto said: "Humans inherit a basic visual system through genetics. That system provides very selective information about the world around us. It has evolved to provide only the information that we need to survive - for example, we cannot see most electromagnetic radiation or follow the leg movement of a galloping horse.

"Of course our visual systems can be influenced by social factors, like fashion and the number of abstract images that we expose ourselves to, but evolution had given us some genetically determined responses to certain shapes and forms. In popular abstract works such as Matisse's The Snail (1963), Mondrian's Composition with Red, Blue and Yellow (1930), and Malevich's Supremus No. 50 (1915), the artists start with a blank canvas and arrange shapes and colours in a way that is aesthetically pleasing, using their own brain to monitor the effect.

"We like to look at the human body or parts of the body like the face and hands, stylised representations like stick figures and organic forms of the kind incorporated into the work of Salvador Dali and Francis Bacon. Certain landscapes and horizontal and vertical lines are also popular because they resonate with our visual systems, which have been tuned by evolution and experience to respond particularly to these biologically and socially important stimuli.

“We know that neurons in the brain need to be kept active to flourish and develop, so it is important for the visual system to be stimulated and sometimes pushed to the limit to function effectively. As with other adaptive behaviours, we have evolved a mechanism for encouraging this by rewarding ourselves with good feelings. Perhaps we enjoy looking at faces, landscapes and Mondrian's work because it is good for us and good for our brains."

Dr Latto added: "Artists were experimenting with abstract shapes long before scientists began analysing our nature of perception. Through observation or trial-and-error, artists have been identifying these aesthetic primitives - critical shapes and arrangements - and have indirectly defined the nature of our visual processes. In purely abstract painting, as with much music, form is all we have. Popular works have shown that essentially we like looking at what we are good at seeing."

Sleep helps people learn complicated tasks

Sleep also helps people recover forgotten skills

Sleep helps the mind learn complicated tasks and helps people recover learning they otherwise thought they had forgotten over the course of a day, research at the University of Chicago shows.

Using a test that involved learning to play video games, researchers showed for the first time that people who had "forgotten" how to perform a complex task 12 hours after training found that those abilities were restored after a night's sleep.

"Sleep consolidated learning by restoring what was lost over the course of a day following training and by protecting what was learned against subsequent loss," said Howard Nusbaum, Professor of Psychology at the University of Chicago, and a researcher in the study. "These findings suggest that sleep has an important role in learning generalized skills in stabilizing and protecting memory."

The results demonstrate that this consolidation may help in learning language processes such as reading and writing as well as eye-hand skills such as tennis, he said.

For the study, researchers tested about 200 college students, most of whom were women, who had little previous experience playing video games. The team reported the findings in the paper, "Consolidation of Sensorimotor Learning During Sleep," in the current issue of Learning and Memory. Joining Nusbaum in the research were lead author Timothy Brawn, a graduate student in Psychology at the University; Kimberly Fenn, now an Assistant Professor of Psychology at Michigan State University; and Daniel Margoliash, Professor in the Departments of Organismal Biology & Anatomy and Psychology at the University.

The team had students learn video games containing a rich, multisensory virtual environment in which players must use both hands to deal with continually changing visual and auditory signals. The first-person navigation games require learning maps of different environments.

For the study, researchers used first-person shooter games, with the goal of killing enemy bots (software avatars that play against the participant) while avoiding being killed.

The subjects were given a pre-test to determine their initial performance level on the games. Then they were trained to play the games and later tested on their performance. One group was trained in the morning and then tested 12 hours later after being awake for that time. A second group was trained in the morning and then tested the next day, 24 hours after being trained. Another group was trained in the evening, then tested 12 hours after a night's sleep and a fourth group was trained in the evening and then also tested 24 hours after training.

When trained in the morning subjects showed an 8 percentage point improvement in accuracy immediately after training. However after 12 waking hours following training, subjects lost half of that improvement when tested in the evening. When subjects were tested the next morning 24 hours after training, they showed a 10 percentage point improvement over their pre-test performance. "The students probably tested more poorly in the afternoon because following training, some of their waking experiences interfered with training. Those distractions went away when they slept and the brain was able to do its work," Nusbaum said.

Among the students who received evening training, scores improved by about 7 percentage points, and went to 10 percentage points the next morning and remained at that level throughout the day.

The study follows Fenn, Nusbaum and Margoliash's earlier work, published in Nature, which showed for the first time that sleep consolidates perceptual learning of synthetic speech.

"In that study we showed that if after learning, by the end of the day, people 'forgot' some of what was learned, a night's sleep restored this memory loss," Nusbaum said. "Furthermore a night's sleep protected memory against loss over the course of the next day." The latest study expanded that work to show that sleep benefits people learning complicated tasks as well, Nusbaum said.

Gulf War research panel finds 1 in 4 veterans suffers from illness caused by toxic exposure

Washington, DC – (Nov. 17, 2008) – At least one in four of the 697,000 U.S. veterans of the 1991 Gulf War suffer from Gulf War illness, a condition caused by exposure to toxic chemicals, including pesticides and a drug administered to protect troops against nerve gas, and no effective treatments have yet been found, a federal panel of scientific experts and veterans concludes in a landmark report released Monday.

The Congressionally-mandated Research Advisory Committee on Gulf War Veterans' Illnesses presented the report today to Secretary of Veterans Affairs James Peake at VA headquarters in Washington.

Scientific staff support to the Committee is provided by the Boston University School of Public Health (BUSPH). The full report is posted at: http://sph.bu.edu/insider/racreport "The extensive body of scientific research now available consistently indicates that Gulf War illness is real, that it is the result of neurotoxic exposures during Gulf War deployment, and that few veterans have recovered or substantially improved with time," the report says.

The 450-page report brings together for the first time the full range of scientific research and government investigations on Gulf War illness and resolves many questions about the condition. "Veterans of the 1990-1991 Gulf War had the distinction of serving their country in a military operation that was a tremendous success, achieved in short order. But many had the misfortune of developing lasting health consequences that were poorly understood and, for too long, denied or trivialized," the Committee's report says.

The report found that Gulf War illness fundamentally differs from stress-related syndromes described after other wars. "Studies consistently indicate that Gulf War illness is not the result of combat or other stressors, and that Gulf War veterans have lower rates of posttraumatic stress disorder than veterans of other wars," the Committee wrote.

The report concludes: "A renewed federal research commitment is needed … to achieve the critical objectives of improving the health of Gulf War veterans and preventing similar problems in future deployments. This is a national obligation, made especially urgent by the many years that Gulf War veterans have waited for answers and assistance."

Panel Chairman James H. Binns, a former Principal Deputy Assistant Secretary of Defense, said the report "provides a blueprint for the new Administration to focus resources on improving the health of Gulf War veterans and avoiding similar consequences in future military deployments."

Committee Scientific Director Roberta White, PhD, associate dean for research at Boston University's School of Public Health, stated: "Veterans of the first Gulf War have been plagued by ill health since their return 17 years ago. Although the evidence for this health phenomenon is overwhelming, veterans repeatedly find that their complaints are met with cynicism and a 'blame the victim' mentality that attributes their health problems to mental illness or non-physical factors."

White said the Committee's findings "clearly substantiate veterans' beliefs that their health problems are related to exposures experienced in the Gulf theatre. It provides a state-of-the-art review of knowledge about Gulf War veterans' health concerns that can guide clinicians and researchers, and offers a scientific rationale for the new Administration to further our understanding of these health problems -- most importantly, by funding treatment trials to develop effective treatments of the veterans' symptoms."

Large numbers of British Gulf War veterans also are ill. "Recognition of the full extent of the illnesses suffered by these veterans of the conflict and the obligation owed to them is long overdue," said Marshal of The Royal Air Force Lord David Craig, Chief of the Defence Staff (the British equivalent of Chairman of the Joint

Chiefs) during the 1990-1991 Gulf War. "They are victims of the war, as much as any one struck by a bullet or shell. Moreover, medical treatments for their conditions are needed to protect current and future military personnel at similar risk."

The Committee evaluated evidence related to a broad spectrum of Gulf War-related exposures. Its review included hundreds of studies of Gulf War veterans, extensive research in other human populations, studies on toxic exposures in animal models, and government investigations related to events and exposures in the Gulf War.

Gulf War illness is typically characterized by a combination of memory and concentration problems, persistent headaches, unexplained fatigue and widespread pain, and may also include chronic digestive problems, respiratory symptoms and skin rashes.

The new report says that scientific evidence "leaves no question that Gulf War illness is a real condition," and it cites dozens of research studies that have identified "objective biological measures" that distinguish veterans with the illness from healthy controls. Those measures relate to structure and functioning of the brain, functioning of the autonomic nervous system, neuroendocrine and immune alterations, and variability in enzymes that protect the body from neurotoxic chemicals.

The panel cited two Gulf War exposures consistently found to be causally associated with Gulf War illness: (1) the drug pyridostigmine bromide (PB), given to troops to protect against nerve gas, and (2) pesticides that were widely used, and often overused, during the Gulf War.

The Committee found that an association between Gulf War illness and several other exposures could not be ruled out. These included low-level exposures to nerve agents, extended exposure to smoke from oil well fires, receipt of large numbers of vaccines, and combinations of neurotoxic exposures.

Department of Defense reports indicate that about 100,000 U.S. troops were potentially exposed to low-level nerve agents as a result of large-scale U.S. demolitions of Iraqi munitions near Khamisiyah, Iraq in 1991. In 2007, a federally funded study led by White, chair of Environmental Health at the Boston University School of Public Health, found evidence that low-level exposure to nerve gas could have caused lasting brain deficits in Persian Gulf troops. The extent of the changes – less brain "white matter" and reduced cognitive function -- corresponded to the extent of the exposure, that study found.

In addition, the Committee said, Gulf War veterans have significantly higher rates of amyotrophic lateral sclerosis (ALS) than other veterans, and troops who were downwind from the Khamisiyah demolitions have died from brain cancer at twice the rate of other Gulf War veterans.

The report found that historically, federal Gulf War research programs have not been effective in addressing Gulf War illness. While the Committee applauded promising new programs at VA and DOD, it noted that overall federal funding for Gulf War research had declined dramatically in recent years. The panel urged policymakers to devote $60 million annually for such programs.

The Committee further recommended that the VA instruct the Institute of Medicine (IOM) to re-do its previously completed Gulf War and Health reports, saying the IOM's series of reports have been "skewed and limited by a restrictive approach to the scientific tasks mandated by Congress, an approach directed by VA in commissioning the reports."

The Research Advisory Committee on Gulf War Veterans' Illnesses is a panel of prominent scientists and veterans, charged with reviewing federal research on the health of Gulf War veterans. The Committee was mandated by Congress and appointed by the Secretary of Veterans Affairs. Additional information about the Committee and its activities can be found on its website: www.va.gov/RAC-GWVI.

Non-white med students reject therapies associated with their culture

Survey of medical students measures attitude of complementary and alternative medicine during 4 years of medical training

WASHINGTON, DC -- Non-white medical students are more likely to embrace orthodox medicine and reject therapies traditionally associated with their cultures. That is one finding from an international study that measures the attitudes of medical students toward complementary and alternative medicine (CAM). While seemingly counter-intuitive, white students view CAM more favorably than their non-white counterparts, the study authors say.

CAM is the common, collective term that describes non-orthodox therapies considered not intrinsic to the politically dominant health system of a particular society or culture.

Despite the growing popularity of CAM, many medical schools do not include CAM teachings within basic medical education. So researchers at four medical schools (Peninsula, UK; Birmingham, UK; Georgetown, USA; and Auckland, NZ) conducted two surveys to measure the attitudes of medical students toward CAM

during their first and fourth year of medical training in schools that offer some CAM education either at the undergraduate or graduate level. The study is published online in Medical Teacher.

"The first study we conducted with first-year medical students indicated that overall, students wanted more information about CAM in their curriculum," said Hakima Amri, PhD, director of the Complementary and Alternative Medicine Program at Georgetown University Medical Center, the only science-based CAM Master's program at an academic institution in the United States. Amri is a co-investigator and the lead author of the US component of the study. "Our follow-up study measured attitude changes about CAM during medical training. We didn't observe a significant change in overall attitude between the first and fourth year, but we did spot some other interesting trends."

Amri says in the first study, U.S. medical students wanted more courses about CAM than students in Hong Kong, for example. (The Hong Kong school was not included in the 2nd survey of fourth year students.) The second study continued to support that trend with the least interest in CAM measured in Asian and black students.

Amri also noted the polarization observed in the second survey. She says, overall, females, older students and those who had used CAM had more positive attitudes towards holistic treatment of health conditions and became more positive in their attitude over time. However, males and non-CAM users had more negative tendencies toward the effectiveness of CAM therapies and continued to become more negative over time.

"One explanation for the decrease in positive attitude about CAM may result from the students' increased medical knowledge and contact with skeptical clinicians, which are not counter-balanced by CAM teaching," Amri explains.

Survey Methodology

Researchers used a survey called Integrative Medicine Attitude Questionnaire (IMAQ), which included 28 questions relevant to CAM, with each item accompanied by a 7-point Likert scale (point scale with responses ranging from strongly disagree to absolutely agree plus don't know). The IMAQ include three major foci: Attitudes toward holism; effectiveness, credibility and value of CAM; and focus on the doctor-patient relationship, reflection and self-care.

The IMAQ also asked questions about students' age, gender, race, specialty choice, whether they had used CAM or seen a CAM practitioner previously and whether they were interested in or had already undertaken a CAM course.

A total of 604 first-year medical students at six schools completed the questionnaire. Only students who indicated willingness to complete the second questionnaire were contacted to participate in the second survey three years later. A total of 154 out of 487 (31.6 percent) of fourth year students at four schools completed the questionnaire.

The authors note limitations of the study and recommend additional research to understand more about attitude change over time with respect to CAM practices.

In addition to Amri, authors include Charlotte Rees, Peninsula Medical School, UK; Sheila Greenfield, University of Birmingham, UK; Andy M. Wearn, University of Birmingham, and Ian Dennis, University of Auckland, NZ. Amri's work is supported by a grant from the National Institutes of Health's National Center for Complementary and Alternative Medicine. The authors report no disclosures.

Water vapor confirmed as major player in climate change

Water vapor is known to be Earth's most abundant greenhouse gas, but the extent of its contribution to global warming has been debated. Using recent NASA satellite data, researchers have estimated more precisely than ever the heat-trapping effect of water in the air, validating the role of the gas as a critical component of climate change.

Andrew Dessler and colleagues from Texas A&M University in College Station confirmed that the heat-amplifying effect of water vapor is potent enough to double the climate warming caused by increased levels of carbon dioxide in the atmosphere.

With new observations, the scientists confirmed experimentally what existing climate models had anticipated theoretically. The research team used novel data from the Atmospheric Infrared Sounder (AIRS) on NASA's Aqua satellite to measure precisely the humidity throughout the lowest 10 miles of the atmosphere. That information was combined with global observations of shifts in temperature, allowing researchers to build a comprehensive picture of the interplay between water vapor, carbon dioxide, and other atmosphere-warming gases. The NASA-funded research was published recently in the American Geophysical Union's Geophysical Research Letters.

"Everyone agrees that if you add carbon dioxide to the atmosphere, then warming will result," Dessler said. "So the real question is, how much warming?"

The answer can be found by estimating the magnitude of water vapor feedback. Increasing water vapor leads to warmer temperatures, which causes more water vapor to be absorbed into the air. Warming and water absorption increase in a spiraling cycle.

Water vapor feedback can also amplify the warming effect of other greenhouse gases, such that the warming brought about by increased carbon dioxide allows more water vapor to enter the atmosphere.

"The difference in an atmosphere with a strong water vapor feedback and one with a weak feedback is enormous," Dessler said.

Climate models have estimated the strength of water vapor feedback, but until now the record of water vapor data was not sophisticated enough to provide a comprehensive view of at how water vapor responds to changes in Earth's surface temperature. That's because instruments on the ground and previous space-based could not measure water vapor at all altitudes in Earth's troposphere -- the layer of the atmosphere that extends from Earth's surface to about 10 miles in altitude.

AIRS is the first instrument to distinguish differences in the amount of water vapor at all altitudes within the troposphere. Using data from AIRS, the team observed how atmospheric water vapor reacted to shifts in surface temperatures between 2003 and 2008. By determining how humidity changed with surface temperature, the team could compute the average global strength of the water vapor feedback.

"This new data set shows that as surface temperature increases, so does atmospheric humidity," Dessler said. "Dumping greenhouse gases into the atmosphere makes the atmosphere more humid. And since water vapor is itself a greenhouse gas, the increase in humidity amplifies the warming from carbon dioxide."

Specifically, the team found that if Earth warms 1.8 degrees Fahrenheit, the associated increase in water vapor will trap an extra 2 Watts of energy per square meter (about 11 square feet).

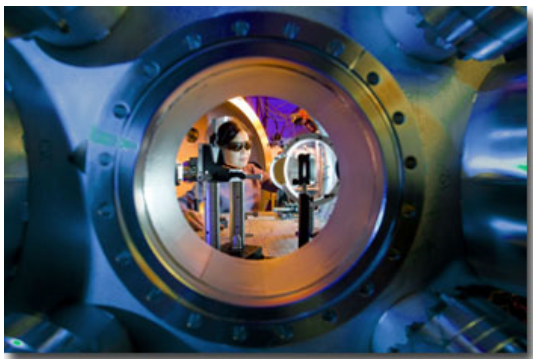
"That number may not sound like much, but add up all of that energy over the entire Earth surface and you find that water vapor is trapping a lot of energy," Dessler said. "We now think the water vapor feedback is extraordinarily strong, capable of doubling the warming due to carbon dioxide alone."

