Erectile dysfunction may signal a broken heart

ED not only interferes with romance, it warns of future heart disease

Erectile dysfunction is always a matter of the heart, but new research shows that more than romance is at stake. Two new studies of men with type 2 diabetes found that erectile dysfunction (ED) was a powerful early warning sign for serious heart disease, including heart attack and death.

One of the studies also showed that cholesterol-lowering medications could cut the risk of heart problems by about one-third—and suggested that Viagra and other compounds in the same drug family might offer similar protection.

The research, which was published in the May 27, 2008, issue of the Journal of the American College of Cardiology (JACC), underscores the importance of encouraging men to report ED to their physicians, and of focusing treatment not only on overcoming sexual dysfunction but also on improving overall cardiovascular health.

"The development of erectile dysfunction should alert both patients and healthcare providers to the future risk of coronary heart disease," said Peter Chun-Yip Tong, Ph.D., an associate professor in the Department of Medicine & Therapeutics at The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong. "Other risk factors such as poor blood glucose control, high blood pressure, high cholesterol levels, smoking and obesity should be reviewed and addressed aggressively."

Diabetes, erectile dysfunction and heart disease share an ominous link: damage to the blood vessels by high blood sugar levels. The same process that hinders the extra blood flow needed to maintain an erection can have even more serious consequences in the heart. "The first event is probably endothelial dysfunction—when the smoothness and reactivity of the blood vessel are damaged," said Dr. Tong. "This process encourages local inflammation on the inner surface of the blood vessels and the deposition of cholesterol, resulting in formation of clots and atherosclerosis. Therefore, there is a high risk of blockage of blood vessels in the heart, which can lead to a heart attack."

Men typically show signs of ED more than three years before the onset of symptoms of coronary heart disease. In one study of diabetic men, symptoms of ED always preceded coronary symptoms.

In the Hong Kong-based study, Dr. Tong and his colleagues set out to determine whether ED could be used as an early warning sign of poor cardiovascular health. Researchers recruited 2,306 men with type 2 diabetes, performing a thorough medical evaluation of diabetic control and complications, including damage to the kidneys, eyes and cardiovascular system. At the beginning of the study, just over one-quarter of the study participants had ED. None of the participants had any signs or history of heart disease, vascular disease or stroke.

The researchers followed-up the patients for an average of four years. During that time, 123 men either suffered a heart attack, died from heart disease, developed chest pain caused by clogged arteries, or needed bypass surgery or a catheter procedure to restore blood flow to the heart. Men who had ED at the beginning of the study were far more likely to develop one of these signs of coronary heart disease—or a "CHD event"—than were men who initially did not have ED. Statistical analysis showed that out of every 1,000 diabetic men with ED, 19.7 could be expected to experience a CHD event each year, as compared to only 9.5 of 1,000 diabetic men without ED.

The research team then performed an analysis that included many different characteristics that, like erectile dysfunction, were associated with the development of CHD, including age, high blood pressure, the need for cholesterol- or blood-pressure-lowering medications, the duration of diabetes, and damage to the kidneys or the eyes as a result of diabetes. Even when these characteristics were taken into account, ED was found to be an independent early warning sign of coronary heart disease. In fact, ED signaled a 58 percent increase in the risk of CHD. Only spillage of large amounts of protein in the urine—a sign of extensive kidney damage—was a stronger warning sign, doubling the risk of heart disease.

The second study, conducted by researchers from four medical centers in Italy, focused on 291 men who not only had type 2 diabetes but also silent CHD discovered by stress testing and confirmed by x-ray angiography. Of these, 118 had ED at the beginning of the study. Lead investigator Carmine Gazzaruso, M.D., Ph.D., and his colleagues followed-up patients for an average of nearly four years, documenting major adverse cardiac events (MACE), which they defined as not only CHD events but also stroke, mini-stroke (transient ischemic attacks) and arterial disease in the legs. They found that patients who had ED at the beginning of the study were twice as likely to suffer a major adverse cardiac event when compared to those without ED.

The study also showed that among patients who were taking cholesterol-lowering statins, the risk of MACE was reduced by one third (hazard ratio, 0.66, p = 0.036). Viagra and other medications in a family known as 5-

phosphodiesterase (5PDE) inhibitors also appeared to reduce the MACE risk (hazard ratio, 0.68); however this finding was just beyond the cusp of being statically significant (p = 0.056).

"These are important studies," said Robert A. Kloner, M.D., Ph.D., F.A.C.C., a professor of medicine at the Keck School of Medicine at the University of Southern California, and director of research for the Heart Institute at Good Samaritan Hospital in Los Angeles. "While we have known that ED shares many common risk factors with CHD, such as hypertension, smoking, dyslipidemia and diabetes, what is new here is that ED remained a significant risk factor for developing heart disease after controlling for other cardiovascular risk factors.

"Men should know that ED is a true harbinger of atherosclerotic coronary heart disease," he said.

Dr. Kloner, who wrote an editorial about the new studies in the same issue of JACC, also noted that not only have statins been shown to reduce the risk of cardiovascular illness in diabetic patients, controlling blood pressure and other risk factors is also critical.

"In diabetic patients, it is important to not only control the blood sugar level, but also to keep blood pressure below 130/80 mmHg and reduce 'bad' (low-density-lipoprotein, or LDL) cholesterol to less than 100 mg/dL. If a patient smokes, a smoking cessation program is crucial," Dr. Kloner said.

Dr. Tong said that he and his colleagues are continuing to analyze a database of nearly 10,000 patients with diabetes in an attempt to answer several remaining questions about the link between ED, diabetes and heart disease. For example, will improvements in the control of blood sugar and other cardiovascular risk factors reduce the likelihood of developing erectile dysfunction or suffering a heart attack or other serious heart disease" Are patients who have ED in addition to diabetes-related eye problems and kidney problems at higher risk for death or cardiovascular disease" And if so, how great is the increased risk"

"All of these questions are relevant to those who suffer from diabetes," Dr. Tong said. "The information we find will help patients to focus on improving their own health."

Dr. Tong reports no conflicts of interest related to this topic.

Researchers bring new meaning to the term 'computer bug'

US researchers have created 'living computers' by genetically altering bacteria. The findings of the research, published in BioMed Central's open access Journal of Biological Engineering, demonstrate that computing in living cells is feasible, opening the door to a number of applications including data storage and as a tool for manipulating genes for genetic engineering.

A research team from the biology and the mathematics departments of Davidson College, North Carolina and Missouri Western State University, Missouri, USA added genes to Escherichia coli bacteria, creating bacterial computers able to solve a classic mathematical puzzle, known as the burnt pancake problem.

The burnt pancake problem involves a stack of pancakes of different sizes, each of which has a golden and a burnt side. The aim is to sort the stack so the largest pancake is on the bottom and all pancakes are golden side up. Each flip reverses the order and the orientation (i.e. which side of the pancake is facing up) of one or several consecutive pancakes. The aim is to stack them properly in the fewest number of flips.

In this experiment, the researchers used fragments of DNA as the pancakes. They added genes from a different type of bacterium to enable the E. coli to flip the DNA 'pancakes'. They also included a gene that made the bacteria resistant to an antibiotic, but only when the DNA fragments had been flipped into the correct order. The time required to reach the mathematical solution in the bugs reflects the minimum number of flips needed to solve the burnt pancake problem.

"The system offers several potential advantages over conventional computers" says lead researcher, Karmella Haynes. "A single flask can hold billions of bacteria, each of which could potentially contain several copies of the DNA used for computing. These 'bacterial computers' could act in parallel with each other, meaning that solutions could potentially be reached quicker than with conventional computers, using less space and at a lower cost." In addition to parallelism, bacterial computing also has the potential to utilize repair mechanisms and, of course, can evolve after repeated use.

Notes to Editors:

1. Engineering bacteria to solve the Burnt Pancake Problem

Karmella A Haynes, Marian L Broderick, Adam D Brown, Trevor L Butner, James O Dickson, W L Harden, Lane H Heard, Eric L Jessen, Kelly J Malloy, Brad J Ogden, Sabriya Rosemond, Samantha Simpson, Erin Zwack, A M Campbell, Todd T Eckdahl, Laurie J Heyer and Jeffrey L Poet

Journal of Biological Engineering (in press)

During embargo, article available here: http://www.jbioleng.org/imedia/1008546980173560_article.pdf?random=51141 After the embargo, article available at the journal website: <u>http://www.jbioleng.org/</u>

Tasmanian tiger DNA 'lives' again

* 01:00 20 May 2008 * NewScientist.com news service * Emma Young

Seventy years after the ferocious Tasmanian tiger went extinct, its marsupial DNA has been resurrected inside mice. This is the first time that genetic material from an extinct animal has functioned inside a living host.

The technique has huge potential, say the researchers. For instance, it might help to reveal how dinosaurs or Neanderthals looked.

Andrew Pask at the University of Melbourne, Australia, and colleagues extracted DNA from four 100-year-old Tasmanian tiger, or thylacine, samples. The samples were taken from three infant animals preserved in alcohol and one adult pelt.



The DNA was badly fragmented, but the team managed to isolate one specific DNA sequence from each of the animals. This 17 base-pair fragment does not code for a gene, but it is needed to switch on the gene for collagen, which is essential for bone and cartilage formation.

Bigger questions

The team then copied the DNA snippet, coupled it with a gene that produces a blue pigment, and injected it into very early mouse embryos. When the fetuses were 14 days old, the team studied them, and found that the thylacine genetic material was functioning – as indicated by the blue stain.

"We could see it very clearly in the developing cartilage," says Pask.

Other researchers have resurrected extinct DNA inside cell lines in the lab. "But you can't assess exactly what genes do and their entire function in a cell line," Pask says.

Having shown that ancient DNA can function in a living animal, the team plans to use the same technique to investigate specific biological questions – such as, why the marsupial thylacine has a body shape more like a dog than a kangaroo.

This work isn't a step towards cloning the entire thylacine, Pask stresses. All the known thylacine DNA samples are too badly degraded for that to be possible.

Mammoth revival

But it should also be possible to use this technique with other, much older extinct specimens, including some for which their DNA is much better preserved – such as the mammoth, various dinosaurs and Neanderthals.

This technique could help to reveal the function of genes found in Neanderthals, but not humans, says Palk. The work is very exciting, says Mike Archer, at the University of New South Wales, Sydney, who initiated work into the recovery of ancient DNA from extinct Australian species.

Archer hopes that developments in technology will also improve the prospects for cloning at least some recently extinct species.

Whether or not that ever happens for the thylacine, "you could say extinction isn't forever – at least not if you are a gene", says Marilyn Renfree of Melbourne University, a co-author of the new paper. *Journal reference: PloS ONE (DOI: 10.1371/journal.pone.0002240)*

Researchers find smallpox drug may also target adenovirus

One cause of the common cold, adenovirus also causes death in organ transplant recipients

st. LOUIS — Scientists at Saint Louis University have made two key discoveries that could lead to the first-ever human testing of a drug to target the adenovirus, which causes a number of severe upper-respiratory infections and is one of many viruses that causes the common cold.

There are currently no drugs approved specifically to treat adenovirus infections in large part because there has been no animal model in which to test drug candidates, a key prerequisite before testing in humans.

SLU researchers and their collaborators, however, have made two breakthrough findings: an animal model suitable for adenovirus testing – in this case using Syrian hamsters – and a drug that successfully attacks the adenovirus in those animals. The drug, hexadecyloxypropyl-cidofovir or CMX001, is currently under development by Chimerix, Inc. as a biodefense agent to meet the threat of smallpox or monkeypox viruses and as an antiviral agent in transplant patients.

The SLU research is published the week of May 19 in an early online edition of the Proceedings of the National Academy of Sciences.

"This is exciting news and a major step forward in finding a drug to treat adenovirus infections in humans," said William Wold, Ph.D., professor and chair of the department of molecular microbiology and immunology at the Saint Louis University School of Medicine and the study's lead author.

One of the key obstacles to finding an animal model for adenovirus testing involves the fact that the virus is generally species-specific; meaning the human version of the virus doesn't replicate well in animals commonly used in laboratory research.

The SLU researchers, however, found that the adenovirus replicates in Syrian hamsters (also called golden hamsters) with suppressed immune systems in much the same manner as it replicates in humans whose immune systems are weakened – making Syrian hamsters ideal for animal model testing.

"We are pleased to see that CMX001, a drug candidate showing broad antiviral activity that is being developed under a federal grant for smallpox, also has potential benefit against adenovirus," said George R. Painter, Ph.D., president and CEO of Chimerix.

Said Samuel Stanley Jr., director of the Midwest Regional Center of Excellence for Biodefense and Emerging Infectious Diseases Research (MRCE): "It is exciting to see work funded by the National Institute of Allergy and Infectious Diseases' MRCE program lead to potential new therapies for this important virus."

There are 52 known serotypes, or strains, of adenovirus in humans. They generally cause acute upper respiratory infections including colds, tonsillitis and ear infections, but they can also cause conjunctivitis, gastroenteritis and bladder infections.

Most people are able to recover from an adenovirus infection, but in some young children and people with weakened immune systems, adenovirus infections can turn virulent and even deadly. Adenovirus can also cause disease and even death in organ transplant recipients. Severe adenovirus outbreaks have occurred among groups of military recruits likely due to crowded living conditions.

CMX001 is an oral pro-drug, or derivative, of cidofovir, a drug developed by Gilead Sciences, Inc. to treat a type of retinitis in AIDS patients. Chimerix licensed from Gilead the rights to develop CMX001.

Cidofovir has long been a possible candidate to treat a number of virus infections, including the herpes virus, poxvirus and adenovirus infections in humans. The drug, however, is quite toxic to the liver and kidneys and is not available in oral form, which limits widespread use.

Using the new animal model, the SLU researchers found that CMX001 provided protection from the adenovirus when it was administered prophylactically (before infection with the virus) or therapeutically (after infection). The scientists found that the drug worked by greatly reducing the ability of the virus to replicate in key organs, mostly notably the liver.

The SLU team also found that CMX001 was much less toxic and far more powerful than cidofovir. In addition, scientists discovered, two weeks after infection with the virus CMX001 had reduced the viral load in the liver and blood to undetectable levels.

In addition to Wold and Painter, others who participated in the research include Karoly Toth, D.V.M., Jacqueline F. Spencer, John E. Sagartz, D.V.M., Ph.D., and R. Mark Buller, Ph.D., all of the Saint Louis University School of Medicine.

Vaccine triggers immune response, prevents Alzheimer's

A vaccine created by University of Rochester Medical Center scientists prevents the development of Alzheimer's disease-like pathology in mice without causing inflammation or significant side effects.

Vaccinated mice generated an immune response to the protein known as amyloid-beta peptide, which accumulates in what are called "amyloid plaques" in brains of people with Alzheimer's. The vaccinated mice demonstrated normal learning skills and functioning memory in spite of being genetically designed to develop an aggressive form of the disease.

The Rochester scientists reported the findings in an article in the May issue of Molecular Therapy, the journal of The American Society of Gene Therapy.

"Our study demonstrates that we can create a potent but safe version of a vaccine that utilizes the strategy of immune response shaping to prevent Alzheimer's-related pathologies and memory deficits," said William Bowers, associate professor of neurology and of microbiology and immunology at the Medical Center and lead author of the article. "The vaccinated mice not only performed better, we found no evidence of signature amyloid plaque in their brains."

Alzheimer's is a progressive neurodegenerative disease associated with dementia and a decline in performance of normal activities. Hallmarks of the disease include the accumulation of amyloid plaques in the brains of patients and the loss of normal functioning tau, a protein that stabilizes the transport networks in neurons. Abnormal tau function eventually leads to another classic hallmark of Alzheimer's, neurofibrillary

tangle in nerve cells. After several decades of exposure to these insults, neurons ultimately succumb and die, leading to progressively damaged learning and memory centers in the brain.