Because the new precise observations agree with existing assessments of water vapor's impact, researchers are more confident than ever in model predictions that Earth's leading greenhouse gas will contribute to a temperature rise of a few degrees by the end of the century.

"This study confirms that what was predicted by the models is really happening in the atmosphere," said Eric Fetzer, an atmospheric scientist who works with AIRS data at NASA's Jet Propulsion Laboratory in Pasadena, Calif. "Water vapor is the big player in the atmosphere as far as climate is concerned."

Billions of particles of anti-matter created in laboratory

LIVERMORE, Calif. – Take a gold sample the size of the head of a push pin, shoot a laser through it, and suddenly more than 100 billion particles of anti-matter appear. The anti-matter, also known as positrons, shoots out of the target in a cone-shaped plasma “jet.” This new ability to create a large number of positrons in a small laboratory opens the door to several fresh avenues of anti-matter research, including an understanding of the physics underlying various astrophysical phenomena such as black holes and gamma ray bursts. Anti-matter research also could reveal why more matter than anti-matter survived the Big Bang at the start of the universe.



Physicist Hui Chen sets up targets for the anti-matter experiment at the Jupiter laser facility.

“We’ve detected far more anti-matter than anyone else has ever measured in a laser experiment,” said Hui Chen, a Livermore researcher who led the experiment. “We’ve demonstrated the creation of a significant number of positrons using a short-pulse laser.”

Chen and her colleagues used a short, ultra-intense laser to irradiate a millimeter-thick gold target. “Previously, we concentrated on making positrons using paper-thin targets,” said Scott Wilks, who designed and modeled the experiment using computer codes. “But recent simulations showed that millimeter-thick gold would produce far more positrons. We were very excited to see so many of them.”

In the experiment, the laser ionizes and accelerates electrons, which are driven right through the gold target. On their way, the electrons interact with the gold nuclei, which serve as a catalyst to create positrons. The electrons give off packets of pure energy, which decays into matter and anti-matter, following the predictions by Einstein’s famous equation that relates matter and energy. By concentrating the energy in space and time, the laser produces positrons more rapidly and in greater density than ever before in the laboratory.

"By creating this much anti-matter, we can study in more detail whether anti-matter really is just like matter, and perhaps gain more clues as to why the universe we see has more matter than anti-matter," said Peter Beiersdorfer, a lead Livermore physicist working with Chen.

Particles of anti-matter are almost immediately annihilated by contact with normal matter, and converted to pure energy (gamma rays). There is considerable speculation as to why the observable universe is apparently almost entirely matter, whether other places are almost entirely anti-matter, and what might be possible if anti-matter could be harnessed. Normal matter and anti-matter are thought to have been in balance in the very early universe, but due to an "asymmetry" the anti-matter decayed or was annihilated, and today very little anti-matter is seen.

Over the years, physicists have theorized about anti-matter, but it wasn't confirmed to exist experimentally until 1932. High-energy cosmic rays impacting Earth's atmosphere produce minute quantities of anti-matter in the resulting jets, and physicists have learned to produce modest amounts of anti-matter using traditional particle accelerators. Anti-matter similarly may be produced in regions like the center of the Milky Way and other galaxies, where very energetic celestial events occur. The presence of the resulting anti-matter is detectable by the gamma rays produced when positrons are destroyed when they come into contact with nearby matter.

Laser production of anti-matter isn't entirely new either. Livermore researchers detected anti-matter about 10 years ago in experiments on the since-decommissioned Nova "petawatt" laser – about 100 particles. But with a better target and a more sensitive detector, this year's experiments directly detected more than 1 million particles. From that sample, the scientists infer that around 100 billion positron particles were produced in total.

Until they annihilate, positrons (anti-electrons) behave much like electrons (just with an opposite charge), and that's how Chen and her colleagues detected them. They took a normal electron detector (a spectrometer) and equipped it to detect particles with opposite polarity as well.

"We've entered a new era," Beiersdorfer said. "Now, that we've looked for it, it's almost like it hit us right on the head. We envision a center for antimatter research, using lasers as cheaper anti-matter factories."

Chen will present her work at the American Physical Society's Division of Plasma Physics meeting Nov. 17-21 at the Hyatt Regency Reunion in Dallas. S.C. Wilks, E. Liang, J. Myatt, K. Cone ,L. Elberson, D.D. Meyerhofer, M. Schneider, R. Shepherd, D. Stafford, R. Tommasini, P. Beiersdorfer are the collaborators on this project.

Two cancer drugs prevent, reverse type 1 diabetes, UCSF study shows

Two common cancer drugs have been shown to both prevent and reverse type 1 diabetes in a mouse model of the disease, according to research conducted at the University of California, San Francisco. The drugs – imatinib (marketed as Gleevec) and sunitinib (marketed as Sutent) – were found to put type 1 diabetes into remission in 80 percent of the test mice and work permanently in 80 percent of those that go into remission.

The findings may offer a new weapon against this autoimmune disease, formerly called juvenile-onset diabetes, for which few drugs have been developed to address the underlying causes, the lead scientists say.

"There are very few drugs to treat type 1 diabetes, especially after disease onset, so this benefit, with a drug already proven to be safe and effective in cancer patients, is very promising," said Jeffrey Bluestone, PhD, director of the Diabetes Center at UCSF and an expert in the study of autoimmunity. "The fact that the treated mice maintained normal blood glucose levels for some time after the drug treatment was stopped suggests that imatinib and sunitinib may be 'reprogramming' their immune systems in a permanent way."

Bluestone is the A.W. and Mary Margaret Clausen Distinguished Professor of the Diabetes Center at UCSF and a senior author on the paper.

Both drugs treat cancer by inhibiting a small subset of the more than 500 tyrosine kinases, which are enzymes that modify cells' signaling proteins through a simple biochemical change. Kinases are ubiquitous agents of cell growth and proliferation, and are also involved in many diseases such as inflammation and cancer. In the immune system, tyrosine kinases are thought to be key to nearly every aspect of immunity, from the signaling that initiates a response by the immune system's T and B cells to later stages of inflammation that can cause tissue damage.

Because type 1 diabetes is caused by an autoimmune response that destroys insulin-secreting cells in the pancreas, the scientists sought to determine if one or more of the tyrosine kinases blocked by the two cancer drugs might also be responsible for the destructive inflammation in the pancreas. If so, the drugs might be promising candidates to treat diabetes.

Using a well-established mouse model for diabetes, known as the non-obese diabetic (NOD) mouse, they found that treating mice with imatinib or sunitinib before the onset of autoimmune diabetes prevented the development of the disease. Findings showed that the drugs' benefits lasted well after the seven-week treatment. Studies with mice that already had diabetes showed that imatinib put the disease into permanent remission in 80 percent of the mice after only eight to 10 weeks of treatment.

The scientists aimed to determine which of the tyrosine kinases targeted by the two cancer drugs might be responsible for triggering diabetes. To their surprise, a few of the drugs' primary targets did not appear crucial to the diabetes treatment's success. Instead, they found that the drugs' rapid benefit appears to derive from the ability to block receptors of a tyrosine kinase not known to be implicated in diabetes, an enzyme known as platelet-derived growth factor receptor, or PDGFR. This kinase regulates cell growth and division, and also plays a key role in inflammation in a variety of settings.

"This study opens up a new area of research in the field of type 1 diabetes, and importantly, opens up exciting opportunities for developing new therapies to treat this disease and other autoimmune diseases," said Arthur Weiss, MD, PhD, UCSF professor of rheumatology and a senior author on the paper.

Weiss is the Ephraim P. Engleman Distinguished Professor and chief of rheumatology at UCSF. The scientists will continue to study the effects of PDGFR in type 1 diabetes and have now applied for funding to perform a safety and efficacy clinical trial in patients.

Lead author of the paper is Cedric Louvet, PhD, postdoctoral fellow in the UCSF Diabetes Center. Coauthors are Shirley Zhu, PhD, UCSF Diabetes Center; Gregory Szot, PhD; Jiena Lang, BS; Michael Lee, MS, and Nicholas Martinier, BS, UCSF Diabetes Center Islet Transplant Facility; and Gideon Bollag, PhD, Plexxikon, Inc., Berkeley, Calif.

The research was funded by the National Institutes of Health and the Juvenile Diabetes Research Foundation.

Gingko biloba does not appear to prevent dementia, Alzheimer's disease

Use of the herb Ginkgo biloba, claimed to have beneficial effects on memory and cognition, was not effective in reducing the rate of dementia or Alzheimer's disease among more than 1,500 elderly study participants after several years of use, according to a study in the November 19 issue of JAMA.

Dementia, especially Alzheimer's disease (AD), is a prevalent chronic disease currently affecting more than 5 million people in the United States and is a leading cause of age-related disability and long-term care placement, according to background information in the article. Ginkgo biloba is prescribed in some areas of the world for preservation of memory; however, there are no medications approved for prevention of dementia, and to date, no clinical trial of adequate design and size has evaluated the safety and effectiveness of Ginkgo biloba in the primary prevention of dementia.

Steven T. DeKosky, M.D., of the University of Pittsburgh, Pa., at the time of the study, and the Ginkgo Evaluation of Memory (GEM) Study Investigators, assessed the effectiveness of Ginkgo biloba in dementia prevention. The study was a randomized, placebo-controlled clinical trial conducted at five academic medical centers in the United States between 2000 and 2008 with a median (midpoint) follow-up of 6.1 years. The trial included 3,069 community volunteers age 75 years or older with normal cognition (n = 2,587) or mild cognitive impairment (MCI; n = 482) at study entry, who were assessed every 6 months for dementia. Participants were randomized to receive either a twice-daily dose of 120-mg extract of Ginkgo biloba (n = 1,545) or placebo (n = 1,524).

The researchers found that during the intervention period, 523 participants were diagnosed with dementia, 246 (16.1 percent) in the placebo group and 277 (17.9 percent) in the Ginkgo biloba group. Of the total dementia cases, 92 percent were classified as possible or probable AD, or AD with evidence of vascular disease of the brain. The rate of total dementia did not differ between participants assigned to Ginkgo biloba vs. placebo (3.3 dementia cases/100 persons, per year exposed, among persons randomized to Ginkgo biloba vs. 2.9/100 persons, per year exposed, among persons randomized to placebo). The rate of Alzheimer-type dementia also did not differ between the two treatment groups (3.0/100 persons, per year exposed vs. 2.6/100 persons, per year exposed). Ginkgo biloba also had no effect on the rate of progression to dementia in participants with MCI.

The adverse event profiles for Ginkgo biloba and placebo were similar and there were no statistically significant differences in the rate of serious adverse events.

"Based on the results of this trial, Ginkgo biloba cannot be recommended for the purpose of preventing dementia," the authors write.

"These results confirm that randomized trials remain critical to the spectrum of translational research necessary to develop new therapies and to determine whether the purported in-vitro, epidemiologic, and surrogate measures of therapeutic benefit are true not only for traditional pharmaceutical therapies but also for complementary therapies. Of almost equal importance from these results is the provision of a strong rationale for including older individuals in randomized trials testing promising interventions for preventing or delaying dementia onset." *(JAMA. 2008;300[19]:2253-2262. Available pre-embargo to the media at www.JAMAmedia.org)*

Editor's Note: Dr. DeKosky is now with the University of Virginia School of Medicine, Charlottesville. Please see the article for additional information, including other authors, author contributions and affiliations, financial disclosures, funding and support, etc.

Editorial: Ginkgo Biloba Extract and Preventing Alzheimer Disease

In an accompanying editorial, Lon S. Schneider, M.D., of the University of Southern California, Los Angeles, comments on the findings of DeKosky and colleagues.

"Despite 2 decades of research with standardized extracts of Ginkgo biloba, considerable uncertainty about its pharmacology and clinical effects remains. Preclinical scientific reports exude promise but generally have not identified the relevant active molecules of this biochemically complex extract, and the preclinical promise has not translated to clinical research benefits. The clinical research, in turn, has not adequately defined potential cognitive indications, potentially effective dosing ranges, pharmacodynamic markers, or convincing evidence for efficacy for any one cognitive condition. The GEM study adds to the substantial body of evidence that Ginkgo biloba extract as it is generally used does not prevent dementia in individuals with or without cognitive impairment and is not effective for Alzheimer disease."

(JAMA. 2008;300[19]:2306-2308. Available pre-embargo to the media at www.JAMAmedia.org)

Found: An Ancient Monument to the Soul

By JOHN NOBLE WILFORD

In a mountainous kingdom in what is now southeastern Turkey, there lived in the eighth century B.C. a royal official, Kuttamuwa, who oversaw the completion of an inscribed stone monument, or stele, to be erected upon his death. The words instructed mourners to commemorate his life and afterlife with feasts "for my soul that is in this stele."

University of Chicago archaeologists who made the discovery last summer in ruins of a walled city near the Syrian border said the stele provided the first written evidence that the people in this region held to the religious concept of the soul apart from the body. By contrast, Semitic contemporaries, including the Israelites, believed that the body and soul were inseparable, which for them made cremation unthinkable, as noted in the Bible.

Circumstantial evidence, archaeologists said, indicated that the people at Sam'al, the ancient city, practiced cremation. The site is known today as Zincirli (pronounced ZIN-jeer-lee). Other scholars said the find could lead to important insights into the dynamics of cultural contact and exchange in the borderlands of antiquity where Indo-European and Semitic people interacted in the Iron Age.

DISCOVERY An inscription on a stone monument in Turkey from the eighth century B.C. indicated a belief that the body and soul were separate. **University of Chicago**

The official's name, for example, is Indo-European: no surprise, as previous investigations there had turned up names and writing in the Luwian language from the north. But the stele also bears southern influences. The writing is in a script derived from the Phoenician alphabet and a Semitic language that appears to be an archaic variant of Aramaic.

The discovery and its implications were described last week in interviews with archaeologists and a linguist at the University of Chicago, who excavated and translated the inscription. "Normally, in the Semitic cultures, the soul of a person, their vital essence, adheres to the bones of the deceased," said David Schloen, an archaeologist at the university's Oriental Institute and director of the excavations. "But here we have a culture that believed the soul is not in the corpse but has been transferred to the mortuary stone."

A translation of the inscription by Dennis Pardee, a professor of Near Eastern languages and civilization at Chicago, reads in part: "I, Kuttamuwa, servant of [the king] Panamuwa, am the one who oversaw the production of this stele for myself while still living. I placed it in an eternal chamber [?] and established a feast at this chamber: a bull for [the god] Hadad, a ram for [the god] Shamash and a ram for my soul that is in this stele."

Dr. Pardee said the word used for soul, nabsh, was Aramaic, a language spoken throughout northern Syria and parts of Mesopotamia in the eighth century. But the inscription seemed to be a previously unrecognized dialect. In Hebrew, a related language, the word for soul is nefesh.

In addition to the writing, a pictorial scene chiseled into the well-preserved stele depicts the culture's view of the afterlife. A bearded man wearing a tasseled cap, presumably Kuttamuwa, raises a cup of wine and sits before a table laden with food, bread and roast duck in a stone bowl.

In other societies of the region, scholars say, this was an invitation to bring customary offerings of food and drink to the tomb of the deceased. Here family and descendants supposedly feasted before a stone slab in a kind of chapel. Archaeologists have found no traces there of a tomb or bodily remains.

Joseph Wegner, an Egyptologist at the University of Pennsylvania, who was not involved in the research, said cult offerings to the dead were common in the Middle East, but not the idea of a soul separate from the body - except in Egypt.

In ancient Egypt, Dr. Wegner noted, the human entity has separate components. The body is important, and the elite went to great expense to mummify and entomb it for eternity. In death, though, a life force or spirit known as ka was immortal, and a soul known as ba, which was linked to personal attributes, fled the body after death.

Dr. Wegner said the concept of a soul held by the people at Sam'al "sounds vaguely Egyptian in its nature." But there was nothing in history or archaeology, he added, to suggest that the Egyptian civilization had a direct influence on this border kingdom.

Other scholars are expected to weigh in after Dr. Schloen and Dr. Pardee describe their findings later this week in Boston at meetings of the American Schools of Oriental Research and the Society of Biblical Literature.

Lawrence E. Stager, an archaeologist at Harvard who excavates in Israel, said that from what he had learned so far the stele illustrated "to a great degree the mixed cultural heritage in the region at that time" and was likely to prompt "new and exciting discoveries in years to come."

Gil Stein, director of the Oriental Institute, said the stele was a "rare and most informative discovery in having written evidence together with artistic and archaeological evidence from the Iron Age."

The 800-pound basalt stele, three feet tall and two feet wide, was found in the third season of excavations at Zincirli by the Neubauer Expedition of the Oriental Institute. The work is expected to continue for seven more years, supported in large part by the Neubauer Family Foundation of Chicago.

The site, near the town of Islahiye in Gaziantep province, was controlled at one time by the Hittite Empire in central Turkey, then became the capital of a small independent kingdom. In the eighth century, the city was still the seat of kings, including Panamuwa, but they were by then apparently subservient to the Assyrian Empire. After that empire's collapse, the city's fortunes declined, and the place was abandoned late in the seventh century.