The mice that received the vaccines were genetically engineered to express large amounts of amyloid beta protein. They also harbored a mutation that causes the tau-related tangle pathology. Prior to the start of the vaccine study, the mice were trained to navigate a maze using spatial clues. They were then tested periodically during the 10-month study on the amount of time and distance traveled to an escape pod and the number of errors made along the way.

"What we found exciting was that by targeting one pathology of Alzheimer's — amyloid beta — we were able to also prevent the transition of tau from its normal form to a form found in the disease state," Bowers said.

The goal of the vaccine is to prompt the immune system to recognize amyloid beta protein and remove it. To create the vaccine, Bowers and the research group use a herpes virus that is stripped of the viral genes that can cause disease or harm. They then load the virus container with the genetic code for amyloid beta and interleukin-4, a protein that stimulates immune responses involving type 2 T helper cells, which are lymphocytes that play an important role in the immune system.

The research group tested several versions of a vaccine. Mice were given three injections of empty virus alone, a vaccine carrying only the amyloid beta genetic code, or a vaccine encoding both amyloid beta and interlueikin-4, which was found to be the most effective.

"We have learned a great deal from this ongoing project," Bowers said. "Importantly, it has demonstrated the combined strengths of the gene delivery platform and the immune shaping concept for the creation of customized vaccines for Alzheimer's disease, as well as a number of other diseases. We are currently working on strategies we believe can make the vaccine even safer."

Bowers expects the vaccine eventually to be tested in people, but due to the number of studies required to satisfy regulatory requirements, it could be three or more years before human trials testing this type of Alzheimer's vaccine occur.

Grants from the National Institutes of Health supported the study. In addition to Bowers, authors of the Molecular Therapy article include Maria E. Frazer, Jennifer E. Hughes, Michael A. Mastrangelo and Jennifer Tibbens of the Medical Center and Howard J. Federoff of Georgetown University Medical Center.

The photonic beetle

Nature builds diamond-like crystals for future optical computers

SALT LAKE CITY - Researchers have been unable to build an ideal "photonic crystal" to manipulate visible light,

impeding the dream of ultrafast optical computers. But now, University of Utah chemists have discovered that nature already has designed photonic crystals with the ideal, diamond-like structure: They are found in the shimmering, iridescent green scales of a beetle from Brazil.

"It appears that a simple creature like a beetle provides us with one of the technologically most sought-after structures for the next generation of computing," says study leader Michael Bartl, an assistant professor of chemistry and adjunct assistant professor of physics at the University of Utah. "Nature has simple ways of making structures and materials that are still unobtainable with our million-dollar instruments and engineering strategies."

The study by Bartl, University of Utah chemistry doctoral student Jeremy Galusha and colleagues is set to be published later this week in the journal Physical Review E.

The beetle is an inch-long weevil named Lamprocyphus augustus. The discovery of its scales' crystal structure represents the first time scientists have been able to work with a material with the ideal or "champion" architecture for a photonic crystal.



This inch-long beetle from Brazil accomplished a task that so far has stymied human researchers. University of Utah chemists determined the beetle glows iridescent green because it evolved a crystal structure in its scales that is like the crystal structure of diamonds. Such a structure is considered an ideal architecture for "photonic crystals" that will be needed to manipulate visible light in ultrafast optical computers of the future. Jeremy Galusha, University of Utah

"Nature uses very simple strategies to design structures to manipulate light – structures that are beyond the reach of our current abilities," Galusha says.

Bartl and Galusha now are trying to design a synthetic version of the beetle's photonic crystals, using scale material as a mold to make the crystals from a transparent semiconductor.

The scales can't be used in technological devices because they are made of fingernail-like chitin, which is not stable enough for long-term use, is not semiconducting and doesn't bend light adequately.

The University of Utah chemists conducted the study with coauthors Lauren Richey, a former Springville High School student now attending Brigham Young University; BYU biology Professor John Gardner; and Jennifer Cha, of IBM's Almaden Research Center in San Jose, Calif.

Ouest for the Ideal or 'Champion' Photonic Crystal

Researchers are seeking photonic crystals as they aim to develop optical computers that run on light (photons) instead of electricity (electrons). Right now, light in near-infrared and visible wavelengths can carry data and communications through fiberoptic cables, but the data must be converted from light back to electricity before being processed in a computer.

The goal – still years away – is an ultrahigh-speed computer with optical integrated circuits or chips that run on light instead of electricity.

"You would be able to solve certain problems that we are not able to solve now," Bartl says. "For certain problems, an optical computer could do in seconds what regular computers need years for."

Researchers also are seeking ideal photonic crystals to amplify light and thus make solar cells more efficient, to capture light that would catalyze chemical reactions, and to generate tiny laser beams that would serve as light sources on optical chips.

"Photonic crystals are a new type of optical materials that manipulate light in non-classic ways," Bartl says. Some colors of light can pass through a photonic crystal at various speeds, while other wavelengths are reflected as the crystal acts like a mirror.

Bartl says there are many proposals for how light could be manipulated and controlled in new ways by photonic crystals, "however we still lack the proper materials that would allow us to create ideal photonic crystals to manipulate visible light. A material like this doesn't exist artificially or synthetically."

The ideal photonic crystal – dubbed the "champion" crystal – was described by scientists elsewhere in 1990. They showed that the optimal photonic crystal – one that could manipulate light most efficiently – would have the same crystal structure as the lattice of carbon atoms in diamond. Diamonds cannot be used as photonic crystals because their atoms are packed too tightly together to manipulate visible light.

When made from an appropriate material, a diamond-like structure would create a large "photonic bandgap," meaning the crystalline structure prevents the propagation of light of a certain range of wavelengths. Materials with such bandgaps are necessary if researchers are to engineer optical circuits that can manipulate visible light.

On the Path of the Beetle: From BYU to Belgium and Brazil

The new study has its roots in Richey's science fair project on iridescence in biology when she was a student at Utah's Springville High School. Gardner's group at BYU was helping her at the same time Galusha was using an electron microscope there and learned of Richey's project.

Richey wanted to examine an iridescent beetle, but lacked a complete specimen. So the researchers ordered Brazil's Lamprocyphus augustus from a Belgian insect dealer.



This microscopic image shows individual scales attached to the exoskeleton of the beetle Lamprocyphus augustus, and how the scales glow iridescent green because the fingernail-like material in the scales has a diamond-like crystal structure that reflects green light. University of Utah chemists are among researchers seeking to create a material with the same structure, which is considered ideal for future optical computers that would run at ultrahigh speeds on light rather than electricity. Michael Bartl, University of Utah

The beetle's shiny, sparkling green color is produced by the crystal structure of its scales, not by any pigment, Bartl says. The scales are made of chitin, which forms the external skeleton, or exoskeleton, of most insects and is similar to fingernail material. The scales are affixed to the beetle's exoskeleton. Each measures 200 microns (millionths of a meter) long by 100 microns wide. A human hair is about 100 microns thick.

Green light – which has a wavelength of about 500 to 550 nanometers, or billionths of a meter – cannot penetrate the scales' crystal structure, which acts like mirrors to reflect the green light, making the beetle appear iridescent green.

Bartl says the beetle was interesting because it was iridescent regardless of the angle from which it was viewed - unlike most iridescent objects - and because a preliminary electron microscope examination showed its scales did not have the structure typical of artificial photonic crystals.

"The color and structure looked interesting," Bartl says. "The question was: What was the exact threedimensional structure that produces these unique optical properties""

The Utah team's study is the first to show that "just as atoms are arranged in diamond crystals, so is the chitin structure of beetle scales," he says.

Galusha determined the 3-D structure of the scales using a scanning electron microscope. He cut a cross section of a scale, and then took an electron microscope image of it. Then he used a focused ion beam – sort of a tiny sandblaster that shoots a beam of gallium ions – to shave off the exposed end of the scale, and then took another image, doing so repeatedly until he had images of 150 cross-sections from the same scale.

Then the researchers "stacked" the images together in a computer, and determined the crystal structure of the scale material: a diamond-like or "champion" architecture, but with building blocks of chitin and air instead of the carbon atoms in diamond.

Next, Galusha and Bartl used optical studies and theory to predict optical properties of the scales' structure. The prediction matched reality: green iridescence.

Many iridescent objects appear that way only when viewed at certain angles, but the beetle remains iridescent from any angle. Bartl says the way the beetle does that is an "ingenious engineering strategy" that approximates a technology for controlling the propagation of visible light.

A single beetle scale is not a continuous crystal, but includes some 200 pieces of chitin, each with the diamond-based crystal structure but each oriented a different direction. So each piece reflects a slightly different wavelength or shade of green.

"Each piece is too small to be seen individually by your eye, so what you see is a composite effect," with the beetle appearing green from any angle, Bartl explains.

Scientists don't know how the beetle uses its color, but "because it is an unnatural green, it's likely not for camouflage," Bartl says. "It could be to attract mates."

The study was funded by the National Science Foundation, American Chemical Society, the University of Utah and Brigham Young University.

Bypass not to blame for heart patients' mental decline

Finding removes stigma from viable treatment, Hopkins researchers say

Heart patients often experience lasting problems with memory, language, and other cognitive skills after bypass surgery. However, these problems aren't caused by the surgery itself or the pump used to replace heart function during surgery, a new study by Johns Hopkins researchers suggests. The findings may lead to better approaches to prevent cognitive decline regardless of which treatment heart disease patients receive.

The study, published in the May Annals of Neurology, compared cognitive function of patients who received cardiac bypass surgery with that of patients who received other treatments for coronary artery disease, including pharmaceuticals and stents. After testing all the study subjects periodically in a variety of cognitive areas for six years after their treatments, the researchers found that both groups experienced an almost identical decline in cognitive function. The results suggest that the disease itself, and not any particular treatment, is the cause for cognitive decline.

Previous studies have linked bypass surgery to patients' mental decline, with many doctors blaming the bypass pump that keeps blood flowing through the body during surgery. This research led many doctors to avoid recommending surgery to their patients. However, Hopkins researcher Guy McKhann explains that previous studies hadn't compared patients who had bypass surgery to those who had other treatments instead. As such, it's been unknown whether mental decline is a consequence of surgery using the bypass pump, heart troubles, part of the normal aging process, or another cause altogether.

To gather evidence, McKhann and other Hopkins researchers recruited 152 heart disease patients who were scheduled to undergo bypass surgery and 92 patients whose doctors planned to treat their heart disease in other ways, including stents and medications. The patients, mostly men, had an average age of about 64.

Before their treatments, the researchers gave each of the patients a battery of 15 different mental tests meant to examine cognitive functions including memory, motor speed, attention, and the ability to plan ahead. Then, at three months, one year, three years, and six years after treatment, the researchers gave the volunteers the same tests to see whether their cognitive function had changed.

When they compared the two groups' results, the researchers found similar results. Both groups started out with comparable cognitive abilities, which improved slightly for about a year after treatment. However, over the next five years, most of the patients experienced a similar decline of cognitive function in almost every area tested, regardless of whether they had surgery or another treatment.

These results suggest that neither bypass surgery nor the pump itself causes cognitive decline, says McKhann. He says that the finding may help the stigma that prevents some doctors from recommending bypass surgery.

"We don't think fear of mental changes should be a factor in deciding what kinds of treatments you have for your heart," he adds.

Since both groups of patients scored lower than healthy patients on similar cognitive tests in other studies, McKhann notes that he and other researchers believe that coronary artery disease is the culprit. However, he says, he and his colleagues don't believe that cognitive decline is an inevitable consequence of heart disease.

"If we take a very aggressive approach to treating risk factors for heart disease, including keeping a handle on diabetes, blood pressure, and weight, patients may be able to avoid these cognitive problems," McKhann says.

Other Hopkins researchers who participated in the study include Ola Selnes, Ph.D., Maura Grega, R.N., M.S.N., Maryanne Bailey, Luu Pham, M.S., Scott Zeger, Ph.D., and William Baumgartner, M.D. The study was supported by grants from the National Institute of Neurological Disorders and Stroke, the Charles A. Dana Foundation, and the Johns Hopkins Medical Institution GCRC. For more information, go to: http://www.jhsph.edu/mindbodyresearch/faculty/guymckhann.html http://www.hopkinsneuro.org/

Old antibiotic may find new life as a stroke treatment

An old intravenous antibiotic may have new life as a stroke treatment, researchers say.

Minocycline appears to reduce stroke damage in multiple ways – inhibiting white blood cells and enzymes that, at least acutely, can destroy brain tissue and blood vessels, respectively, says Dr. David Hess, chair of the Department of Neurology in the Medical College of Georgia School of Medicine. The broad-spectrum antibiotic also seems to reduce cell suicide in the minutes and hours following a stroke, enabling more cells to recover.

He and other researchers leading a clinical trial that will study the drug in 60 stroke patients in Georgia, Kentucky and Oregon say they believe the antibiotic will be a safe, effective adjunct therapy for tPA, the only FDA-approved drug therapy for strokes.

"It's a safe drug that is easy to give and tolerate, that gets into the brain well, and may reduce bleeding, the primary side effect of tPA," says Dr. Hess, principal investigator on the \$1.8 million National Institute of Neurological Disorders and Stroke-funded clinical trial. "We think it will make strokes smaller and patient outcomes better."

Their animal studies have shown the drug, given within six hours of a stroke, then every 12 hours for up to three days - the peak time of inflammation - reduces stroke damage by up to 40 percent.

"We know it's safe in humans and we know the concentrations we need to see improvement in the brains of rats can be achieved safely in humans," says Dr. Susan C. Fagan, professor of pharmacy at the University of Georgia, assistant dean for the MCG program of the UGA College of Pharmacy and study co-investigator. "That's an important consideration."

The drug's safety and optimal stroke dose are the primary focus of the phase-one clinical trial in stroke patients who arrive at MCG, University of Kentucky or Oregon Health & Science University within six hours of symptom onset and with measurable neurological symptoms. Every study patient will get one of four doses, starting with 200 milligrams, the most common dose already used, and increasing incrementally up to 700 milligrams. They'll get half their first dose at subsequent 12-hour intervals for a three-day period then be followed for 90 days.

"We are going to be drawing samples from patients to make sure we achieve the concentrations that we want in the blood, plus we want to define the half-life in stroke patients to see if it's different than in the younger patients who take it for other reasons,' says Dr. Fagan. Newer intravenous antibiotics have replaced minocycline in the United States, but an oral version is used to treat conditions such as acne and rheumatoid arthritis. "If the half-life is longer, we can give it less frequently. We are really fine-tuning the dose," she says. They'll do this by looking in the blood for biomarkers, indicators of inflammation, to see if inflammatory factors go up after three days. "It may give us a clue we should treat patients longer," says Dr. Fagan, a coinvestigator on the studies leading to minocycline's use in rheumatoid arthritis.

One way minocycline fights inflammation is by inhibiting microglial cells, white blood cells activated by a stroke, says Dr. Hess. "When they get activated, they get angry and produce materials that damage the brain. The inflammatory cascade is bad and good. Early on it's bad, later on it may actually do some good things," he says. Typically these microglial cells are sentinel immune cells for the brain, helping eliminate infections and secreting factors that support neurons. However, acutely in a stroke, brain tissue can become their target. "They are basically cleaning house at first, then later, they are supportive, releasing growth factors and promoting the growth of new blood vessels," adds Dr. Fagan.

Minocycline also blocks matrix metallo-proteinases, also released during stroke, which destroy the basement membrane of blood vessels. The presence of these enzymes also is a mixed bag. "If you want angiogenesis – you want to make new blood vessels – you need MMPs around to get rid of the old ones, like tearing down an old building to build a new one," says Dr. Hess. However, in patients lucky enough to get the clot buster tPA, the enzyme increases the major risk factor: bleeding. Dr. Hess notes that while this initial clinical trial is in ischemic strokes, he thinks minocycline also may be useful in hemorrhagic strokes, which account for about 12 percent of strokes, where clearly blocking MMPs would come in handy.