A German expedition, from 1888 to 1902, was the first to explore the city's past. It uncovered thick city walls of stone and mud brick and monumental gates lined with sculpture and inscriptions. These provided the first direct evidence of Indo-European influence on the kingdom. After the Germans suspended operations, the ruins lay unworked until the Chicago team began digging in 2006, concentrating on the city beyond the central citadel, which had been the focus of the German research. Much of the 100-acre site has now been mapped by remote-sensing magnetic technology capable of detecting buried structures.

This summer, on July 21, workers excavating what appeared to be a large dwelling came upon the rounded top of the stele and saw the first line of the inscription. Dr. Schloen and Amir Fink, a doctoral student in archaeology at Tel Aviv University, bent over to read.

Almost immediately, they and others on the team recognized that the words were Semitic and the name of the king was familiar; it had appeared in the inscriptions found by the Germans. As the entire stele was exposed, Dr. Schloen said, the team made a rough translation, and this was later completed and refined by Dr. Pardee.

Then the archaeologists examined more closely every aspect of the small, square room in which the stele stood in a corner by a stone wall. Fragments of offering bowls to the type depicted in the stele were on the floor. Remains of two bread ovens were found.

"Our best guess is that this was originally a kitchen annexed to a larger dwelling," Dr. Schloen said. "The room was remodeled as a shrine or chapel - a mortuary chapel for Kuttamuwa, probably in his own home." They found no signs of a burial in the city's ruins. At other ancient sites on the Turkish-Syrian border, cremation urns have been dated to the same period. So the archaeologists surmised that cremation was also practiced at Sam'al.

Dr. Stager of Harvard said the evidence so far, the spread of languages and especially the writing on stone about a royal official's soul reflected the give-and-take of mixed cultures, part Indo-European, part Semitic, at a borderland in antiquity.

Brain Compound 'Throws Gasoline Onto The Fire' Of Schizophrenia

COLUMBUS, Ohio – New research has traced elevated levels of a specific compound in the brain to problem-solving deficits in patients with schizophrenia.

The finding suggests that drugs used to suppress the compound, called kynurenic acid, might be an important supplement to antipsychotic medicines, as these adjuncts could be used to treat the disorder's most resistant symptoms – cognitive impairments.

Though schizophrenia is commonly characterized by hallucinations and delusions, patients also have problems with what is known as cognitive flexibility or executive decision-making. Many patients can set a goal and plan one way to achieve it, but cannot adjust their thinking if circumstances force them to consider alternative strategies.

"We've got this core cluster of symptoms that is the Achilles heel for these individuals, and we're not really doing a good job of treating them," said John P. Bruno, professor of psychology, psychiatry and neuroscience at Ohio State University and principal investigator of the research.

Bruno and colleagues have combined advanced animal modeling of schizophrenia-related chemical changes in the brain with the observation that the production of too much kynurenic acid is linked to troubled thinking that affects the research animals' behavior.

The compound is present in all human brains and has some useful functions. But in excessive amounts, the researchers found, kynurenic acid interferes with other chemical processes that govern the ability to pay attention and think strategically under changing conditions.

"If we try to make predictions about how disabled patients with schizophrenia will be and how likely are they to be integrated into the social fabric, it's the severity of the cognitive deficits that are most predictive," Bruno said. "Antipsychotics are particularly good at what we call positive symptoms, but these same drugs are very poor at treating the cognitive deficits. "There are a lot of therapeutic strategies for dealing with schizophrenia, but one which has not been explored, and which we think has a great deal of promise, has to do with regulating production of kynurenic acid," Bruno said. He described the research Tuesday (11/18) at the Society for Neuroscience meeting in Washington, D.C.

Bruno and colleagues tested kynurenic acid's effects on cognitive abilities in rats. Seven rats were given a compound that stimulated excess production of the molecule in their brains, while a control group of rats received no such stimulation. All of the rats were subjected to a test gauging their ability to make what is called an extra-dimensional set shift, requiring them to change response strategies based on changing contingencies – in this case, in a quest to find food. Only 28 percent of the rats with elevated kynurenic acid were able to solve problems to receive a food reward, compared to 100 percent of the control animals. Before the intervention, all of the animals were equally able to find the food under changing circumstances.

The kynurenic acid essentially exacerbates a phenomenon already observed in patients with schizophrenia – the fact that two neurotransmitters in their brains are not as active as they need to be to allow for normal problem-solving capabilities.

These two neurotransmitters critical to normal cognition are acetylcholine and glutamate. Their activity is partially regulated by what are called alpha-7 receptors, a class of proteins involved in the brain's chemical communication system. In the case of schizophrenia, these neurotransmitters are already at abnormally low levels, most likely because of genetic mutations. Excess levels of kynurenic acid inhibit the work of the alpha-7 receptors, meaning they suppress the release of these neurotransmitters even more.

"So we've already got problems with these neurotransmitters, and then to make matters worse, we've got all this extra kynurenic acid antagonizing the alpha-7 receptors, which just throws gasoline onto the fire," Bruno said. "If we can design drugs that are able to inhibit the enzymes that are responsible for overproducing kynurenic acid, we may improve cognitive performance in these patients."

Antipsychotic agents used to control hallucinations and delusions act on different neurotransmitters. Agents targeting kynurenic acid production could be part of a medication cocktail that could restore additional neurochemistry responsible for cognition, Bruno said.

Bruno's research group is able to precisely gauge the effects of the compound on neurotransmitters in the brain because of the animal model used for the research. Schizophrenia was once considered too complex a disorder to model in an animal brain, but Bruno and colleagues have developed a rat model to focus on specific cognitive deficits traced to the part of the brain known as the prefrontal cortex.

An element of the modeling is the painless use of microelectrodes in the animals' brains to measure neurotransmitter levels before and after introduction of the agent that elevates kynurenic acid. The real-time measurements allow the scientists to prove the causal relationship between the elevated compound and the reduced presence of the neurotransmitters.

"No one is claiming that we're producing rats with schizophrenia. What we can do is model the neural side pathologies and see if those pathologies lead to behavioral impairments that look like what see on the clinical side. When we get both of those to line up as we have in this model, we have a valid model to ask questions about developing novel therapeutics," Bruno said. "This has allowed us to move from molecules to neurotransmitters to cognitive behavior all in one fell swoop. These findings set the foundation for several years of research that we hope will have some very big implications."

This work is supported, in part, by the National Institutes of Health.

Coauthors on the studies are Ohio State researchers and graduate students Amy Zmarowski, Katie Alexander, Åsa Konradsson, Clelland Gash and Julie Brooks, as well as Robert Schwarcz and Hui-Qiu Wu of the University of Maryland School of Medicine.

It's confirmed: Matter is merely vacuum fluctuations

* 19:00 20 November 2008 **by Stephen Battersby**

Matter is built on flaky foundations. Physicists have now confirmed that the apparently substantial stuff is actually no more than fluctuations in the quantum vacuum. The researchers simulated the frantic activity that goes on inside protons and neutrons. These particles provide almost all the mass of ordinary matter.

Each proton (or neutron) is made of three quarks - but the individual masses of these quarks only add up to about 1% of the proton's mass. So what accounts for the rest of it?

Theory says it is created by the force that binds quarks together, called the strong nuclear force. In quantum terms, the strong force is carried by a field of virtual particles called gluons, randomly popping into existence and disappearing again. The energy of these vacuum fluctuations has to be included in the total mass of the proton and neutron.

But it has taken decades to work out the actual numbers. The strong force is described by the equations of quantum chromodynamics, or QCD, which are too difficult to solve in most cases.

So physicists have developed a method called lattice QCD, which models smooth space and time as a grid of separate points. This pixellated approach allows the complexities of the strong force to be simulated approximately by computer.

Gnarly calculation

Until recently, lattice QCD calculations concentrated on the virtual gluons, and ignored another important component of the vacuum: pairs of virtual quarks and antiquarks. Quark-antiquark pairs can pop up and momentarily transform a proton into a different, more exotic particle. In fact, the true proton is the sum of all these possibilities going on at once.

Virtual quarks make the calculations much more complicated, involving a matrix of more than 10,000 trillion numbers, says Stephan Dürr of the John von Neumann Institute for Computing in Jülich, Germany, who led the team. "There is no computer on Earth that could possibly store such a big matrix in its memory," Dürr told New Scientist, "so some trickery goes into evaluating it."

Crunch time

Several groups have been working out ways to handle these technical problems, and five years ago a team led by Christine Davies of the University of Glasgow, UK, managed to calculate the mass of an exotic particle called the B_c meson. That particle contains only two quarks, making it simpler to simulate than the three-quark proton. To tackle protons and neutrons, Dürr's team used more than a year of time on the parallel computer network at Jülich, which can handle 200 teraflops - or 200 trillion arithmetical calculations per second. Even so, they had to tailor their code to use the network efficiently. "We spent an enormous effort to make sure our code would make optimum use of the machine," says Dürr.

Without the quarks, earlier simulations got the proton mass wrong by about 10%. With them, Dürr gets a figure within 2% of the value measured by experiments.

Higgs field

Although physicists expected theory to match experiment eventually, it is an important landmark. "The great thing is it shows that you can get close to experiments," says Davies. "Now we know that lattice QCD works, we want to make accurate calculations of particle properties, not just mass." That will allow physicists to test QCD, and look for effects beyond known physics. For now, Dürr's calculation shows that QCD describes quark-based particles accurately, and tells us that most of our mass comes from virtual quarks and gluons fizzing away in the quantum vacuum.

The Higgs field is also thought to make a small contribution, giving mass to individual quarks as well as to electrons and some other particles. The Higgs field creates mass out of the quantum vacuum too, in the form of virtual Higgs bosons. So if the LHC confirms that the Higgs exists, it will mean all reality is virtual.

For Tasmanian Devils, Hope Against a Wily Cancer

By ERICA REX

They’re inky black, pointy-eared, furry and, in a fierce sort of way, cute. And in May of this year, they were added to Australia’s endangered species list.

Ordinarily solitary, Tasmanian devils commune only to feast on carrion and to mate in short-lived passionate couplings during which they tear each other to ribbons. Their spine-decalcifying caterwauls - a sequence of whuffings, snarlings and growlings - have evoked satanic visions since the first European settlers arrived on the island of Tasmania over a century ago. 2Parents used to tell their kids: ‘Don’t go out into the bush because the devil will get you,’ ” recalled Dr. Greg Woods, an associate professor of immunology at Menzies Research Institute in Hobart, Tasmania’s capital.

But in the past decade, the Tasmanian devil has been trapped in a purgatory of its own. Since 1996, a deadly cancer, devil facial tumor disease, has preyed on the devil. Its population plummeted to fewer than 50,000 from about 150,000, said Dr. Hamish McCallum, senior scientist with the Devil Facial Tumour Disease Program at the University of Tasmania.

The devils' situation is dire. Yet as more has been learned about the disease, hope has appeared. Scientists have begun an experimental inoculation program, and this year, Dr. Woods identified one devil able to mount an antibody response to the tumor.

PROGRESS An inoculation worked for Cedric, a Tasmanian devil in captivity. **G.M. Woods**

The devil, Cedric, is a 3-year-old male from western Tasmania who has been living in captivity for several months. Dr. Woods inoculated Cedric and his half-brother, Clinky, who was also disease-free at the time, with irradiated - that is, dead - devil tumor cells. Although they had the same mother, Cedric and Clinky had different fathers. Dr. Woods repeated the vaccination three times. He then administered live tumor cells to both. Cedric mounted an immune response and lived. Clinky did not develop an immune response, and he succumbed to the cancer. His father's genetics made Clinky's immune system more like that of the devils found in eastern Tasmania.

All mammalian immune systems rely on certain cells to recognize invaders. Demarcation of "otherness" at the cellular level is carried out in a part of the mammalian genome called the major histocompatibility complex, or M.H.C. An animal's ability to fight off disease depends on this group of genes. M.H.C. is responsible for the cell markers that flag the difference between cells that are "self" and those that are "nonself." But the tumor's M.H.C. is what makes it deadly to the devil.

"The tumor has no foreign cell surface markers," said Dr. Katherine Belov, a scientist in the Australasian Wildlife Genomics Group at the University of Sidney. "If tumor cells get into a devil, its own immune system should be able to see the cells as foreign. That doesn't happen because the tumor's cells look like devils' own cells." Dr. Belov likened the process to genetic matching for an organ transplant: "You have to have the same genes at the M.H.C. as your donor. If they're different, you'll reject the organ."

If the tumor were a needed organ, devils would be perfect recipients. In other words, the devils' M.H.C. is identical to that of the tumor. The devil and the tumor are genetic clones. Not recognizing a foreign cell, the immune system does not create antibodies.

Devil facial tumor disease first showed up in a 1996 photo taken by a Dutch wildlife photographer, Christo Baars, while he was visiting at Mount William in northeastern Tasmania. Sightings of ailing devils - their lips and jaws deformed by tumors, their noses and eyes obscured by swollen, ulcerating wounds - increased in frequency, notably in the east and north. The disease is always fatal. The devils die of starvation and dehydration when the growths in their jaws and throats make eating and drinking impossible.

Until recently, scientists were at a loss to explain the cancer's cause or mode of transmission. "We'd predicted they'd be vulnerable to viruses" because they are an inbred population, Dr. Woods said. "That what got them was a cancer took everyone by surprise." But this cancer, Dr. Woods and his colleagues found, was unlike any the researchers had seen before. "In all other cancers, what you've got is your own cells gone haywire, whereas in this particular cancer, the cells are not from the host, they're from a different animal," Dr. McCallum said. "The tumor itself is the infectious agent."

The tumor plaguing the devil is a clone, derived from one devil. When animals bite each other in the face, as they do during mating season, tumor cells are passed from host to host.

The Tasmanian devil is about the size of a corgi when fully grown and is the largest surviving carnivorous marsupial. The animal became legally protected in 1941, when farmers and settlers hunted them aggressively, believing the nocturnal scavengers were preying on livestock. Both agriculture and population growth have contributed to fragmentation of the devils' habitat. From 1900 to the present, the human population of Tasmania increased almost threefold, to just less than 500,000. Once widespread, devil populations became more isolated, inbred and genetically similar.

Cedric was the first devil to be inoculated successfully using killed cancer cells. Dr. Woods has since found a second devil that was able to mount an immune response. Three other inoculated devils from eastern Tasmania have developed the disease, supporting Dr. Woods's hypothesis that devils from the west have maintained greater genetic diversity.

Saving the devil from extinction has become a conservation imperative. According to Dr. McCallum, without major intervention, the devil will be extinct in five years.

Dr. Woods said he would begin the search for naturally resistant devils early next year. He posits that the devils' best bet lies within its own genome.

Yet even if more M.H.C.-different devils are found, Dr. Belov thinks the immunological arms race is far from over. She has already seen some evidence that the tumor is adapting. Whereas before, the tumors were clonal, "now we're seeing slight variation - slight chromosomal differences. They've begun to evolve from original clone or cell," she said. "If it does evolve immune evasion strategies, such as turning off the M.H.C. altogether, the tumor has potential to infect M.H.C.-different individuals. If it down regulates its cell surface M.H.C. - that is, switches off its M.H.C. altogether - the tumor not only has potential to infect M.H.C.-different individuals, but it may also cross the species barrier."

If that happened, the most likely victim would be the devil's closest living relative, the spotted-tail quoll. Another carnivorous marsupial indigenous to Tasmania, the quoll has a white-dotted reddish to dark chocolate brown coat and is about the size of a small house cat. Even now, it is considered an endangered species.

Exercise increases brain growth factor and receptors, prevents stem cell drop in middle age

BETHESDA, Md. (Nov. 18, 2008) – A new study confirms that exercise can reverse the age-related decline in the production of neural stem cells in the hippocampus of the mouse brain, and suggests that this happens because exercise restores a brain chemical which promotes the production and maturation of new stem cells.

Neural stem cells and progenitor cells differentiate into a variety of mature nerve cells which have different functions, a process called neurogenesis. There is evidence that when fewer new stem or progenitor cells are produced in the hippocampus, it can result in impairment of the learning and memory functions. The hippocampus plays an important role in memory and learning.

The study, "Exercise enhances the proliferation of neural stem cells and neurite growth and survival of neuronal progenitor cells in dentate gyrus of middle-aged mice," was carried out by Chih-Wei Wu, Ya-Ting Chang, Lung Yu, Hsiun-ing Chen, Chauying J. Jen, Shih-Ying Wu, Chen-Peng Lo, Yu-Min Kuo, all of the National Cheng Kung University Medical College in Taiwan. The study appears in the November issue of the Journal of Applied Physiology, published by The American Physiological Society.

Rise in corticosterone or fall in nerve growth factor?

The researchers built on earlier studies that found that the production of stem cells in the area of the hippocampus known as the dentate gyrus drops off dramatically by the time mice are middle age and that exercise can slow that trend. In the current study, the researchers wanted to track these changes in mice over time, and find out why they happen.

One hypothesis the researchers investigated is that the age-related decline in neurogenesis is tied to a rise in corticosterone in middle age. Elevation of corticosterone has been associated with a drop in the production of new stem cells in the hippocampus.

The second hypothesis is that nerve growth factors -- which encourage new neural cell growth but which decrease with age -- account for the drop in neurogenesis. Specifically, the study looked at whether a decrease in brain-derived neurotrophic growth factor leads to a decline in new neural stem cells.