Minocycline also works by blocking apoptosis, or cell suicide, an observation originally made by MCG Cell Biologist Zheng Dong. "It does this by increasing a protein called bcl-2, which helps cells survive," says Dr. Hess.

The antibiotic's potential usefulness in protecting brain cells began surfacing in scientific literature within the last few years. "It was so interesting to us because we knew that a lot of the limitations of other drugs that had been tried in rodents but didn't work in stroke patients were that they didn't cross into the brain," Dr. Fagan says. "We knew that minocycline did based on previous experiments and the fact that many people who take it for acne or rheumatoid arthritis get dizzy. So we were encouraged by this.

"We wanted something we could give at least three hours after stroke or later. In our studies in animal models, we found at delayed time intervals it was profoundly neuroprotective," says Dr. Fagan. "We studied it at multiple time points at multiple doses and, in fact, some of the most important work we did was finding out how the rodent dose really could be translated to humans," she says, referencing work published in Experimental Neurology in 2004.

For the clinical trial, Wyeth Pharmaceuticals will make the sterile powder used for injection available from Japan, where it's still in use.

At MCG, Dr. Hess as well as MCG Neurologists Chris Hall, Fenwick Nichols and Jeff Switzer are enrolling patients in the study. Other MCG contributors include Biostatistician Jennifer Waller and Physiologist Adviye Ergul. For more information about the study, contact Joanne Rogalsky-Nacca, study coordinator, at 706-721-2675 or <u>jrnacca@mcg.edu</u>.

Plant flavonoid found to reduce inflammatory response in the brain

Researchers at the University of Illinois report this week that a plant compound found in abundance in celery and green peppers can disrupt a key component of the inflammatory response in the brain. The findings have implications for research on aging and diseases such as Alzheimer's and multiple sclerosis.

The study appears this week in Proceedings of the National Academy of Sciences.

Inflammation can be a blessing or a blight. It is a critical part of the body's immune response that in normal circumstances reduces injury and promotes healing. When it goes awry, however, the inflammatory response can lead to serious physical and mental problems.

Inflammation plays a key role in many neurodegenerative diseases and also is implicated in the cognitive and behavioral impairments seen in aging.

The new study looked at luteolin (LOO-tee-OH-lin), a plant flavonoid known to impede the inflammatory response in several types of cells outside the central nervous system. The purpose of the study was to determine if luteolin could also reduce inflammation in the brain, said animal sciences professor and principal investigator Rodney Johnson.

"One of the questions we were interested in is whether something like luteolin, or other bioactive food components, can be used to mitigate age-associated inflammation and therefore improve cognitive function and avoid some of the cognitive deficits that occur in aging," Johnson said.

The researchers first studied the effect of luteolin on microglia. These brain cells are a key component of the immune defense. When infection occurs anywhere in the body, microglia respond by producing inflammatory cytokines, chemical messengers that act in the brain to orchestrate a whole-body response that helps fight the invading microorganism.

This response is associated with many of the most obvious symptoms of illness: sleepiness, loss of appetite, fever and lethargy, and sometimes a temporary diminishment of learning and memory. Neuroinflammation can also lead some neurons to self-destruct, with potentially disastrous consequences if it goes too far.

Graduate research assistant Saebyeol Jang studied the inflammatory response in microglial cells. She spurred inflammation by exposing the cells to lipopolysaccharide (LPS), a component of the cell wall of many common bacteria.

Those cells that were also exposed to luteolin showed a significantly diminished inflammatory response. Jang showed that luteolin was shutting down production of a key cytokine in the inflammatory pathway, interleukin-6 (IL-6). The effects of luteolin exposure were dramatic, resulting in as much as a 90 percent drop in IL-6 production in the LPS-treated cells.

"This was just about as potent an inhibition as anything we had seen previously," Johnson said.

But how was luteolin inhibiting production of IL-6"

Jang began by looking at a class of proteins involved in intracellular signaling, called transcription factors, which bind to specific "promoter" regions on DNA and increase their transcription into RNA and translation into proteins.

Using electromobility shift assays, which measure the binding of transcription factors to DNA promoters, Jang eventually determined that luteolin inhibited IL-6 production by preventing activator protein-1 (AP-1) from binding the IL-6 promoter.

AP-1 is in turn activated by JNK, an upstream protein kinase. Jang found that luteolin inhibited JNK phosphorylation in microglial cell culture. The failure of the JNK to activate the AP-1 transcription factor prevented it from binding to the promoter region on the IL-6 gene and transcription came to a halt.

To see if luteolin might have a similar effect in vivo, the researchers gave mice luteolin-laced drinking water for 21 days before injecting the mice with LPS.

Those mice that were fed luteolin had significantly lower levels of IL-6 in their blood plasma four hours after injection with the LPS. Luteolin also decreased LPS-induced transcription of IL-6 in the hippocampus, a brain region that is critical to spatial learning and memory.

The findings indicate a possible role for luteolin or other bioactive compounds in treating neuroinflammation, Johnson said.

"It might be possible to use flavonoids to inhibit JNK and mitigate inflammatory reactions in the brain," he said. "Inflammatory cytokines such as interleukin-6 are very well known to inhibit certain types of learning and memory that are under the control of the hippocampus, and the hippocampus is also very vulnerable to the insults of aging," he said. "If you had the potential to decrease the production of inflammatory cytokines in the brain you could potentially limit the cognitive deficits that result."

Editor's note: To reach Rodney Johnson, call 217-333-2118; e-mail: <u>rwjohn@uiuc.edu</u>.

Beringia: humans were here

It was an extraordinary ancient land filled with fantastic creatures and intrepid people. **ALEX ROSLIN** Special to The Gazette Saturday, May 17, 2008

Beringia is thought by a handful of renegade scientists to be a prehistoric homeland for aboriginal people who later spread across the Americas and the key to one of archeology's greatest Holy Grails - figuring out how humans first got to this continent.

This July, Jacques Cinq-Mars, a renowned archeologist living in Longueuil, is heading to Beringia - a vast territory that once spanned the Yukon, Alaska and Siberia - in hopes of resolving a controversy he unleashed nearly 20 years ago when he chanced upon a curious-looking cave in the Yukon's Keele Mountain Range, perched on a ridge high above the Bluefish River.

Here, at a site known as the Bluefish Caves, Cinq-Mars's team discovered something that would turn archeology on its ear and has fuelled debate ever since - a chipped mammoth bone that appeared to have been fashioned into a small harpoon point. Radiocarbon dating showed the bone to be 28,000 years old.

The find stunned archeologists who had long presumed the first people to enter the Americas did so 13,000 years ago via a land bridge from Siberia after the end of the last Ice Age.

Until that point, routes from Alaska down into the Americas were blocked off by glaciers up to four kilometres thick, which would have cut off any possibility of migration for thousands of years.

But scientists have unearthed a growing number of ancient human sites across the continent that date back much more than 13,000 years. How did those people get here? No one knows for sure.

Cinq-Mars, a retired former curator at the Canadian Museum of Civilization, believes the answers lie in the lost land of Beringia.

Named after 18th-century Danish explorer Vitus Bering, this territory emerged from under the sea when advancing glaciers locked up seawater and caused ocean levels to fall 120 metres. The 1,000-kilometre-wide land bridge that joined the two continents was so arid it remained a glacier-free oasis of grassland steppes that teemed with life at the height of the Ice Age.

People here lived alongside giant and outlandish animals - beavers the size of today's bears, fearsome carnivorous bears that would have dwarfed today's grizzlies, sloths as big as oxen, mastodons, lions and woolly rhinos and camels.

Cinq-Mars, who has been exploring Beringia since his student days in 1966, believes the region was not only a way-point for people migrating into the Americas, but also a homeland for aboriginal people for millennia as they sought refuge during the Ice Age.

If he is right, his finds at the Bluefish Caves and even older mammoth bone flakes found by another Canadian team at nearby Beringian sites mean people were already trundling around in the Americas long before the Ice Age. (Radiocarbon dating puts the age of the mammoth bone flakes found by the Archeological Survey of Canada team at 40,000 years old.) Nearly 20 years after the initial mammoth bone find was publicized in the early 1990s, however, much of the archeological establishment remains skeptical about Cinq-Mars's discoveries in Beringia. His finds clash with a long-held view known as the "Clovis First" theory, which is based on 13,000-year-old spear points found near Clovis, New Mexico, in the 1930s.