Variables studied

The researchers trained young (3 months), adult (7 months), early middle-aged (9 months), middle-aged (13 months) and old (24 months) mice to run a treadmill for up to one hour a day.

The study tracked neurogenesis, age, exercise, serum corticosterone levels and brain-derived neurotrophic factor (BDNF) and its receptor TrkB levels in the hippocampus. The researchers focused on middle age as a critical stage for the decline of neurogenesis in the mice.

As expected, the study found that neurogenesis drops off sharply in middle-aged mice. For example, the number of neural progenitor and mitotic (dividing) cells in the hippocampus of middle-aged mice was only 5% of that observed in the young mice.

The researchers also found that exercise significantly slows down the loss of new nerve cells in the middle-aged mice. They found that production of neural stem cells improved by approximately 200% compared to the middle-aged mice that did not exercise. In addition, the survival of new nerve cells increased by 170% and growth by 190% compared to the sedentary middle-aged mice. Exercise also significantly enhanced stem cell production and maturation in the young mice. In fact, exercise produced a stronger effect in younger mice compared to the older mice.

How does this happen?

Based on these results, it appears that nerve growth factor has more to do with these findings than the corticosterone:

* The middle-aged exercisers had more brain-derived neurotrophic factor and its receptor, TrkB, compared to the middle-aged mice that did not exercise. This suggests that exercise promotes the production of brain-derived neurotrophic factor which, in turn, promotes differentiation and survival of new brain cells in the hippocampus.

* Exercise did not change the basal level of serum corticosterone in middle-aged mice. This suggests that the reduction of neurogenesis during aging is not due to the drop in corticosterone levels.

Funding: National Science Council of Taiwan

Scientists find facial scars increase attractiveness

Men with facial scars are more attractive to women seeking short-term relationships, scientists at the University of Liverpool have found.

It was previously assumed that in Western cultures scarring was an unattractive facial feature and in non-Western cultures they were perceived as a sign of maturity and strength. Scientists at Liverpool and Stirling University, however, have found that Western women find scarring on men attractive and may associate it with health and bravery.

Researchers investigated how scarring might impact on mate choice for men and women seeking both long-term and short-term relationships. They found that women preferred men with facial scars for short-term relationships and equally preferred scarred and un-scarred faces for long-term relationships. Men, however, regarded women with and without facial scars as equally attractive for both types of relationship.

Dr Rob Burriss, from the University's School of Biological Sciences, explains: "Male and female participants were shown images of faces that displayed scarring from injury or illness, and were asked to rate how attractive they found the person for long-term and short-term relationships.

"Women may have rated scarring as an attractive quality for short-term relationships because they found it be a symbol of masculinity, a feature that is linked to high testosterone levels and an indicator of good genetic qualities that can be passed on to offspring. Men without scars, however, could be seen as more caring and therefore more suitable for long-term relationships.

"The results demonstrate that we may have more in common with non-Western cultures than previously thought. The perception that scarring is a sign of strength is a view shared by the Yanomamö tribe of Venezuela for example, who use face-paint to accentuate scars that result from ritualised club fights designed to test a man's endurance against repeated strikes to the head.

"The assumption that scarring is a sign of bravery is also consistent with the historical tradition of academic fencing in Western culture, whereby scarring on a man was often evidence of his courage and ability to withstand an opponent's blow."

The research is published in the journal of Personality and Individual Differences.

Members of the public are invited to take part in the online face preference studies by logging on to Dr Burriss' webpage at ***http://www.oraclelab.co.uk/***

Antibiotics Can Cause Pervasive, Persistent Changes to the Microbial Community in the Human Gut, MBL and Stanford Scientists Report

MBL, WOODS HOLE, MA - Using a novel technique developed by Mitchell Sogin of the Marine Biological Laboratory (MBL) to identify different types of bacteria, scientists have completed the most precise survey to date of how microbial communities in the human gut respond to antibiotic treatment.

Sogin, director of the MBL's Josephine Bay Paul Center, and Susan Huse of the MBL, along with David Relman and Les Dethlefsen of Stanford University, identified pervasive changes in the gut microbial communities of three healthy humans after a five-day course of the antibiotic Ciprofloxacin. Their results are reported in the Nov. 18 issue of PloS Biology.

Using very conservative criteria, the scientists identified at least 3,300 to 5,700 different taxa (genetically distinct types) of bacteria in the human distal gut, and antibiotic treatment influenced the abundance of about a third of those taxa.

"You clearly get shifts in the structure of the microbial community with antibiotic treatment," says Sogin. "Some bacteria that were in low abundance prior to treatment may become more abundant, and bacteria that were dominant may decrease in abundance. When you get these shifts, they may be persistent. Some individuals may recover quickly, and others won't recover for many months."

In all the individuals tested in this study, the bacterial community recovered and closely resembled its pre-treatment state within four weeks after the antibiotic course ended, but several bacterial taxa failed to recover within six months.

This raises questions about the health effects of perturbations to the human-microbial symbiosis in the gut, such as may occur with antibiotic treatment. Because specific microbial populations mediate many chemical transformations in the gut - and previous studies have related these processes to cancer and obesity, among other conditions - changes in the composition of the gut microbiota could have important, but as yet undiscovered, health effects.

“When you change the microbial population structure in the gut, you may affect how that population is keeping indigenous pathogens at manageable levels,” says Sogin. Bacteria that do not normally cause problems may begin to grow more rapidly, and cause disease.

The study is part of a large, international effort to fully characterize the microbiota in the human gut, which is the highest-density natural bacterial ecosystem known. Up to 100 trillion microbial cells reside in the gut, and this community plays essential roles in nutrition, development, metabolism, pathogen resistance, and regulation of immune responses.

Until recently, descriptions of human-associated microbiota were constrained by techniques of cultivating (and thus identifying) bacteria. Less than 20-40% of the microbes in the human distal gut, for example, have been cultured in the laboratory. Since the late 1980s, however, cultivation-independent microbial surveys have been developed that identify community members by genetic sequencing. Sogin’s technique, for example, which was used in this study, characterizes microbial populations by sequencing short, hypervariable regions of one gene common to all microbes, the 16S rRNA gene. This pyrosequencing technique reveals greater taxonomic richness in microbial samples at a fraction of the cost of traditional sequencing technologies.

Citation:

Dethlefsen, L., S. Huse, M.L. Sogin, and D.A. Relman (Nov. 18, 2008). The pervasive effects of an antibiotic on the human gut microbiota, as revealed by deep 16S rRNA sequencing. PLoS Biology Vol. 6, No. 11, e280 doi:10.1371/ journal.pbio.0060280.

Real-life 'gremlin' rediscovered in the wild

* 11:42 19 November 2008 **by Reuters and New Scientist staff**

On a misty mountaintop on the Indonesian island of Sulawesi, scientists have observed a living pygmy tarsier - one of the planet's smallest and rarest primates - for the first time in more than 80 years.

Over a two-month period, the scientists used nets to trap three furry, mouse-sized pygmy tarsiers - two males and one female - on Mount Rore Katimbo in Lore Lindu National Park. They spotted a fourth one that got away.

The tarsiers, which some scientists believed were extinct, may not have been overly thrilled to be found. One of them bit Sharon Gursky-Doyen, from Texas A&M University, who took part in the expedition. "I'm the only person in the world to ever be bitten by a pygmy tarsier," says Gursky-Doyen. "My assistant was trying to hold him still while I was attaching a radio collar around his neck," she says. "It's very hard to hold them because they can turn their heads around 180°. As I was trying to close the radio collar, he turned his head and nipped my finger." The collars were being attached so the tarsiers' movements could be tracked through their remote habitat.

The pygmy tarsier, a primate that has not been seen alive since 1921 and was thought extinct, has been rediscovered in Indonesia **(Image: Sharon Gursky-Doyen/Texas A and M University)**

Clawed primate

Tarsiers are primates - the mammalian group that includes lemurs, monkeys, apes and people. The handful of tarsier species live on various Asian islands.

As their name indicates, pygmy tarsiers are small - weighing about 2 ounces (50 grams). They have large eyes and large ears, and they have been described as looking a bit like one of the creatures in the 1984 movie Gremlins. They are nocturnal insectivores and are unusual among primates in that they have claws rather than finger nails.

Pygmy tarsiers had not been seen alive by scientists since 1921. In 2000, Indonesian scientists who were trapping rats in the Sulawesi highlands accidentally trapped and killed a pygmy tarsier. "Until that time, everyone really didn't believe that they existed, because people had been going out looking for them for decades and nobody had seen them or heard them," says Gursky-Doyen.

Her group observed the first live pygmy tarsier in August at an elevation of about 6900 feet (2103 metres).

"Everything was covered in moss and the clouds are right at the top of that mountain. It's always very, very foggy; very, very dense. It's cold up there," says Gursky-Doyen. "When you're 1° from the equator, you expect to be hot. You don't expect to be shivering most of the time. That's what we were doing."

Research By K-State Aging Experts Is Helping Nursing Home Staff Become More Comfortable Dealing With Residents' Sexual Expression

MANHATTAN -- "Do not disturb" signs aren't just for newlyweds anymore.

They are also a way to give nursing home residents some privacy for sexual expression, according to Kansas State University aging experts. "By law you can't always lock a room, but you can offer residents some privacy," said Gayle Doll, who directs K-State's Center on Aging.

She said semi-private rooms pose a problem for nursing home residents who want to engage in sexual activity, either alone or with a partner. That's why two of the center's researchers are looking at ways to make nursing home staff more comfortable accommodating the sexual needs of residents.

Doll said that because nursing home staff don't receive any education in this area, they tend to either ignore or condemn these needs. "We just want people to start talking about these issues," she said. "Once you start talking about it with nursing home staff, everyone has a story."

Majka Jankowiak and Laci Cornelison, research assistants at the Center on Aging, studied nursing home staff attitudes about sexuality in three Kansas nursing homes. The research was presented in October at the American Association of Homes and Services for the Aging conference.

The researchers surveyed the staff before and after a workshop they presented. The surveys, as well as anecdotal feedback from the participants, showed a marked change in attitudes. "They really felt this was a topic that they needed to be educated on," Jankowiak said. "Part of it is that American society is not supportive of older people and sex. It's been a taboo, and it's an even bigger taboo in nursing homes. After the presentation, the participants felt more confident talking about it and dealing with sexual expression of residents."

These shifting attitudes translated into a positive experience for one particular couple, Cornelison said. A married couple moved into a nursing home room with two hospital beds. One spouse had to have a leg elevated, but it was on the same side as the partner's bed, which made it hard for them to hold hands. Some staff members didn't see the importance of allowing the couple intimacy and said the problem couldn't be fixed. "But someone who had been to our presentation encouraged everyone to move the furniture," Cornelison said.

The researchers said that sexuality and nursing home residents brings up issues beyond just acknowledging and accommodating sexual expression. HIV and other sexually transmitted diseases can be concerns for a generation that may have not have the same awareness that younger people do.

Also, adult children may have concerns about their parent's safety or how a new relationship will affect the family or their inheritance. The researchers are developing materials to help family members deal with these questions. "What they fear is exploitation or that the role the parent played will go away," Doll said.

In addition, Alzheimer's and dementia raise questions about the ability to consent, and these conditions also may spur sexual behavior that's inappropriate. "Even though we advocate for residents' rights, there are things that are inappropriate," Doll said. "But staff must be able handle this without residents feeling embarrassed. Inappropriate behavior can just come from people needing relationships, not necessarily sexual ones."

Doll said the researchers hope to see federal guidelines developed to help all nursing homes deal with sexuality in a positive way, especially as baby boomers age and bring their attitudes about sex with them to the nursing home. "Nursing homes are the second most regulated industry next to nuclear power, and yet these regulations don't address sexuality," Doll said.

The Psychology of Déjà vu

All of us have experienced being in a new place and feeling certain that we have been there before. This mysterious feeling, commonly known as déjà vu, occurs when we feel that a new situation is familiar, even if there is evidence that the situation could not have occurred previously. For a long time, this eerie sensation has been attributed to everything from paranormal disturbances to neurological disorders. However, in recent years, as more scientists began studying this phenomenon, a number of theories about déjà vu have emerged, suggesting that it is not merely a glitch in our brain’s memory system. A new report by Colorado State University psychologist Anne M. Cleary, published in Current Directions in Psychological Science, a journal of the Association for Psychological Science, describes recent findings about déjà vu, including the many similarities that exist between déjà vu and our understanding of human recognition memory.

Recognition memory is the type of memory that allows us to realize that what we are currently experiencing has already been experienced before, such as when we recognize a friend on the street or hear a familiar song on the radio. The brain fluctuates between two different types of recognition memory: recollection and

familiarity. Recollection-based recognition occurs when we can pinpoint an instance when a current situation has previously occurred. For example, seeing a familiar man at a store and realizing that we've seen him before on the bus. On the other hand, familiarity-based recognition occurs when our current situation feels familiar, but we don't remember when it has happened before. For example, we see that familiar man in the store, but we just can't remember where we know him from. Déjà vu is believed to be an example of familiarity-based recognition - during déjà vu, we are convinced that we recognize the situation, but we are not sure why.

Cleary conducted experiments testing familiarity-based recognition in which participants were given a list of celebrity names. Later on, they were shown a collection of celebrity photographs; some photographs corresponded to the names on the list, other photographs did not. The volunteers were told to identify the celebrities in the photographs and indicate how likely it was the celebrity's names were on the list they had seen previously. The findings were surprising. Even when the volunteers were unable to identify a celebrity by photo, they had a sense of which names they had studied earlier and which they had not. That is, they couldn't identify the source of their familiarity with the celebrity, but they knew the celebrity was familiar to them. Cleary repeated the experiment substituting famous places (such as Stonehenge and the Taj Majal) for celebrities and got similar results. These findings indicate that the participants stored a little bit of the memory, but it was hazy, so they were not able to connect it to the new experience.

Cleary also ran experiments to figure out what features or elements of situations could trigger feelings of familiarity. She had participants study a random list of words. During a word recognition test, some of the words on the test resembled the earlier words, although only in sound (e.g. lady sounds similar to eighty), but the volunteers reported a sense of familiarity for the new words, even when they could not recall the earlier-presented, similar-sounding words that were the source of this familiarity. Previous research has also shown that people feel familiarity when shown a visual fragment containing isolated geometric shapes from an earlier experience. This suggests that familiar geometric shapes may create the sense that an entire new scene has been viewed before.

These results support the idea that events and episodes which we experience are stored in our memory as individual elements or fragments of that event. Déjà vu may occur when specific aspects of a current situation resemble certain aspects of previously occurring situations; if there is a lot of overlap between the elements of the new and old situations, we get a strong feeling of familiarity. "Many parallels between explanations of déjà vu and theories of human recognition memory exist", Cleary concludes, "Theories of familiarity-based recognition and the laboratory methods used to study it may be especially useful for elucidating the processes underlying déjà vu experiences."

For more information about this report, please contact Anne M. Cleary (anne.cleary@colostate.edu)
Wray Herbert discusses this study in his blog, "We're Only Human..." (http://www.psychologicalscience.org/onlyhuman/)

Woman receives windpipe built from her stem cells

* 00:01 19 November 2008 **by Andy Coghlan**

A Colombian woman has become the world's first recipient of windpipe tissue constructed from a combination of donated tissue and her own cells.

Stem cells harvested from the woman's bone marrow were used to populate a stripped-down section of windpipe received from a donor, which was then transplanted into her body in June.

"Surgeons can now start to see and understand the very real potential for adult stem cells and tissue engineering to radically improve their ability to treat patients," says Martin Birchall, professor of surgery at the University of Bristol, UK, and a member of the team which constructed the windpipe tissue. "We believe this success has proved that we are on the verge of a new age in surgical care."

Claudia Castillo is the first person to receive a windpipe transplant made partly from her own cells **(Image: University of Barcelona)**

Tuberculosis damage

Claudia Castillo, the 30-year-old patient, had suffered a collapse of the tracheal branch of her windpipe leading to her left lung following a severe tuberculosis infection. Left barely able to breathe, the decision was taken in March to attempt the windpipe reconstruction.

Spanish doctors started the process by taking a 7-centimetre section of windpipe from a deceased donor.

Researchers at the University of Padua, Italy, led by Maria Teresa Conconi, then used detergent and enzymes to purge the donated windpipe of all the donor's cells. After six weeks, all that was left was a solid scaffold of connective tissue.

Meanwhile, Birchall and his colleagues in Bristol took the stem cells from the patient's bone marrow and coaxed them in the lab into developing into the cartilage cells that normally coat windpipes.

Finally, the patient's cells were coated onto the donated tracheal scaffold over four days in a special bioreactor built at the Polytechnic of Milan in Italy.

No rejection

The patient received the finished organ in June at the Hospital Clinic, Barcelona, where surgeon Paolo Macchiarini replaced Castillo's damaged trachea with the newly constructed tissue. Now, five months later, the patient is fit and well, and there have been no signs yet that her body is rejecting the graft.

The construction of the windpipe is the second organ produced outside the body using stem cells or cells from the patient's own body.

In 2006, Anthony Atalaat Wake Forest University Medical School in Winston-Salem, North Carolina, revealed that his team had fitted seven children with bladders reconstructed from their own tissue.

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The smart way to study

UC San Diego researchers report on how to improve long-term learning

Combine the aphorisms that "practice makes perfect" and "timing is everything" into one and you might get something resembling findings published in this month's issue of Psychological Science. Proper spacing of lessons, the researchers report, can dramatically enhance learning. And larger gaps between study sessions result in better recall of facts. Conversely: Cramming – whether it's math for a midterm or a foreign language in anticipation of a trip abroad – is not effective in the long haul.

Led by Hal Pashler and John Wixted, professors of psychology at UC San Diego, the study has implications for education. In light of the study, the coauthors write, "it appears no longer premature for psychologists to offer some rough practical guidelines to those who wish to use study time in the most efficient way possible to promote long-term retention."

More than 1,000 subjects participated in three sessions. In the first session, they were taught a set of such obscure but true facts as Norway is the European nation that consumes the most spicy Mexican food and Rudyard Kipling invented snow golf. The second session was a review of the same facts. The time between the sessions ranged from several minutes to several months. Study time was held constant in all the conditions. After some further delay, up to about one year, subjects were then tested.

Not surprisingly, when the interval between the second session and the test was increased, memory got worse – reflecting the familiar curve of forgetting. The interesting finding, however, was that increasing the time between the study sessions reduced the rate of forgetting. This reduction in forgetting was very large – sometimes increasing the likelihood that information would be recalled in the final session by 50 percent.

"The finding that greater spacing between study sessions can enhance later memory was expected, given prior research going back over a century. The results of our study revealed a number of new facts that were not known, however," said Pashler, who heads the Attention and Perception Lab at UCSD. "First, the study used much longer time intervals than in prior research, and it turned out that effects were larger than those seen in earlier studies using much shorter time periods. Second, the results showed that there is an optimal value for the delay between the initial study and the final test, and that this optimal delay varies with the final retention interval: the longer the final retention interval, the longer the optimum delay between study and review."

The results suggest, Pashler said, the optimal amount of time over which learning should take place depends upon how long the information needs to be retained: "If you want to remember information for just a week, it is probably best if study sessions are spaced out over a day or two. On the other hand, if you want to remember information for a year, it is best for learning to be spaced out over about a month."

Extrapolating from the results, he added, "it seems plausible that whenever the goal is for someone to remember information over a lifetime, it is probably best for them to be re-exposed to it over a number of years." "The results imply," said Pashler, "that instruction that packs a lot of learning into a short period is likely to be extremely inefficient, at least for remembering factual information." In a general way, Pashler said, the results also support the use of software designed to provide spaced review, such as the open-source **Mnemosyne Project.**

Coauthors of the paper are Nicholas Cepeda of York University and UC San Diego, Doug Rohrer of the University of South Florida, and Edward Vul of UC San Diego and MIT.

The study was funded by grants from the National Science Foundation and the Institute of Education Sciences, U.S. Department of Education.

Scientists Are High On Idea That Marijuana Reduces Memory Impairment

Written by Emily Caldwell

COLUMBUS, Ohio – The more research they do, the more evidence Ohio State University scientists find that specific elements of marijuana can be good for the aging brain by reducing inflammation there and possibly even stimulating the formation of new brain cells.

The research suggests that the development of a legal drug that contains certain properties similar to those in marijuana might help prevent or delay the onset of Alzheimer's disease. Though the exact cause of Alzheimer's remains unknown, chronic inflammation in the brain is believed to contribute to memory impairment.

Any new drug's properties would resemble those of tetrahydrocannabinol, or THC, the main psychoactive substance in the cannabis plant, but would not share its high-producing effects. THC joins nicotine, alcohol and caffeine as agents that, in moderation, have shown some protection against inflammation in the brain that might translate to better memory late in life. "It's not that everything immoral is good for the brain. It's just that there are some substances that millions of people for thousands of years have used in billions of doses, and we're noticing there's a little signal above all the noise," said Gary Wenk, professor of psychology at Ohio State and principal investigator on the research.

Wenk's work has already shown that a THC-like synthetic drug can improve memory in animals. Now his team is trying to find out exactly how it works in the brain.

The most recent research on rats indicates that at least three receptors in the brain are activated by the synthetic drug, which is similar to marijuana. These receptors are proteins within the brain's endocannabinoid system, which is involved in memory as well as physiological processes associated with appetite, mood and pain response. This research is also showing that receptors in this system can influence brain inflammation and the production of new neurons, or brain cells.

"When we're young, we reproduce neurons and our memory works fine. When we age, the process slows down, so we have a decrease in new cell formation in normal aging. You need those cells to come back and help form new memories, and we found that this THC-like agent can influence creation of those cells," said Yannick Marchalant, a study coauthor and research assistant professor of psychology at Ohio State.

"Could people smoke marijuana to prevent Alzheimer's disease if the disease is in their family? We're not saying that, but it might actually work. What we are saying is it appears that a safe, legal substance that mimics those important properties of marijuana can work on receptors in the brain to prevent memory impairments in aging. So that's really hopeful," Wenk said. Marchalant described the research in a poster presentation Wednesday (11/19) at the Society for Neuroscience meeting in Washington, D.C.

Knowing exactly how any of these compounds work in the brain can make it easier for drug designers to target specific systems with agents that will offer the most effective anti-aging benefits, said Wenk, who is also a professor of neuroscience and molecular virology, immunology and medical genetics.

"Could people smoke marijuana to prevent Alzheimer's disease if the disease is in their family? We're not saying that, but it might actually work. What we are saying is it appears that a safe, legal substance that mimics those important properties of marijuana can work on receptors in the brain to prevent memory impairments in aging. So that's really hopeful," Wenk said. One thing is clear from the studies: Once memory impairment is evident, the treatment is not effective. Reducing inflammation and preserving or generating neurons must occur before the memory loss is obvious, Wenk said.

Marchalant led a study on old rats using the synthetic drug, called WIN-55212-2 (WIN), which is not used in humans because of its high potency to induce psychoactive effects.

The researchers used a pump under the skin to give the rats a constant dose of WIN for three weeks – a dose low enough to induce no psychoactive effects on the animals. A control group of rats received no intervention. In follow-up memory tests, in which rats were placed in a small swimming pool to determine how well they use visual cues to find a platform hidden under the surface of the water, the treated rats did better than the control rats in learning and remembering how to find the hidden platform.

"Old rats are not very good at that task. They can learn, but it takes them more time to find the platform. When we gave them the drug, it made them a little better at that task," Marchalant said.

In some rats, Marchalant combined the WIN with compounds that are known to block specific receptors, which then offers hints at which receptors WIN is activating. The results indicated the WIN lowered the rats' brain inflammation in the hippocampus by acting on what is called the TRPV1 receptor. The hippocampus is responsible for short-term memory.

With the same intervention technique, the researchers also determined that WIN acts on receptors known as CB1 and CB2, leading to the generation of new brain cells – a process known as neurogenesis. Those results led the scientists to speculate that the combination of lowered inflammation and neurogenesis is the reason the rats' memory improved after treatment with WIN.

The researchers are continuing to study the endocannabinoid system's role in regulating inflammation and neuron development. They are trying to zero in on the receptors that must be activated to produce the most benefits from any newly developed drug.

What they already know is THC alone isn't the answer.

"The end goal is not to recommend the use of THC in humans to reduce Alzheimer's," Marchalant said. "We need to find exactly which receptors are most crucial, and ideally lead to the development of drugs that specifically activate those receptors. We hope a compound can be found that can target both inflammation and neurogenesis, which would be the most efficient way to produce the best effects."

The National Institutes of Health supported this work.

Coauthors on the presentation are Holly Brothers and Lauren Burgess, both of Ohio State's Department of Psychology.
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Uncovering secrets of life in the ocean

Researchers unravel how the very first eyes in evolution might have worked and how they guide the swimming of marine plankton towards light

Larvae of marine invertebrates – worms, sponges, jellyfish - have the simplest eyes that exist. They consist of no more than two cells: a photoreceptor cell and a pigment cell. These minimal eyes, called eyespots, resemble the 'proto-eyes' suggested by Charles Darwin as the first eyes to appear in animal evolution. They cannot form images but allow the animal to sense the direction of light. This ability is crucial for phototaxis – the swimming towards light exhibited by many zooplankton larvae. Myriads of planktonic animals travel guided by light every day. Their movements drive the biggest transport of biomass on earth.

The larvae of marine ragworm Platynereis dumerilii have the simplest eyes that exist. They resemble the first eyes that developed in animal evolution and allow the larvae to navigate guided by light. **EMBL**

"For a long time nobody knew how the animals do phototaxis with their simple eyes and nervous system," explains Detlev Arendt, whose team carried out the research at EMBL. "We assume that the first eyes in the animal kingdom evolved for exactly this purpose. Understanding phototaxis thus unravels the first steps of eye evolution."

Studying the larvae of the marine ragworm Platynereis dumerilii, the scientists found that a nerve connects the photoreceptor cell of the eyespot and the cells that bring about the swimming motion of the larvae. The photoreceptor detects light and converts it into an electrical signal that travels down its neural projection, which makes a connection with a band of cells endowed with cilia. These cilia - thin, hair-like projections - beat to displace water and bring about movement.

Shining light selectively on one eyespot changes the beating of the adjacent cilia. The resulting local changes in water flow are sufficient to alter the direction of swimming, computer simulations of larval swimming show.

The second eyespot cell, the pigment cell, confers the directional sensitivity to light. It absorbs light and casts a shadow over the photoreceptor. The shape of this shadow varies according to the position of the light source and is communicated to the cilia through the signal of the photoreceptor.

"Platynereis can be considered a living fossil," says Gáspár Jékely, former member of Arendt's lab who now heads a group at the MPI for Developmental Biology, "it still lives in the same environment as its ancestors millions of years ago and has preserved many ancestral features. Studying the eyespots of its larva is probably the closest we can get to figuring out what eyes looked like when they first evolved."

It is likely that the close coupling of light sensor to cilia marks an important, early landmark in the evolution of animal eyes. Many contemporary marine invertebrates still employ the strategy for phototaxis.

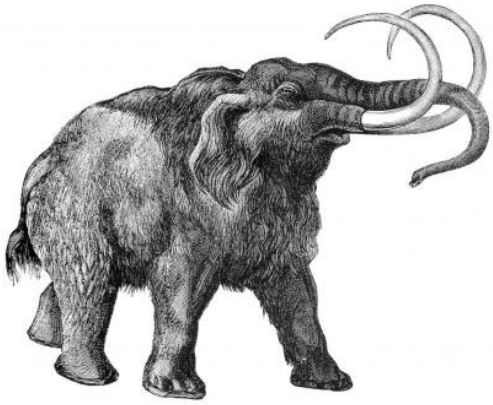
Regenerating a Mammoth for $10 Million

By NICHOLAS WADE

Scientists are talking for the first time about the old idea of resurrecting extinct species as if this staple of science fiction is a realistic possibility, saying that a living mammoth could perhaps be regenerated for as little as $10 million. The same technology could be applied to any other extinct species from which one can obtain hair, horn, hooves, fur or feathers, and which went extinct within the last 60,000 years, the effective age limit

for DNA. Though the stuffed animals in natural history museums are not likely to burst into life again, these old collections are full of items that may contain ancient DNA that can be decoded by the new generation of DNA sequencing machines.

If the genome of an extinct species can be reconstructed, biologists can work out the exact DNA differences with the genome of its nearest living relative. There are talks on how to modify the DNA in an elephant's egg so that after each round of changes it would progressively resemble the DNA in a mammoth egg. The final-stage egg could then be brought to term in an elephant mother, and mammoths might once again roam the Siberian steppes. The same would be technically possible with Neanderthals, whose full genome is expected to be recovered shortly, but there would be several ethical issues in modifying modern human DNA to that of another human species.



Drawing of a woolly mammoth. Copyright-free illustration (from Dover books)

A scientific team headed by Stephan C. Schuster and Webb Miller at Pennsylvania State University reports in Thursday's issue of Nature that it has recovered a large fraction of the mammoth genome from clumps of mammoth hair. Mammoths, ice-age relatives of the elephant, were hunted by the modern humans who first learned to inhabit Siberia some 22,000 years ago. The mammoths fell extinct in both their Siberian and North American homelands toward the end of the last ice age, some 10,000 years ago.

Dr. Schuster and Dr. Miller said there was no technical obstacle to decoding the full mammoth genome, which they believe could be achieved for a further $2 million. They have already been able to calculate that the mammoth's genes differ at some 400,000 sites on its genome from that of the African elephant.

There is no present way to synthesize a genome-size chunk of mammoth DNA, let alone to develop it into a whole animal. But Dr. Schuster said a shortcut would be to modify the genome of an elephant's cell at the 400,000 or more sites necessary to make it resemble a mammoth's genome. The cell could be converted into an embryo and brought to term by an elephant, a project he estimated would cost some $10 million. "This is something that could work, though it will be tedious and expensive," he said.

There have been several Russian attempts to cultivate eggs from frozen mammoths that look so perfectly preserved in ice. But the perfection is deceiving since the DNA is always degraded and no viable cells remain. Even a genome-based approach would have been judged entirely impossible a few years ago and is far from reality even now.

Still, several technical barriers have fallen in surprising ways. One barrier was that ancient DNA is always shredded into tiny pieces, seemingly impossible to analyze. But a new generation of DNA decoding machines use tiny pieces as their starting point. Dr. Schuster's laboratory has two, known as 454 machines, each of which costs $500,000.

Ball of permafrost-preserved mammoth hair containing thick outer-coat and thin under-coat hairs. Stephan Schuster lab, Penn State

Another problem has been that ancient DNA in bone, the usual source, is heavily contaminated with bacterial DNA. Dr. Schuster has found that hair is a much purer source of the host's DNA, with the keratin serving to seal it in and largely exclude bacteria.

A third issue is that the DNA of living cells can be modified only very laboriously and usually at one site at a time. Dr. Schuster said he had been in discussion with George Church, a well-known genome technologist at Harvard Medical School, about a new method Dr. Church has invented for modifying some 50,000 genomic sites at a time.

The method has not yet been published, and until other scientists can assess it they are likely to view genome engineering on such a scale as being implausible. Rudolph Jaenisch, a biologist at the Whitehead Institute in Cambridge, said the proposal to resurrect a mammoth was "a wishful-thinking experiment with no realistic chance for success."

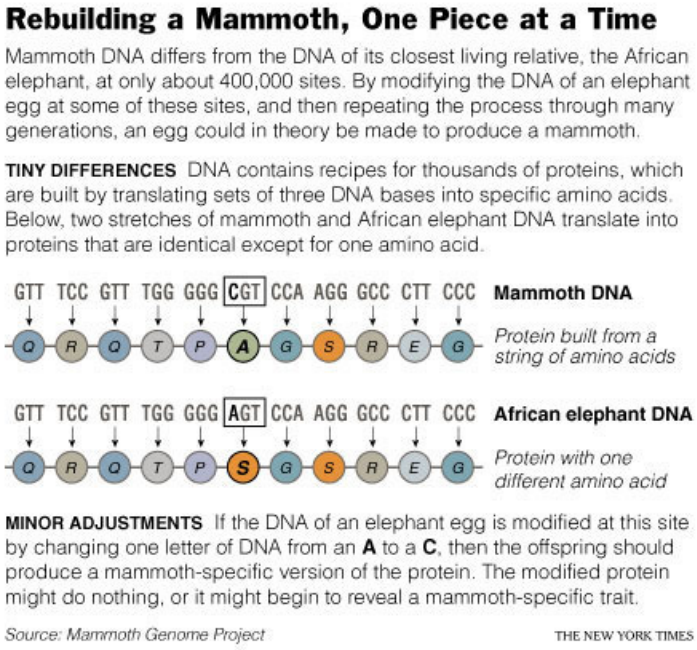
Dr. Church, however, said that there had recently been enormous technical improvements in decoding genomes and that he expected similar improvements in genome engineering. In his new method, some 50,000 corrective DNA sequences are injected into a cell at one time. In the laboratory, the cell would then be grown and tested and its descendants subjected to further rounds of DNA modification until judged close enough to that of the ancient species. In the case of resurrecting the mammoth, Dr. Church said, the process would begin by taking a skin cell from an elephant and converting it to the embryonic state with a method developed last year by Dr. Shinya Yamanaka for reprogramming cells.

Asked if the mammoth project might indeed happen, Dr. Church said that "there is some enthusiasm for it," although making zoos better did not outrank fixing the energy crisis on his priority list.

Dr. Schuster believes that museums could prove gold mines of ancient DNA because any animal remains containing keratin, from hooves to feathers, could hold enough DNA for the full genome to be recovered by the new sequencing machines.

The full genome of the Neanderthal, an ancient human species probably driven to extinction by the first modern humans that entered Europe some 45,000 years ago, is expected to be recovered shortly. If the mammoth can be resurrected, the same would be technically possible for Neanderthals.

But the process of genetically engineering a human genome into the Neanderthal version would probably raise many objections, as would several other aspects of such a project. "Catholic teaching opposes all human cloning, and all production of human beings in the laboratory, so I do not see how any of this could be ethically acceptable in humans," said Richard Doerflinger, an official with the United States Conference of Catholic Bishops.



Dr. Church said there might be an alternative approach that would "alarm a minimal number of people." The workaround would be to modify not a human genome but that of the chimpanzee, which is some 98 percent similar to that of people. The chimp's genome would be progressively modified until close enough to that of Neanderthals, and the embryo brought to term in a chimpanzee. "The big issue would be whether enough people felt that a chimp-Neanderthal hybrid would be acceptable, and that would be broadly discussed before anyone started to work on it," Dr. Church said.