The Clovis theory, which dominated archeological thinking until recent years, holds that people first spilled into the Americas across the Siberian land bridge only after retreating glaciers opened passages through Canada to the south.

Archeologists who question Clovis First have been branded as renegades, said Raymond Le Blanc, an archeologist at the University of Alberta. "It's almost like admitting you saw a UFO," he said.

Le Blanc was a grad student on Cinq-Mars's team at the Bluefish Caves in the mid-1970s, when the exploration there started. (It took another 15 years to analyze the material uncovered and publish the results.) Far from being a ticket to fame and fortune, bucking the Clovis First doctrine has meant "you become part of the fringe. It's not great for your career. It becomes a little more difficult to get (research) money," he said.

Indeed, since the potentially stunning finds in Beringia, Cinq-Mars said he has struggled to cobble together research funds to continue the exploration and analyze what's been found.

"My biggest problem is getting access to funding. This is a scientific gold mine we've been sitting on for years, but many people just didn't give a hoot. There has been and still is very strong resistance. Clovis First has been the credo of archeology for decades," he said.

The waters have been muddled by scientific acrimony about the Bluefish Cave mammoth bone evidence. Some of Cinq-Mars's detractors say the bone could have been chipped at a later point long after the mammoth died or through natural processes like erosion or falling rocks.

"I'm very, very skeptical about cave data," said Bob Gall, a veteran archeologist with the U.S. National Park Service in Fairbanks, Alaska.

"They're occupied by animals and people, and material rolls down slopes. You have rock falls and material that's really difficult to sort out." Even if the mammoth bone was indeed modified by a person, Gall said it's still not clear when that would have happened. "From the time that elephant died, up until the present, it could have been modified by man," he said.

Subsequent research showed the bone was indeed likely to have been chipped by humans shortly after the mammoth died, but the questions have lingered, with many scientists saying more confirming data is needed.

That, in turn, has led to an archeological Catch-22: Little funding is available to pursue the Beringia research. "There are more things from that site we could date, but there has been a lack of money," Le Blanc said.

Complicating the search for confirming evidence is the fact that the best human sites to explore in the region are now probably at the bottom of the Bering Strait, said Ruth Gotthardt, an archeologist with the Yukon government. "The evidence is not co-operating," she said.

But now, the region is seeing renewed scientific interest as evidence emerges to suggest Cinq-Mars may have been on the right track after all.

Since the mid-1970s, more than two dozen other possible sites predating Clovis have been unearthed across North and South America. Perhaps the most famous is a 14,500-year-old settlement at Monte Verde, Chile, including a human footprint, tools and living quarters for 20 to 30 people.

Initially dismissed by archeologists, the Monte Verde site has become widely accepted as legitimate in recent years.

In 2004, the Clovis theory suffered another indirect blow when scientists in Siberia - in what used to be the western edge of Beringia - found a 30,000-year-old human site with tools fashioned from mammoth and rhino tusks.

The discovery showed humans had adapted to the extreme cold of the Far North thousands of years earlier than previously thought. It has also rejuvenated interest in Beringia, Le Blanc said. "If people got to the Arctic, I don't see why they couldn't have penetrated farther east." Meanwhile, Cinq-Mars has been amassing evidence from European researchers that shows chipped mammoth bones were used there as spear points more than 200,000 years ago - more evidence that the bone chips in Beringia were a widespread ancient technology.

And in July, Cinq-Mars plans to return to the region that ignited the controversy 30 years ago with hopes of finding more clues. He has received funds from the Yukon's Gwitchin First Nation in order to explore several sites, including the Bluefish Caves.

"There are layers there that have yet to be looked at which are likely to be older (than the original Bluefish find)," he said.

Cinq-Mars also has another mission for this trip - helping the Gwitchin village of Old Crow create a cultural centre to showcase the region's rich history.

In August, Le Blanc will also be poking around at another site called Gwizi Cave, about 60 kilometres to the north of Cinq-Mars's expedition. Le Blanc believes it, too, could yield more ancient remains.

Finding undisputed evidence of a pre-Ice Age human presence there, both men said, would force scientists to rewrite the history of the Americas.

"Beringia is the only site that explains the pre-Clovis finds," Le Blanc said. "The area has profound importance."

Following a trail of archeological clues over the millennia

40,000 to 28,000 years ago: Age of chipped mammoth bones found at the Yukon's Bluefish Caves and nearby sites in the 1970s and '80s by archeologist Jacques Cinq-Mars and his team.

30,000 years ago: Siberian mammoth hunters were found to have penetrated far into the Arctic by this period. 23,000 years ago: The Ice Age entombs the northern hemisphere in glaciers, cutting off routes from Siberia to the south.

15,000 to 17,000 years ago: Archeologists say people were living at Cactus Hill, Virginia, where stone tools and charcoal from a fire pit have been dated to this period.

14,500 years ago: Humans were living in Monte Verde in southern Chile, where human tools, a dwelling structure and a person's footprint have been dated to this period.

14,000 years ago: Archeologists believe this is when receding glaciers probably first opened an ice-free corridor through Canada between Alaska and the rest of the Americas. The conundrum: How did people get to Cactus Hill and Monte Verde before this?

13,000 years ago: People were living near Clovis, New Mexico, where tools from this era were found in the 1930s. This find gave rise to the widely held Clovis First theory that people spread through the Americas only after the Ice Age. 11,000 years ago: As the Ice Age ends, melting glaciers raise sea levels 120 metres, submerging the land bridge between Alaska and Siberia.

Nanotubes' toxic effects 'similar to asbestos'

* 18:00 20 May 2008 * NewScientist.com news service * Colin Barras

Injecting carbon nanotubes into mice shows they can trigger similar toxic responses to asbestos fibres, causing a strong immune response and possibly cancer in the abdominal cavity, researchers say.

But another recent study suggests the tiny tubes, which are increasingly appearing in commercial and industrial products, are not dangerous when inhaled, probably because they do not persist in the body as asbestos fibres do.

Carbon nanotubes (CNTs) first came to the attention of researchers in the early 1990s. Incredibly strong for their size and able to function as both conductors and semiconductors, the tiny structures are thought to be ideal for applications that range from drug delivery to space elevators.

But under a microscope, some CNTs look identical to asbestos fibres, leading to concerns that they could cause similar health problems. Occupational exposure to asbestos led to widespread lung disease, and cancers known as mesothelioma, in the 20th century.

Deadly lookalike

Asbestosis research revealed a checklist of features that makes the fibres dangerous, says Ken Donaldson at the University of Edinburgh, UK.

Ever since, it was presumed that any needle-like fibres around 20 micrometers long with an ability to persist in the body could have similarly dangerous effects. Donaldson and colleagues have now shown this holds true for carbon nanotubes.

When they injected multi-walled carbon nanotubes – composed of a hierarchy of tubes within tubes – into the abdominal cavity of mice, they saw a strong immune reaction within seven days to tubes longer than 20 micrometers. Lesions known as granulomas had developed in the tissue surrounding the abdominal organs.

The granulomas form when the macrophage immune cells that usually swallow and neutralise foreign particles take on the tubes. The cells get ruptured and die when they try to swallow fibres longer than 20 micrometers.

Highly charged

But Donaldson points out that his study does not reveal whether nanotubes are able to persist in the body long enough to reach the areas he directly injected them into. "We need to show this result in an inhalation study," he says.

James Bonner at the North Carolina State University, Raleigh, US, will shortly publish one of the first such studies. He says the results suggest that nanotubes do not persist long enough to cause damage.

In his experiments, mice breathed air containing 40-micrometer-long multi-walled nanotubes. "Very little inflammatory or fibrogenic effect was observed," he says.

Donaldson notes that determining the true risks of nanotubes will involve measuring the ways in which people will be exposed to them, something studies on toxicity cannot judge.