Surgeons perform world's first pediatric robotic bladder reconstruction

A 10-year-old Chicago girl born with an abnormally small bladder that made her incontinent has become the first patient to benefit from a new robotic-assisted bladder-reconstruction method developed by surgeons at the University of Chicago Medical Center. The surgeons describe their innovative technique in the December 2008 issue of the journal Urology. They have now performed the operation, using the DaVinci robotic surgical system, six times, with good results and no significant complications.

The first patient, treated Feb. 21, 2008, suffered from a very small, spasmodic bladder, a birth defect that led to gradual kidney damage and loss of urinary control.

"We refer to this condition as neurogenic bladder," said team leader Mohan S. Gundeti, MD, assistant professor of surgery and chief of pediatric urology at the University of Chicago's Comer Children's Hospital. "Her bladder could barely hold six ounces. Worse, it produced frequent involuntary contractions, which forced the urine back up into the kidneys, where it slowly but inevitably causes damage, including frequent infections."

The girl always felt that she urgently had to go to the bathroom. She stopped drinking juice or soda. She even cut back on water, to less than two cups a day. Medication helped a little, but despite two years of trying different treatments, the problem continued to get worse and began to cause kidney damage, which made surgery necessary.

Although Gundeti had performed the operation to enlarge and relax a tiny spasmodic bladder many times, it had never been done robotically--an approach that has produced quicker recovery, less pain and minimal scars in other procedures.

"This is a major, lengthy operation," he said, "essentially five smaller procedures done in sequence."

Known as an augmentation ileocystoplasty with Mitrofanoff appendicovesicostomy, the surgery normally begins with a big incision, about six inches long, from above the navel down to the pubic area, followed by placement of retractors to pull the stomach muscles out of the way.

"The robotic approach enabled us to avoid that entire incision, which causes significant post-operative pain, presents an infection risk and leaves a big scar," Gundeti said.

Instead, the robotic tools enter the abdomen through five small, dime-sized holes. In this operation, the surgeons use about 12 inches of intestine to reconstruct a larger bladder, "more than twice the original size," said Gundeti. "Plus, it can no longer contract with the same force."

Then they converted the appendix into a "continent conduit," a drain for the new, expanded bladder, with one end implanted into the wall of the bladder and the other end leading outside the body through small outlet in the lower abdomen. A skin flap covers the fleshy appendix opening.

"No one had ever done the full operation this way," Gundeti said. "It requires a lot of familiarity with both the open operation and considerable laparoscopic experience."

This first case took about ten hours, compared to six-to-eight hours for an open procedure. The team included Gundeti and adult urologists Arieh Shalhav and Gregory Zagaja, as well as follows, residents and the nursing team. The team was able to reduce OR time in the subsequent cases.

After such a long, complicated operation, "I expected my daughter to be covered with bandages and gauze and tape, to have a big swollen belly with a big wound," the patient's mother recalled. "But there was none of that. I was stunned. Her belly was flat and normal, no bandages, not even a band-aid, just a few little cuts that looked like they had been covered with glue. Oh, I thought, she's going to like this. No big scars. She could wear a bikini." "I would not want her to wear a bikini," she added, "but she could."

"Patients like surgery without significant scars," Gundeti said. "We also hope to show that in addition to the benefit of no big wound to heal, just five small punctures, there is less risk of infection, quick recovery and less pain." Pain management for this case consisted of oral medications, rather than the traditional morphine and epidural anesthesia, which is contraindicated in young patients who have had previous spine surgery.

The patient started drinking clear liquids six hours after surgery and eating within 24 hours, which she "greatly appreciated," Gundeti said. She went home about four days after her surgery and within six weeks was completely continent, day and night. "This is a great benefit for the child and her family," Gundeti said.

Although she still has empty her bladder with a regular catheter, it is now easier to do and is far more reliable at retaining urine. "She hasn't had a leak since then," her mother said. "She can drink water, or juice, even soda. She's enjoying the freedom she never had."

Additional authors of the study were Michael Eng, Greg Zagaja and Stuart Reynolds of the University of Chicago Medical Center. A video of one of the cases won the "best video award" at a regional meeting of the American Urological Association.

Mysterious electrons may be sign of dark matter

* 18:30 19 November 2008 **by Jessica Griggs**

Dark matter is proving less shadowy than its name suggests. Its signature may have been detected by a balloon-borne experiment that measured a surprisingly high number of energetic electrons streaming in from space.

High-energy electrons are found throughout space and are accelerated when stars explode in supernovae. But a balloon-borne detector flying over Antarctica called the Advanced Thin Ionization Calorimeter (ATIC) has detected 70 more high-energy electrons than the normal background level attributed to supernova blasts.

John Wefel of Louisiana State University in Baton Rouge, who led the collaboration, says there are two possible explanations.

The electrons could come from a nearby astrophysical object, such as a pulsar, that lies within 3000 light years from Earth. But the team has spent four years trying to fit the signal to such an object and has yet to find a good match.

The alternative is that the electrons were produced when two dark matter particles met and destroyed each other. That hypothesis is strengthened by the electrons' observed energies, which range from 300 to 800 gigaelectronvolts.

"There is nothing that we know of in high-energy physics or astrophysics that happens in this energy range," says Wefel.

Extra dimensions

What's more, the signal peaked at 650 GeV and then rapidly declined to the background level at 800 GeV. According to Wefel, this is the kind of signature you would expect if a type of exotic particle known as a Kaluza Klein particle was the dark matter culprit, with the peak at 650 GeV corresponding to its mass.

This type of particle is a WIMP (weakly interacting massive particle), one of the most promising candidates for dark matter, and comes from theories in which the universe has extra spatial dimensions. These extra dimensions can only be detected by observing WIMPS that have leaked into the four dimensions (three of space and one of time) that are familiar to us.

The past few years have been good for dark matter hunters. In 2007, NASA's WMAP satellite, which measures the big bang's afterglow, picked up an excess of microwaves from around the centre of our galaxy. This 'WMAP haze' could be radiation produced when dark matter particles collide.

Other signals

A few months ago, another group found tantalising hints of dark matter in antimatter measurements taken by a detector known as PAMELA.

So how do the results from ATIC fit in with these?

Even though the data from PAMELA cover a different energy range from the ATIC signal, Wefel believes that "there is no contradiction between ATIC and PAMELA, at least to within the uncertainties on the presently available data", he told New Scientist. "It is possible that we may be observing the same source."

But ATIC has detected 200 times more potential dark matter than WMAP did at the galactic centre. "We need a boost factor of 200 for the results to be compatible," says Wefel. "So either the WMAP haze is wrong, the theory is wrong, or dark matter is not uniformly distributed all over the place."

The search continues

With so many unanswered questions, will we ever be able to say conclusively that dark matter has been spotted? Wefel thinks that experiments such as the recently launched Fermi Gamma Ray Space Telescope should continue to discover new possible sources of dark matter. These sources will need to be studied in other wavelengths and with other instruments in order to determine their properties.

"Then we shall see if any of them have the capability to produce the electron signal that ATIC observed," says Wefel. "How long do you search before you give up? I can't say but I suspect we'll keep going until Fermi and other instruments run out of new source discoveries. Meanwhile other experiments will try to study the electrons in more detail to see if they can 'pin down' the signature of dark matter annihilation."

However the pieces fit together, other experts say the ATIC discovery is intriguing. That's because there are still some questions about what accelerates electrons and other charged particles in space, called cosmic rays.

"Even if it proves not to be dark matter, the puzzle of how very high-energy cosmic rays are produced is still a mystery, and this work will help shed some light on it," thinks Andy Taylor, an astrophysicist from the University of Edinburgh. *Journal reference: Nature (vol 456, p 362)*

Monkey gossip hints at social origins of language

* 19 November 2008 **by David Robson**

The discovery that female macaques are far chattier than males helps bolster the theory that human language evolved to forge social bonds **(Image: Pete Oxford / Naturepl.com)**

WOMEN may be fed up with being stereotyped as the chattier sex, but the cliché turns out to be true - in female-centric monkey groups at least. The gossipy nature of female macaques also adds weight to the theory that human language evolved to forge social bonds.

Many researchers think that language replaced grooming as a less time-consuming way of preserving close bonds in ever-growing societies.

Nathalie Greeno and Stuart Semple from Roehampton University in London hypothesised that if this was true then in species of animals with large social networks, such as macaques, vocal exchanges should be just as important as grooming.

The duo listened to a group of 16 female and eight male macaques living on Cayo Santiago island off Puerto Rico for three months. They counted the grunts, coos and girneys - friendly chit-chat between two individuals - while ignoring calls specific to the presence of food or a predator.

The team found that females made 13 times as many friendly noises as males. "The results suggest that females rely on vocal communication more than males due to their need to maintain the larger social networks," Greeno says.

Females were also much more likely to chat to other females than to males. Greeno suggests this is because female macaques form solid, long-lasting bonds as they stay in the same group for life and rely on their female friends to help them look after their offspring. In contrast, males, who rove between groups throughout their life, chatted to both sexes equally (Evolution and Human Behavior, DOI: 10.1016/j.evolhumbehav.2008.09.002).

The team say this is the first time that sex differences in communication in non-human primates have been identified.

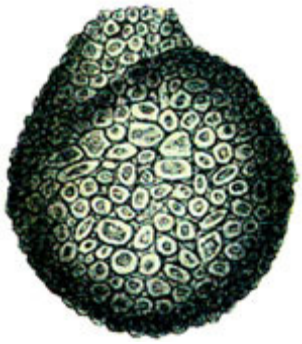
It is not known whether early human societies were female-centric, as macaques are, but the team believe that their findings support the theory that human language evolved to strengthen ties between individuals.

Klaus Zuberbühler from the University of St Andrews in the UK, who studies primate communication, agrees that the findings back the theory of language development.

In all social species, he says, communication "helps individuals navigate their daily social lives, usually by influencing the minds and behaviour of group members". He adds that communication helps resolve the tension between a species' "need to compete and a desire to cooperate".

Deep-sea protists may explain trace fossil evidence attributed to ancient animals

A new discovery challenges one of the strongest arguments in favor of the idea that animals with bilateral symmetry - those that, like us, have two halves that are roughly mirror images of each other - existed before their obvious appearance in the fossil record during the early Cambrian, some 542 million years ago. In the November 25th issue of Current Biology, a Cell Press publication, researchers report the first evidence that trace fossils interpreted by some as the tracks of ancient bilaterians could have instead been made by giant deep-sea protists, like those that can still be found at the seafloor to this day.



Gromia sphaerica

Protists are a diverse group of predominantly microscopic organisms. They are commonly single-celled with a single nucleus, but they may attain larger size by having many nuclei or forming colonies of identical, unspecialized cells. In the new study, the team describes macroscopic groove-like traces produced by living giant protists, known as Gromia sphaerica, which look something like a grape in terms of shape and size. Those grooves bear a remarkable resemblance to the trace fossils from the Precambrian, including ones as much as 1.8 billion years old.

"Our paper gives the precedent of a protozoan that is motile, produces macroscopic traces, and has a large hydrostatically supported body," said Mikhail Matz of the University of Texas at Austin. "With these possibilities demonstrated, pretty much anything within the Precambrian fossil record can in principle be attributed to large protozoans, from the earliest traces and fossils of the Stirling formation that are 1.8 billion years old to the weird Ediacaran biota with which the Precambrian culminated."

This new "protozoan option" takes the edge off the most compelling evidence of primitive bilaterians in the Precambrian that is so important for what has been called the "ancient school," he says. That line of thinking holds that the apparently explosive diversification of multicellular body plans during the Cambrian is an artifact of the fossil record; it suggests that bilaterians actually existed long before the Cambrian and evolved gradually over time. Others think instead that the Cambrian explosion really happened the way it appears that it did and that evolutionary mechanisms must therefore be sought to explain the rapid diversification.

The giant deep sea protist, Gromia sphaerica, approaches three large cup corals growing on a half-buried sea urchin.
Dr. Mikhail Matz, the University of Texas at Austin

"Previously one could say, 'There were traces, therefore there must have been bilaterians,' whereas now it is 'There were traces, therefore there may have been bilaterians,' which is, obviously, not nearly as strong a statement," Matz said.

He calls the findings a "classic case of scientific serendipity." They stumbled upon the giant protists while working on a project exploring the interaction between light and life in the ocean. "We were looking for pretty animals that have eyes, are colored, or glow in the dark," Matz said. "Instead, the most interesting find was the organism that was blind, brainless, and completely covered in mud."

Almost nothing is known about G. sphaerica, he added. His team is now deep sequencing the genes expressed in this giant protist and a few related protozoans to get a better idea about their evolutionary relationships to one another. They also plan to initiate a project on "deep-sea paleontology" to create a catalogue of traces produced by a variety of present-day animals. "There is surprisingly little data on this, so paleontologists have to resort to speculations a lot when interpreting fossil traces," Matz said.

The researchers include Mikhail V. Matz, University of Texas at Austin, Austin, TX; Tamara M. Frank, Harbor Branch Oceanographic Institute at Florida Atlantic University, Fort Pierce, FL; N. Justin Marshall, The University of Queensland, Brisbane, Queensland, Australia; Edith A. Widder, Ocean Research and Conservation Association, Fort Pierce, FL; and Sonke Johnsen, Duke University, Durham, NC, USA.

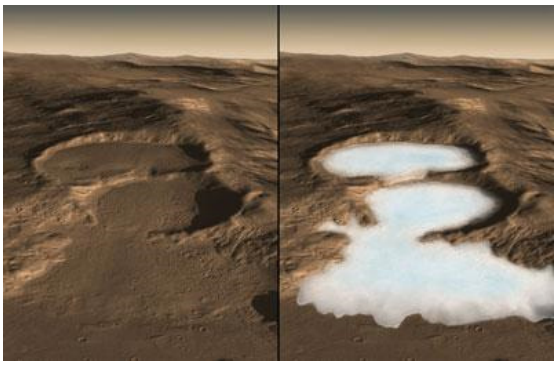
Vast stores of water ice surround Martian equator

* 19:30 20 November 2008 **by Rachel Courtland**

Ice glaciers hundreds of metres deep are lurking just underneath the Martian surface around the planet's mid-latitudes, new radar measurements suggest.

The discovery represents the largest cache of ice yet found beyond Mars's polar regions and bolsters the case that the planet's tilt changes periodically. The ice could also be an ideal place to study the ancient Martian climate and look for evidence of life.

The glaciers, found at latitudes between 30 and 60° in both the northern and southern hemispheres, sit underneath fields of rocky debris. The appearance of the landscape suggests the debris flowed from hills lying up to 20 kilometres away. Mars researchers have debated the origins of these rocky fields, which are called 'lobate debris aprons.' Some suspected that small particles of ice condensed from atmospheric water vapour between rocks and dust; this ice could lubricate the material, allowing it to flow down slopes. Others suggested the rocky aprons actually hid large glaciers.



"There's been this debate about what's inside," says John Holt of the University of Texas at Austin. To investigate, Holt and colleagues used radar aboard NASA's Mars Reconnaissance Orbiter to probe the aprons around hills and mountains in the mid-latitude regions of Mars.

Three Martian craters: the actual surface is on the left, and without debris is on the right. **(Credit: NASA, University of Texas at Austin)**

Tilting axis

Most of the radar signal bounced off the ground, but some reached though the upper layer of rock to bounce around the interior of large ice deposits. The deposits in Mars's eastern Hellas basin alone contain an 800-metre-thick glacier and hide 28,000 cubic kilometres of water ice - enough to coat the entire planet with a layer of water 20 cm thick.

The glaciers likely formed during a time when Mars's pole pointed more towards the Sun, says co-author James Head of Brown University in Providence, Rhode Island. Because Mars lacks a massive moon that can stabilise its tilt, the planet is thought to wobble dramatically every 120,000 years or so.

When its poles were tilted more towards the Sun during one such wobble, the more intense sunlight could have heated ice at the poles. That caused the ice to sublimate into the atmosphere and then condense down into solid ice again in areas near the equator - which at that time were colder, Head says. Rocky debris from nearby slopes then fell on the icy deposits.

Insulating layer

Over time, the upper layer of ice vaporised into the thin Martian atmosphere, concentrating the rocks so they formed an insulating layer. These rocks prevented the glacier from melting entirely when the Sun once again drenched the mid-latitude regions. "It's kind of like the Hotel California. The ice checks in but it doesn't check out. It doesn't go back to the poles," Head told New Scientist. "[The deposits] tell you that significant amounts of water vapour can be transported from the poles to the mid-latitudes and that some of it - a lot of it - is still there."

The relatively warm weather could make the mid-latitude glaciers an ideal site to explore on future Mars missions. Like glaciers in Antarctica's Dry Valleys, the ice deposits could hold gas bubbles that could reveal what the Martian atmosphere was like in the past, allowing researchers to build up a better picture of the planet's past climate, Head says. The ice could also preserve evidence of life. *Journal reference: Science (vol 322, p 1235)*

Lactic acid found to fuel tumors

DURHAM, N.C., and BRUSSELS, BELGIUM - A team of researchers at Duke University Medical Center and the Université catholique de Louvain (UCL) has found that lactic acid is an important energy source for tumor cells. In further experiments, they discovered a new way to destroy the most hard-to-kill, dangerous tumor cells by preventing them from delivering lactic acid.

"We have known for more than 50 years that low-oxygen, or hypoxic, cells cause resistance to radiation therapy," said senior co-author Mark Dewhirst, DVM, Ph.D., professor of radiation oncology and pathology at Duke. "Over the past 10 years, scientists have found that hypoxic cells are also more aggressive and hard to treat with chemotherapy. The work we have done presents an entirely new way for us to go after them."

Many tumors have cells that burn fuel for activities in different ways. Tumor cells near blood vessels have adequate oxygen sources and can either burn glucose like normal cells, or lactic acid (lactate). Tumor cells further from vessels are hypoxic and inefficiently burn a lot of glucose to keep going. In turn, they produce lactate as a waste product.

Tumor cells with good oxygen supply actually prefer to burn lactate, which frees up glucose to be used by the less-oxygenated cells. But when the researchers cut off the cells' ability to use lactate, the hypoxic cells didn't get as much glucose.

For the dangerous hypoxic cells, "it is glucose or death," said Pierre Sonveaux, professor in the UCL Unit of Pharmacology & Therapeutics and lead author of the study, published in the Nov. 20 online edition of the Journal of Clinical Investigation. He formerly worked with Dr. Dewhirst at Duke.

The next challenge was to discover how lactate moved into tumor cells. Because lactate recycling exists in exercising muscle to prevent cramps, the researchers imagined that the same molecular machinery could be used by tumor cells.

"We discovered that a transporter protein of muscle origin, MCT1, was also present in respiring tumor cells," said Dewhirst. The team used chemical inhibitors of MCT1 and cell models in which MCT1 had been deleted to learn its role in delivering lactate. "We not only proved that MCT1 was important, we formally demonstrated that MCT1 was unique for mediating lactate uptake," said Professor Olivier Feron of the UCL Unit of Pharmacology & Therapeutics.

Blocking MCT1 did not kill the oxygenated cells, but it nudged their metabolism toward inefficiently burning glucose. Because the glucose was used more abundantly by the better-oxygenated cells, they used up most of the glucose before it could reach the hypoxic cells, which starved while waiting in vain for glucose to arrive. "This finding is really exciting," Dewhirst said. "The idea of starving hypoxic cells to death is completely novel."

Even though hypoxic tumor cells have been identified as a cause of treatment resistance for decades, there has not been a reliable method to kill them. "They are the population of cells that can cause tumor relapse," said Professor Feron.

A significant advantage of the new strategy is that a new drug does not need to reach hypoxic cells far from blood vessels and it does not need to enter into cells at all – it merely needs to block the transporter molecule that moves the lactose, which is outside of the cells. "This finding will be really important for drug development," said Sonveaux.

The researchers also showed in mice that radiation therapy along with MCT1 inhibition was effective for killing the remaining tumor cells, those nearest the blood vessels. This proved to be a substantial antitumor approach.

The study was funded by grants from the National Institutes of Health; the Belgian American Educational Foundation (BAEF); from governmental foundations, F.R.S.-FNRS, Communauté française de Belgique and Région wallonne; and the J. Maisin and St. Luc Foundations in Belgium. Other authors included, from Duke University Medical Center: Thies Schroeder, Melanie C. Wergin, Zahid N. Rabbani, and Kelly M. Kennedy from the Department of Radiation Oncology; Michael J. Kelley, from the Division of Hematology and Medical Oncology; and Miriam L. Wahl from the Department of Pathology. And from the Université catholique de Louvain (UCL), in Brussels, Belgium: Frédérique Végran, Julien Verrax, and Christophe J. De Saedeleer from the Unit of Pharmacology & Therapeutics; and Caroline Diepart, Bénédicte F. Jordan, and Bernard Gallez of the Unit of Biomedical Magnetic Resonance.

Oh, what a feeling!

Brain-injured recover emotional perception skills

People who have lost the ability to interpret emotion after a severe brain injury can regain this vital social skill by being re-educated to read body language, facial expressions and voice tone in others, according to a new study. The research, published in the Journal of Head Trauma Rehabilitation, reveals that appropriate training can result in significant gains in "emotional perception", which is crucial for successful social communication.

The study involved 18 participants recruited from an outpatient service at the Liverpool Hospital Brain Injury Rehabilitation Unit, in Sydney, Australia. All had experienced a severe traumatic brain injury at least six months earlier and had significantly impaired ability to interpret emotions in others.

Observations by clinicians or the participants themselves had identified chronic social difficulties or isolation, an apparent disregard or a lack of awareness of social cues, or inappropriate social responding.

Someone who has suffered traumatic brain injury - commonly due to a blow to the skull - can lose the ability to accurately read other people's emotional cues, which may make their social behaviour awkward, badly timed or miscalculated, notes the study's lead author, UNSW clinical psychologist, Dr Cristina Bornhofen.

"These people find it difficult to integrate the cluster of non-verbal cues that accompany speech," says Bornhofen. "Their inability to interpret emotional expression causes significant frustration because it impairs their social competence." They may have difficulty interpreting an emotion such as sarcasm, for example, in which a positive verbal message is paired with a voice tone and facial expression intended to convey a meaning opposite to the verbal message.

Traditional treatments have emphasised training in positive social behaviours, such as turn-taking, giving compliments, and reducing undesirable behaviours, such as excessive talking and inappropriate conversation topics, Dr Bornhofen says. However, these programs have had limited success. "Good social communication is possible only if people can effectively use feedback, such as that provided by the emotional responses of others. Behaviourally-oriented programs have tended to neglect this critical aspect of social skills," she says.

Using photographs and videos, the participants were tested before and after the program on an array of outcomes: independent living skills, psycho-social health, and emotional discrimination tasks requiring them to identify emotions such as happiness, sadness, anger, anxiety, disgust and surprise.

Earlier research had suggested that the accurate perception of emotional cues requires a variety of cognitive skills involving several brain regions and pathways, which are yet to be clearly defined. Dr Bornhofen and her co-researcher, Professor Skye McDonald, therefore compared two broadly different treatment regimes, randomly assigning program participants to each treatment.

The first, known as "self-instruction training", taught patients to answer questions by using a set of strategic questions to guide them through emotion discrimination tasks, using questions such as: What is it am I deciding about? What do I already know about it? What do I need to look or listen for?

The second regime, called "errorless learning", began with extremely easy discriminations, providing extensive practice at each stage and strongly discouraged learners from guessing when unsure. For example, repeated practice of identifying patterns associated with basic emotions (such as wide eyes and raised eyebrows in surprise) was carried out using line drawings of basic expressions laid out on a table alongside a card with the words "not sure." Participants were encouraged to point to "not sure" rather than guess the answer, and were positively acknowledged whenever they did so. Both regimes were carefully designed to ensure that participants received comparable levels of positive feedback and therapeutic attention in each.

"The results suggested that self-instruction training was slightly better at improving program participants' ability to judge facial expressions from photographs, and deciding whether someone was speaking sarcastically, on the basis of a speaker's emotional demeanour," says Dr Bornhofen.

Informal subjective reports from treatment group members and their relatives revealed improvements in the participants' ability to understand the emotional state of others during day-to-day interactions and an increased confidence in their ability to successfully engage in social contexts.

The sister of one study participant said: "My brother is engaging better with his children and they are enjoying doing more things with him. He is enjoying a far better relationship with his parents. His anger and frustration have virtually disappeared and he is achieving well at work. His sense of humour has returned and he can laugh off things that would once trouble him deeply. The impact of the program has been life changing."

"The results are cause for optimism that people suffering traumatic brain injuries can be retrained to identify emotions in others, and to begin functioning normally again," says Bornhofen. "Overall, self-instruction training appears to be the most beneficial strategy for teaching emotion perception skills to most traumatically brain injured patients, although further research is required to substantiate this finding. We are continuing research in this direction, and, in the meantime, we are preparing to publish the treatment program in manual form so that clinicians can utilise the best of the materials and techniques in their work with patients.

"As there are currently no other evidence-based treatment materials available for this kind of rehabilitation with people who have brain injuries, we believe the work will be of great assistance. We have already had numerous requests for the program, especially from the U.S., where the growing number of returning armed service personnel with head injuries is raising awareness in this area."

Uncertainty Can Be More Stressful Than Clear Negative Feedback

We are faced with uncertainty every day. Will our investments pay off? Will we get the promotions we are hoping for? When faced with the unknown, most people experience some degree of anxiety and discomfort. Exactly how much anxiety someone experiences during uncertain times depends on his or her personality profile. In particular, it is the personality trait of Neuroticism that predicts how distressed people will be when confronted with the unknown.

In a new study published in Psychological Science, a journal of the Association for Psychological Science, University of Toronto psychologists Jacob Hirsh and Michael Inzlicht examined whether neurotic individuals would react more strongly to clear negative information or to uncertainty. The researchers administered a computerized time-estimation task, in which the participants had to indicate when they thought one second had passed from the appearance of a symbol on the screen. The participants were then given clear positive, clear negative, or uncertain feedback (i.e., a question mark). All the while, the researchers measured the participants' brain activity using electroencephalography (EEG).

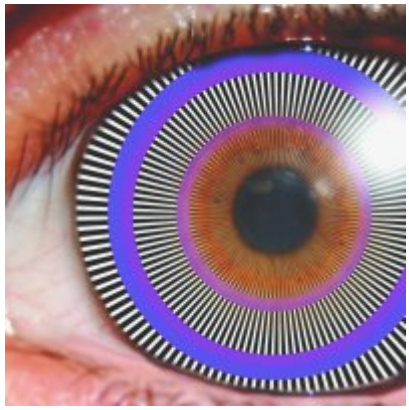
Hirsh and Inzlicht focused on the responses of the anterior cingulate cortex (ACC), a brain area associated with error-monitoring and conflict-related anxiety, instrumental in regulating our behavior to environmental change. The results were clear: stronger responses were observed in this brain region in neurotic individuals when they were given uncertain feedback compared to when they were given unambiguous negative feedback.

In other words, neurotic individuals experience an immediate, uncomfortable response to uncertainty, even more so than when they are faced with clear negative information. This suggests that neurotic individuals

would rather receive clear negative feedback than uncertain feedback, even though the outcome of the uncertain feedback could potentially be positive. “Uncertainty can be very stressful,” says Hirsh, “and high levels of Neuroticism contribute to this dislike of the unknown.” The results of this study have important implications for human behavior, as they suggest that some individuals, namely those high in Neuroticism, “prefer the devil they know over the devil they do not know.”

Barrow scientists solve 200-year-old scientific debate involving visual illusions

Neuroscientists at Barrow Neurological Institute at St. Joseph's Hospital and Medical Center have discovered a direct link between eye motions and the perception of illusory motion that solves a 200-year-old debate.



Stephen Macknik, PhD, director of the Laboratory of Behavioral Neurophysiology; Susana Martinez-Conde, PhD, director of the Laboratory of Visual Neuroscience; Xoana G. Troncoso, PhD; and Jorge Otero-Millan; conducted a study based on the Enigma painting, a visual illusion in which rotational motion is seen within a stationary image. The artwork has been at the center of a debate over whether the brain or the eye is behind the perception of illusory motion.

Dr. Martinez-Conde's laboratory recently discovered that microsaccades, a small, unconscious eye movement that occurs when humans fixate their eyes, are critical to normal vision. The team of scientists conducted the Enigma study to see if microsaccades are also behind the perception of this illusion. Based on their study, the hypothesis suggesting the illusion originates solely in the brain was ruled out.

Participants in the study observed the Enigma illusion while their eye movements were simultaneously recorded with high precision cameras. Microsaccade rates increased before the illusionary motion sped up and decreased before the motion slowed, revealing a direct link between the eye movements and the illusion.

"We have discovered that this illusion originates with eye movements and not solely the brain as previously thought," says Dr. Martinez-Conde. "The findings from the study could help design future prosthetics for patients with brain damage or brain lesions that affect the perception of motion."

Gallery: *Ape artists* raise funds for conservation

* 16:00 20 November 2008 **by Lucy Dodwell**

This painting features the brush strokes of Popi and Katy, two orangutans who recently retired from entertainment, added to a canvas with a black circle painted by Pennsylvania artist Sue Buck

An art exhibition showcasing colourful paintings by bonobos and orangutans is on until the 30th November in West Des Moines, Iowa, US.

Apes Helping Apes is held by the Great Ape Trust, a scientific institute that studies great ape intelligence and behaviour. The proceeds from the sale of the original paintings will go towards raising money to help conserve great apes in the wild.

This painting features the brush strokes of Popi and Katy, two orangutans who recently retired from entertainment, added to a canvas with a black circle painted by Pennsylvania artist Sue Buck *See a gallery of the apes' paintings*

Last year $16,725 was raised by the exhibition and this supported the Gishwati Area Conservation Program in Rwanda and the Ketambe Research Center on the Indonesian island of Sumatra.

Orangutans and bonobos are given the choice of whether they want to paint - and according to the Great Ape Trust, their daily lives are enriched immeasurably by such creative activities. The Trust also states that skills such as choosing canvases and colours and whether to make small, careful marks or big dramatic ones, are all within the ape's control.

Observatory

Invasive Plants in Galápagos May Really Be Native

By HENRY FOUNTAIN

For years, conservationists have been concerned about the impact of invasive plant species in the Galápagos Islands. Hundreds of species have been identified as being nonnative, introduced through human contact. The idea is to remove these plants to help keep the archipelago ecologically pristine.

That’s a worthy goal. But there’s just one problem, according to a study in Science: some of these pariah plants turn out to be native after all. They predate humans in the Galápagos by thousands of years.

The evidence for this is in the form of fossilized pollen grains found in sediment cores from bogs on Santa Cruz island in the heart of the archipelago. Jacqueline F.N. van Leeuwen of the University of Bern in Switzerland and Cynthia A. Froyd of Oxford University in England and colleagues identified pollen of six species that earlier studies had concluded were probably nonnative. Pollen was found in samples up to 8,200 years old; it is generally agreed that the first humans to reach the Galápagos were Europeans, in 1535.

Among the species revealed to be native are billy goat weed (Ageratum conyzoides) and swamp hibiscus (Hibiscus diversifolius). Swamp hibiscus appears to be spreading on Santa Cruz, which had been seen as evidence of its invasiveness, but instead it may just be reclaiming habitat that was lost over time.

Most of these plants are widespread throughout the Pacific, so the researchers suggest that similar paleoecological studies on other islands will help determine whether these species, and perhaps many others, have wrongly been categorized as well.

Hairspray is linked to common genital birth defect, says study

Women who are exposed to hairspray in the workplace during pregnancy have more than double the risk of having a son with the genital birth defect hypospadias, according to a new study published today in the journal Environmental Health Perspectives.

The study is the first to show a significant link between hairspray and hypospadias, one of the most common birth defects of the male genitalia, where the urinary opening is displaced to the underside of the penis. The causes of the condition are poorly understood.

Women have a two to three-fold increased risk of having a son with hypospadias if they are exposed to hairspray in the workplace in their first trimester of pregnancy, according to the new study, by researchers from Imperial College London, University College Cork and the Centre for Research in Environmental Epidemiology in Barcelona.

The study suggests that hairspray and hypospadias may be linked because of chemicals in hairspray known as phthalates. Previous studies have proposed that phthalates may disrupt the hormonal systems in the body and affect reproductive development.

It is thought that hypospadias affects around 1 in 250 boys in the UK and in the USA, although estimates about prevalence vary. Usually, hypospadias can be successfully treated with corrective surgery after a boy reaches his first birthday, but more severe cases can lead to problems with urinating, sexual relations and fertility.

The new research also reveals that taking folic acid supplements in the first three months of pregnancy is associated with a 36 percent reduced risk of bearing a child with the condition. The UK Department of Health already recommends that folic acid supplements are taken up until the twelfth week of pregnancy in order to prevent neural tube defects such as spina bifida.

Previous smaller studies had suggested that hypospadias might be linked to vegetarianism but the new study did not show any increased risk in women who had a vegetarian diet during pregnancy.

Professor Paul Elliott, the corresponding author of the research from the Department of Epidemiology and Public Health at Imperial College London, said: "Hypospadias is a condition that, if left untreated, can cause problems in later life. Although surgery to correct it is usually successful, any surgery will be traumatic for the child and his parents. It is encouraging that our study showed that taking folic acid supplements in pregnancy may reduce the risk of a child being born with the condition. Further research is needed to understand better why women exposed to hairspray at work in the first 3 months of pregnancy may have increased risk of giving birth to a boy with hypospadias."

The researchers reached their conclusions after conducting detailed telephone interviews with 471 mothers whose sons had been referred to surgeons for hypospadias and 490 controls, across 120 London Boroughs and Local Authority Districts.

The questionnaires explored a range of aspects of the women's health and lifestyle, including the mother's occupation and possible exposure to different chemical substances, family history of disease, maternal occupation, vegetarianism, smoking and use of folate supplements.

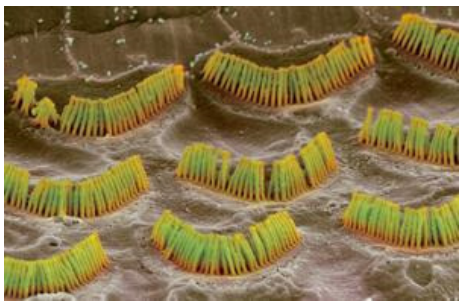
The study was funded by a grant from the UK Health and Safety Executive, the Department of Health, the Department of the Environment, Transport and The Regions and the European Chemical Industry Council.