There is little evidence about exposure so far, says Donaldson. "But the good news is that nanotubes are probably not very 'dirty'," he says. "They are quite highly charged and stick together, so they don't seem to get airborne easily."

Journal reference: Nature Nanotechnology (DOI: 10.1038/nnano.2008.111)

New pharmacological effect of Jianpi Huoxue Decoction

Professor Yi-Yang Hu and his colleagues confirmed that Jianpi Huoxue decoction (JHD) reduced the cytokine expression induced by lipopolysaccharide (LPS) and inhibited some targets in LPS-activated Kupffer cell signal pathway. This may provide new insight on the mechanism of JHD on alcoholic liver injury.

This study, performed by a team led by Professor Hu, from the Institute of Liver Diseases, Shuguang Hospital, affiliated with the Shanghai University of Traditional Chinese Medicine, is described in a research article to be published on March 28, 2008 in the World Journal of Gastroenterology.

This study confirmed one of the possible mechanisms of JHD on alcoholic liver injury, that it inhibits some targets in LPS-activated Kupffer cell signal pathway, such as the specific molecular marker of macrophage, CD68, phosphorylated inhibit- kappaB (p-I kappaB) protein expression, the endotoxin receptor and toll-like receptor (TLR2) mRNA expression.

JHD has proven to be effective in suppressing alcoholic liver and intestinal injury induced by the Lieber-Decarli liquid diet in rats. It has also proven to be effective in suppressing the concentration of LPS in plasma. Study has demonstrated the inhibitory effect of JHD on LPS-induced cytokine secretion pathway, but the relationship between endotoxin receptors and LPS should be investigated in more detail. Such research would contribute to further observing the effect of JHD on endotoxin receptors.

The "two-hits" theory brought great advances in pathogenesis research of alcoholic liver injury (ALD). At present, most attention is focused on the mechanism of the endotoxin or LPS signal pathway involved in ALD. The function of Kupffer cells and their cytokine secretion pathway when exposed to LPS has become the hotspot of this field. This research might provide a new effective method for alcoholic liver injury prevention and treatment.

Professor Hu and his colleagues work in the Institute of Liver Diseases, Shuguang Hospital, affiliated with the Shanghai University of Traditional Chinese Medicine, which focuses on basic research on liver disease prevention and treatment with Chinese traditional medicine.

Reference: Peng JH, Hu YY, Cheng Y, Han C, Xu LL, Feng Q, Chen SD, Tao Q, Li HS, Li XM. Effect of JIANPI HUOXUE decoction on inflammatory cytokine secretion pathway in rat liver with lipopolysaccharide challenge. World J Gastroenterol 2008;14(12):1851-1857 http://www.wjgnet.com/1007-9327/14/1851.asp Correspondence to: Professor Yi-Yang Hu, Institute of Liver Diseases, Shuguang Hospital, affiliated with the Shanghai University of Traditional Chinese Medicine, Shanghai 201203, China. yyhu@citiz.net Telephone: +86-21-51328500 Fax: +86-21-51328500

How can we measure the emotional states of animals?

Sensitivity to reward loss as an indicator of animal emotion and welfare

Rats housed in standard conditions show a stronger response to the loss of an expected food reward than those housed in enriched conditions, perhaps indicating a more negative emotional state, according to new research by scientists at Bristol University Veterinary School, published in this week's issue of Royal Society Biology Letters.

The researchers have developed a new approach to the measurement of animal emotional states based on findings from human psychology that emotions affect information processing. In general, people are more

sensitive to reward losses than gains, but depressed people are particularly sensitive to losses. The researchers wanted to know whether animals' sensitivity to reward loss might also be related to their emotional state.

Many studies have demonstrated beneficial welfare effects of enriched compared to barren housing, and the researchers found that rats housed in standard conditions, previously shown to experience poorer welfare than those housed in enriched conditions, were indeed more sensitive to the unanticipated loss of a food reward. Oliver Burman, Richard Parker, Liz Paul and Mike Mendl from the Centre for Behavioural Biology at Bristol University consider the research indicates that sensitivity to reward reduction may be a valuable new indicator of animal emotion and welfare.

"The study of animal emotion is an important emerging field in subjects ranging from neuroscience to animal welfare research. Whilst we cannot know for sure what other animals feel, our approach may provide improved methods for indirectly measuring animal emotion and welfare," said Professor Mendl.

Dr Burman further explained, "Parallel studies using this approach in humans and animals may also reveal cross-species commonalities in the influence of affect on reward evaluation. Our next step is to see whether other reward evaluation processes involving contrasts between expected and actual rewards also reflect background emotional state."

Incense is psychoactive: Scientists identify the biology behind the ceremony New study in The FASEB Journal shows how and why molecules released from burning incense in religious ceremonies alleviate anxiety and depression

Bethesda, MD—Religious leaders have contended for millennia that burning incense is good for the soul. Now, biologists have learned that it is good for our brains too. In a new study appearing online in The FASEB Journal (http://www.fasebj.org), an international team of scientists, including researchers from Johns Hopkins University and the Hebrew University in Jerusalem, describe how burning frankincense (resin from the Boswellia plant) activates poorly understood ion channels in the brain to alleviate anxiety or depression. This suggests that an entirely new class of depression and anxiety drugs might be right under our noses.

"In spite of information stemming from ancient texts, constituents of Boswellia had not been investigated for psychoactivity," said Raphael Mechoulam, one of the research study's co-authors. "We found that incensole acetate, a Boswellia resin constituent, when tested in mice lowers anxiety and causes antidepressive-like behavior. Apparently, most present day worshipers assume that incense burning has only a symbolic meaning."

To determine incense's psychoactive effects, the researchers administered incensole acetate to mice. They found that the compound significantly affected areas in brain areas known to be involved in emotions as well as in nerve circuits that are affected by current anxiety and depression drugs. Specifically, incensole acetate activated a protein called TRPV3, which is present in mammalian brains and also known to play a role in the perception of warmth of the skin. When mice bred without this protein were exposed to incensole acetate, the compound had no effect on their brains.

"Perhaps Marx wasn't too wrong when he called religion the opium of the people: morphine comes from poppies, cannabinoids from marijuana, and LSD from mushrooms; each of these has been used in one or another religious ceremony." said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal. "Studies of how those psychoactive drugs work have helped us understand modern neurobiology. The discovery of how incensole acetate, purified from frankincense, works on specific targets in the brain should also help us understand diseases of the nervous system. This study also provides a biological explanation for millennia-old spiritual practices that have persisted across time, distance, culture, language, and religion—burning incense really does make you feel warm and tingly all over!"

According to the National Institutes of Health, major depressive disorder is the leading cause of disability in the United States for people ages 15–44, affecting approximately 14.8 million American adults. A less severe form of depression, dysthymic disorder, affects approximately 3.3 million American adults. Anxiety disorders affect 40 million American adults, and frequently co-occur with depressive disorders.

The FASEB Journal (http://www.fasebj.org) is published by the Federation of American Societies for Experimental Biology (FASEB) and is consistently ranked among the top three biology journals worldwide by the Institute for Scientific Information. FASEB comprises 21 nonprofit societies with more than 80,000 members, making it the largest coalition of biomedical research associations in the United States. FASEB advances biological science through collaborative advocacy for research policies that promote scientific progress and education and lead to improvements in human health.

Article details: Incensole acetate, an incense component, elicits psychoactivity by activating TRPV3 channels in the brain. Arieh Moussaieff, Neta Rimmerman, Tatiana Bregman, Alex Straiker, Christian C. Felder, Shai Shoham, Yoel Kashman, Susan M. Huang, Hyosang Lee, Esther Shohami, Ken Mackie, Michael J. Caterina, J. Michael Walker, Ester Fride, and Raphael Mechoulam. Published online before print May 20, 2008 as doi: 10.1096/fj.07-101865. http://www.fasebj.org/cgi/content/abstract/fj.07-101865v1

2008/05/26

Scientists Discover a Molecular Scaffold That Guides Connections Between Brain Cells Non-signaling glial cells can direct synapse formation in the forging of neural networks

Cold Spring Harbor, NY – Brain cells known as neurons process information by joining into complex networks, transmitting signals to each other across junctions called synapses. But "neurons don't just connect to other neurons," emphasizes Z. Josh Huang, Ph.D., "in a lot of cases, they connect to very specific partners, at particular spots."