Light opens up a world of sound for the deaf

* 21 November 2008 **by Rachel Nowak**

INFRARED light can stimulate neurons in the inner ear as precisely as sound waves, a discovery that could lead to better cochlear implants for deaf people.

A healthy inner ear uses hair cells that respond to sound to stimulate neurons that send signals to the brain. But hair cells can be destroyed by disease or injury, or can contain defects at birth, leading to deafness. In such cases, cochlear implants can directly stimulate neurons.



The hearing provided by today's implants is good enough to enable deaf children to develop speech skills that are remarkably similar to hearing children's. Implant users still find it tough to appreciate music, communicate in a noisy environment and understand tonal languages like Mandarin, however. That's because the implants use only 20 or so electrodes, a small number compared to the 3000-odd hair cells in a healthy ear.

Infrared light can stimulate neurons in the inner ear as precisely as sound waves, a discovery that could lead to better cochlear implants **(Image: Steve Gschmeissner/SPL)**

More sources of stimulation should make hearing clearer but more electrodes cannot be packed in because tissue conducts electricity, so signals from different electrodes would interfere. In contrast, laser light targets nerves more precisely and doesn't spread, which could allow an implant to transmit more information to the neurons.

To explore this idea, a team led by Claus-Peter Richter at Northwestern University in Chicago shone infrared light directly onto the neurons in the inner ear of deaf guinea pigs. At the same time, the researchers recorded electrical activity in the inferior colliculus, a relay between the inner ear and the brain cortex, producing a set of frequency "maps". These maps are a good indication of the quality of sound information sent to the brain.

Electrical stimulation of the inner ear by a cochlear implant produces blurred maps, but the light stimulation produced maps that were as sharp as those produced by sound in hearing guinea pigs, says Richter, who presented the findings at the Medical Bionics conference in Lorne, in the Australian state of Victoria, earlier this week.

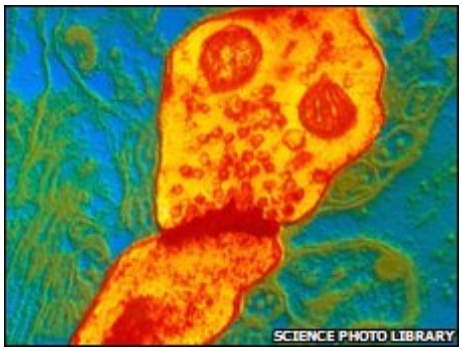
It is a mystery how light stimulates the neurons, as they do not contain light-sensitive proteins. The phenomenon was discovered by surgeons attempting to "weld" nerves with heat from a laser. Richter says the heat that accompanies the light may play a role, and his team is now investigating the long-term effects of heating neurons. Making fibre optics and lasers to target light in the inner ear is the next challenge.

IBM to build brain-like computers

By Jason Palmer Science and technology reporter, BBC News

IBM has announced it will lead a US government-funded collaboration to make electronic circuits that mimic brains. Part of a field called "cognitive computing", the research will bring together neurobiologists, computer and materials scientists and psychologists.

As a first step in its research the project has been granted $4.9m (£3.27m) from US defence agency Darpa. The resulting technology could be used for large-scale data analysis, decision making or even image recognition.



"The mind has an amazing ability to integrate ambiguous information across the senses, and it can effortlessly create the categories of time, space, object, and interrelationship from the sensory data," says Dharmendra Modha, the IBM scientist who is heading the collaboration.

"There are no computers that can even remotely approach the remarkable feats the mind performs," he said.

"The key idea of cognitive computing is to engineer mind-like intelligent machines by reverse engineering the structure, dynamics, function and behaviour of the brain."

Mimicking synapses like this one is crucial to the effort

'Perfect storm'

IBM will join five US universities in an ambitious effort to integrate what is known from real biological systems with the results of supercomputer simulations of neurons. The team will then aim to produce for the first time an electronic system that behaves as the simulations do. The longer-term goal is to create a system with the level of complexity of a cat's brain.

Prof Modha says that the time is right for such a cross-disciplinary project because three disparate pursuits are coming together in what he calls a "perfect storm".

Neuroscientists working with simple animals have learned much about the inner workings of neurons and the synapses that connect them, resulting in "wiring diagrams" for simple brains.

Supercomputing, in turn, can simulate brains up to the complexity of small mammals, using the knowledge from the biological research. Modha led a team that last year used the BlueGene supercomputer to simulate a mouse's brain, comprising 55m neurons and some half a trillion synapses.

"But the real challenge is then to manifest what will be learned from future simulations into real electronic devices - nanotechnology," Prof Modha said.

Technology has only recently reached a stage in which structures can be produced that match the density of neurons and synapses from real brains - around 10 billion in each square centimetre.

Networking

Researchers have been using bits of computer code called neural networks that seek to represent connections of neurons. They can be programmed to solve a particular problem - behaviour that appears to be the same as learning. But this approach is fundamentally different. "The issue with neural networks and artificial intelligence is that they seek to engineer limited cognitive functionalities one at a time. They start with an objective and devise an algorithm to achieve it," Prof Modha says.

"We are attempting a 180 degree shift in perspective: seeking an algorithm first, problems second. We are investigating core micro- and macro-circuits of the brain that can be used for a wide variety of functionalities."

The problem is not in the organisation of existing neuron-like circuitry, however; the adaptability of brains lies in their ability to tune synapses, the connections between the neurons.

Synaptic connections form, break, and are strengthened or weakened depending on the signals that pass through them. Making a nano-scale material that can fit that description is one of the major goals of the project.

"The brain is much less a neural network than a synaptic network," Modha says.

First thought

The fundamental shift toward putting the problem-solving before the problem makes the potential applications for such devices practically limitless. Free from the constraints of explicitly programmed function, computers could gather together disparate information, weigh it based on experience, form memory independently and arguably begin to solve problems in a way that has so far been the preserve of what we call "thinking".

"It's an interesting effort, and modelling computers after the human brain is promising," says Christian Keysers, director of the neuroimaging centre at University Medical Centre Groningen. However, he warns that the funding so far is likely to be inadequate for such an large-scale project.

That the effort requires the expertise of such a variety of disciplines means that the project is unprecedented in its scope, and Dr Modha admits that the goals are more than ambitious.

"We are going not just for a homerun, but for a homerun with the bases loaded," he says.

Nature Medicine study shows Peregrine's bavituximab can cure lethal virus infections

PS-targeting antibodies may represent a new class of drugs with broad potential to treat viral infections

TUSTIN, Calif., November 23, 2008 -- Peregrine Pharmaceuticals, Inc. (NASDAQ: PPHM) today reported publication of data in Nature Medicine that supports the broad anti-viral potential of the company's novel anti-phosphatidylserine (anti-PS) antibody platform, showing that its PS-targeting drug bavituximab can cure lethal virus infections in animal disease models.

Bavituximab is in clinical trials for the treatment of hepatitis C virus (HCV) infection and in preclinical development for the treatment of viral hemorrhagic fevers under a contract worth up to $44.4 million with the bioterrorism program of the U.S. Defense Threat Reduction Agency (DTRA). Bavituximab and other anti-PS antibodies are also being studied preclinically in HIV, cytomegalovirus (CMV) and other serious viral infections.

"Based on these findings, anti-PS antibodies such as bavituximab may represent a completely new class of drugs for the treatment of life-threatening viral infections," said study co-author Dr. Philip Thorpe, professor of pharmacology at UT Southwestern Medical Center and a scientific advisor to Peregrine. "By targeting a property of the host cell rather than the virus itself, anti-PS antibodies have the potential to treat a range of viral infections, and they should be less susceptible to the viral mutations that contribute to the development of drug resistance."

In the research reported today, scientists at UT Southwestern assessed the activity of bavituximab in animal models of two lethal viruses--cytomegalovirus and Lassa fever virus, a hemorrhagic fever virus that is listed as a class A bioterrorism agent by the CDC. Bavituximab showed potent anti-viral activity in both models.

Dr. Melina Soares, lead study author and UT Southwestern instructor of pharmacology, commented, "Recent non-affiliated research has further confirmed that exposed PS has immunosuppressive properties and is also clarifying its involvement during viral infection of cells. Our data go a step further, providing compelling

evidence that exposed PS itself is a promising anti-viral drug target that is involved in the pathogenesis of multiple viruses, suggesting the possibility of achieving broad-spectrum anti-viral effects using a single anti-PS agent. We look forward to further exploring the potential of bavituximab and other anti-PS antibodies against viruses for which there are few or no effective therapeutic options."

In the first study, 100% of mice infected with lethal murine CMV and treated with bavituximab recovered fully, while only 25% of control animals survived. In the second study, guinea pigs were infected with lethal Pichinde virus, which is a model virus for Lassa fever. Fifty percent of the bavituximab-treated group survived, while untreated animals all died. In this study, the anti-viral effect of bavituximab was further augmented by the addition of the standard of care drug ribavirin, with 63% of animals receiving the combination therapy surviving the potentially lethal infection.

"We are extremely pleased to see this research demonstrating the broad anti-viral potential of bavituximab and our anti-PS technology platform published in this highly regarded journal," said Steven W. King, president and CEO of Peregrine. "This new publication is the latest in a series of external validations of our anti-viral program. It follows a recently awarded federal government contract for assessment of anti-PS antibodies to treat viral hemorrhagic fevers, research on the role of PS in viral infections that was published in a leading science journal earlier this year, and a recent presentation on anti-PS antibodies at a global HIV conference."
Mr. King added, "Better prevention and treatment of viral diseases are urgently needed, and we are increasingly optimistic that bavituximab and our other anti-PS antibodies could be valuable contributors to the field."

PS is a lipid molecule normally found on the inside of cell membranes that "flips" and becomes exposed on the outside of the membranes of enveloped viruses and virally infected cells. Exposed PS enables viruses to evade immune recognition and dampens the body's normal responses to infection. By masking the exposed PS, bavituximab and other anti-PS antibodies may block these effects and allow the body to develop a robust immune response to the viral pathogen. Anti-PS antibodies have been shown to help clear infectious virus from the bloodstream and to induce antibody-dependent cellular cytotoxicity, an important anti-viral immune response.

Researchers have found that PS is exposed on the outer membrane of cells infected with HIV, influenza (including avian flu), herpes simplex viruses, hemorrhagic fever viruses, measles and members of the small pox and rabies virus families.

Dr. Barton Haynes, director of Duke University's Human Vaccine Institute and the Center for HIV/AIDS Vaccine Immunology (CHAVI) is currently investigating PS as a potential target for preventing HIV infection. He commented, "Targeting a host cell lipid such as PS as an anti-viral strategy is an intriguing concept that may have relevance for new therapeutic and possibly prophylactic innovations in a number of virus infections."

Peregrine's research assessing the therapeutic potential of anti-PS antibodies against hemorrhagic fever viruses was originally funded by a grant from the National Institutes of Allergy and Infectious Diseases (NIAID). The results discussed in today's study contributed in part to the June 2008 receipt by Peregrine of an award from the biodefense program of the DTRA, an agency of the U.S. Department of Defense, potentially worth up to $44.4 million over five years for the development of bavituximab and similar PS-targeting antibodies as potential therapies against hemorrhagic fever viruses.
The studies reported today were conducted by Drs. Melina Soares and Philip Thorpe and colleagues at UT Southwestern Medical Center and are published in the November 23, 2008 on-line edition and December 2008 published edition of Nature Medicine. For more information, visit http://www.nature.com/nm/index.html

Scripps research team defines new painkilling chemical pathway

Discovery could lead to new pain treatments

Marijuana kills pain by activating a set of proteins known as cannabinoid receptors, which can also regulate appetite, inflammation, and memory. The body also has chemicals known as endocannabinoids that naturally activate these same receptors, namely N-arachidonoyl ethanolamine (AEA) and 2-arachidonoylglycerol (2-AG). These natural components of the cannabinoid system remain the focus of intense efforts to develop new treatments not only for chronic pain, but also for obesity, anxiety, and depression. However, until the new paper, specific methods to study 2-AG signaling have been lacking.

AEA's activity has been well understood for years. In past research, Cravatt and his team identified an enzyme called fatty acid amide hydrolase, or FAAH, that breaks down AEA, effectively reducing its pain killing activity. A number of compounds are now in clinical development that target and breakdown FAAH, allowing AEA to build up, reducing pain. However, FAAH does not control 2-AG metabolism in vivo, and therefore, the potential biological functions and therapeutic potential of this second endocannabinoid have remained largely unknown.

Teasing out 2-AG's specific impacts have proven challenging. Comparable to FAAH, an enzyme called monoacylglycerol lipase (MAGL) breaks down 2-AG. But, despite numerous attempts, no group had been able to develop a chemical that inhibits MAGL specifically.

"The tools - selective and efficacious MAGL inhibitors - just weren't there, " says Jonathan Long, a graduate student of the Scripps Research Kellogg School of Science and Technology who is a member of the Cravatt lab and a first author of the new paper.

But now, a MAGL-specific inhibitor is finally available, thanks to the lab's new work. Key to this success was Activity-Based Protein Profiling, a unique chemical technique the group devised and has used fruitfully in other inhibitor hunts. This system enables the rapid engineering and testing of chemical compounds against many members of enzyme families, in hope of finding effective and selective inhibitors.

For this project, the group developed about 200 compounds and found that one was a highly effective block for MAGL. The scientists dubbed the compound JZL184, named after Long's initials and the order in the series of potential inhibitors tested. JZL184 effectively blocks only MAGL among more than 40 related brain enzymes, which opened the door for the first definitive study of 2-AG's activity.

A New View of 2-AG

Unlike increased AEA, which causes only reduced pain sensation, the team found that MAGL inhibition using JZL184, and the resulting increase in 2-AG concentration, not only reduced pain in mice, but also induced other effects associated with the cannabinoid receptors, namely hypothermia and decreased movement. "This really does suggest a sort of segregation of labor, if you will," says Cravatt of the differential effects of elevating AEA versus 2-AG as part of the overall function of the cannabinoid system. "That, I think, is a truly unique result."

While treatments based on inhibiting FAAH show great promise for controlling pain, manipulating MAGL levels could also be a boon for treatment development, especially if 2-AG's other effects, such as hypothermia, can be managed. "There are so many different types of pain," Cravatt says, "that it's possible some types could be more effectively treated with one treatment than another."

In addition to Cravatt and Long, authors on the paper, titled "Selective blockade of 2-arachidonoylglycerol hydrolysis produces cannabinoid behavioral effects," were Weiwei Li, Lamont Booker, Franciso Pavón, Antonia Serrano, and Loren Parsons, of the Scripps Research Institute, and James Burston, Steven Kinsey, Joel Schlosburg, Dana Selley, and Aron Lichtman, of Virginia Commonwealth University.

This research was supported by the National Institutes of Health, the Helen L. Dorris Child and Adolescent Neuro-Psychiatric Disorder Institute, and the Skaggs Institute for Chemical Biology.

Scientists discover 21st century plague

Bacteria that can cause serious heart disease in humans are being spread by rat fleas, sparking concern that the infections could become a bigger problem in humans. Research published in the December issue of the Journal of Medical Microbiology suggests that brown rats, the biggest and most common rats in Europe, may now be carrying the bacteria.

Since the early 1990s, more than 20 species of Bartonella bacteria have been discovered. They are considered to be emerging zoonotic pathogens, because they can cause serious illness in humans worldwide from heart disease to infection of the spleen and nervous system. "A new species called Bartonella rochalimae was recently discovered in a patient with an enlarged spleen who had travelled to South America," said Professor Chao-Chin Chang from the National Chung Hsing University in Taiwan. "This event raised concern that it could be a newly emerged zoonotic pathogen. Therefore, we decided to investigate further to understand if rodents living close to human environment could carry this bacteria."

Scientists have found that rodents carry several pathogenic species of Bartonella, such as B. elizabethae, which can cause endocarditis and B. grahamii, which was found to cause neuroretinitis in humans. Although scientists are unsure about the main route of transmission, these infections are most likely to be spread by fleas. Ctenophthalmus nobilis, a flea that lives on bank voles, was shown to transmit different species of Bartonella bacteria. These pathogens have also been found in fleas that live on gerbils, cotton rats and brown rats.

"We analysed bacteria found in Rattus norvegicus in Taiwan. The brown rat is also the most common rat in Europe," said Professor Chang. "By analysing the DNA of the bacteria, we discovered a strain that is most closely related to B. rochalimae, which has been isolated recently from a human infection in the United States".

The researchers took samples from 58 rodents, including 53 brown rats, 2 mice (Mus musculus) and 3 black rats (Rattus rattus). 6 of the rodents were found to be carrying Bartonella bacteria; 5 of these were brown rats. Four of the rodents were carrying B. elizabethae, which can cause heart disease in humans, and one of the black rats was found to be harbouring B. tribocorum. However, the scientists noticed one strain that had not been identified in rodents previously. The strain was finally shown to be close to B. rochalimae.

"Because of the small sample size used in this study, we cannot say for sure that the common brown rat is spreading B. rochalimae," said Professor Chang. "However, several different Bartonella bacteria are surely transmitted by rodents. These results raise concerns about the existence of other reservoirs and vectors for this emerging infection. This certainly warrants further investigation."