Dr. Huang, a professor at Cold Spring Harbor Laboratory (CSHL), leads a team that has identified molecules guiding this highly specific neuronal targeting in the developing brains of mice. The researchers report in PLoS Biology that in some cases, these molecular guides -- non-signaling brain cells known as glia -- form a kind of scaffold. This scaffold, in turn, directs the growth of nerve fibers and their connections between specific types of neurons.

As they learn through research like this how the brain develops its complex wiring, the scientists hope they can clarify what goes wrong in disorders like autism.

The Cerebellum's 'Organized Architecture'

Distinctive wiring patterns are unmistakable in the cerebellum, a brain region best known for controlling movement, in both mice and people. Compared to regions involved in more sophisticated functions like vision and thought, "the cerebellum is an easier place to start, because of its very organized architecture," Dr. Huang says, although he notes that other parts of the brain have their own specific wiring patterns.

Central to the wiring architecture of the cerebellum are so-called Purkinje cells, a type of neuron that deploys a bushy array of fibers called dendrites that extend through layers of cerebellar territory. The dendrites gather signals from many other neurons in the cerebellum and send signals to other parts of the body.

The complex wiring pattern emerges during the early growth of the brain, when individual neurons migrate from their places of origin in other brain regions and emit filaments called axons that connect to particular parts of other neurons, such as the dendrites. Dr. Huang likens this process to the address on a letter that brings it from another country directly to your door by specifying the country, state, city, street, and house number. He and other brain researchers have learned much about the higher levels of this addressing scheme, identifying, for instance, chemical signals that guide axons to the right section of the brain, and different signals that lead them to the appropriate layer within that section.

How Neurons Form Synapses

Only recently, however, have Dr. Huang and his colleagues traced the chemical signals leading neurons to form synapses with specific parts of other neurons. Such sub-cellular specificity is critical to ensure the precision and reliability of communication among neurons. Synapses are the tiny gaps across which nerve cells exchange signals, conveyed by chemicals called neurotransmitters.

A few years ago, Dr. Huang's team established that a protein from the immunoglobulin family directs one group of cerebellar neurons to connect with a specific part of Purkinje cells. Immunoglobulin proteins are best known for acting as antibodies in the immune system, where they take on myriad forms to attack new invaders. Here, however, they are observed to be involved in the wiring of the brain.

"The striking feature is that there is a lot of capacity for variety" in immunoglobulin molecules, Dr. Huang explains. In the nervous system, their versatility may help them guide cells to form synapses with specific partners. Intriguingly, Dr. Huang adds, immunoglobulins have been implicated in neural developmental disorders, such as autism. "There is good evidence that these disorders involve miswiring of the nervous system," Dr. Huang says, which may reflect a problem with immunoglobulin-guided synapse formation. A Guiding Scaffold Made of Glial Cells

In the work reported in their newly published paper, Dr. Huang's team traced the sub-cellular targeting of a different set of cerebellar neurons called stellate cells, which make numerous connections to the dendritic "bush" emanating from clumps of Purkinje cells. Unlike the cells they had studied previously, however, these neurons need help to form synapses. The researchers developed sophisticated techniques to label different cell types with chemical markers, and found that non-signaling cells called glia act as a scaffold, guiding the growing axons of the stellate cells and determining where they form synapses to the Purkinje cells.

In this role, the glia act something like "matchmakers" to bring the stellate and Purkinje cells together. But Dr. Huang notes that the scaffold of glia interspersed among the neurons allows each stellate cell to make contact to many different Purkinje cells. A direct attraction between stellate and Purkinje cells, he suggests, might lead two cells two pair up exclusively.

"Bergmann Glia and the Recognition Molecule CHL1 Organize GABAergic Axons and Direct Innervation of Purkinje Cell Dendrites" appears in the April, 2008 edition of the journal PLoS Biology. The complete citation is: Fabrice Ango, Caizhi Wu, Johannes J. Van der Want, Priscilla Wu, Melitta Schachner, Z. Josh Huang http://biology.plosjournals.org/perlserv/?request=get-document&doi=10.1371%2Fjournal.pbio.0060103#aff1. The paper is available online at http://dx.doi.org/10.1371/journal.pbio.0060103

Body's natural painkillers may block phobias

* 21:00 20 May 2008

* NewScientist.com news service

* Alison Motluk

The way humans are conditioned by fearful stimuli is to some extent damped down by the body's own painrelief system, a study suggests. The finding may shine light on the neural mechanisms behind anxieties, phobias and even post-traumatic stress disorder.

Scientists have known for a long time that if you pair an innocuous stimulus (such as a tone) with something aversive (such as a shock to the feet), animals, including humans, will learn to show a "conditioned fear" response.

With repetition, the innocuous stimulus alone brings on the fear response. Both the learning and the initiation of this response take place in a part of the brain known as the amygdala.

One of the more perplexing features of the conditioned fear response is that, when the dreaded stimulus is something painful, people actually tend to experience less pain the more they are exposed to it.

Work in rodents has revealed that this is because opioids – chemicals that have a morphine-like effect on the body – are called into operation during the conditioning and they end up blunting the pain. Blocking the opioids not only stops the pain from being lessened, but also intensifies the learning process.

More fear

Falk Eippert at the University Medical Centre of Hamburg-Eppendorf, Germany, and his colleagues wanted to know if something similar operated in humans.

Thirty male volunteers were asked to watch green triangles and blue pentagons on a screen inside an MRI scanner. One of the symbols was followed half the time by a moderately painful application of heat to the forearm; the other was never followed by pain.

Half the volunteers were infused with naloxone, a drug that blocks the effects of opioids, while the others got saline solution as a control. The researchers were blind as to which group was getting what treatment.

The brain scans showed that in people whose opioid systems had been blocked, the amygdala showed a fear response that did not diminish with exposure. Every time they saw the symbol associated with pain, their amygdalas reacted strongly. In the control group, however, the activation decreased over the course of the experiment.

Because the group receiving naloxone was reacting more fearfully, the researchers speculate, they were learning the association more intensively.

Opioid deficiency

The team also found behavioural evidence that this might be the case. At the beginning of each trial, volunteers had to perform a reaction time task – pressing a button to indicate on which half of the screen the symbol had appeared.

Overall, subjects reacted more quickly to the cue signalling pain than the cue signalling nothing – but the opioid-free subjects reacted significantly faster.

"This natural response advantage to something dangerous was much stronger in the people who received naloxone," says Eippert.

The researchers speculate that opioid deficiency could be a contributing factor to anxiety disorders and exaggerated fear responses. Knock-out mice whose opioid systems have been genetically "switched off" do seem to be prone to anxieties and exaggerated conditioned fear responses, points out Eippert.

"It potentially has far reaching implications," says Jon-Kar Zubieta at the University of Michigan in Ann Arbor, US. There is tremendous variability in how individuals respond to threats and stress, he says, which is thought to relate to the risk developing anxiety disorders.

"This study examines the circuits and neurochemical systems that are likely to underlie that response heterogeneity." The research could help open new avenues for understanding, preventing and treating these types of illnesses, he says.

Journal reference: Journal of Neuroscience (DOI: 10.1523/jneurosci.5336-07.2008)

Well Finding the Best Way to Cook All Those Vegetables By TARA PARKER-POPE

By now, most people know they should be eating more vegetables. But are there ways to get more from the vegetables you already eat?

A growing body of research shows that when it comes to vegetables, it's not only how much we eat, but how we prepare them, that influences the amount of phytochemicals, vitamins and other nutrients that enter our body.

The benefits are significant. Numerous studies show that people who consume lots of vegetables have lower rates of heart disease, hypertension, diabetes, eye problems and even cancer. The latest dietary guidelines call for 5 to 13 servings — that is two and a half to six and a half cups a day. For a person who maintains her weight on a 2,000-calorie-a-day diet, this translates into nine servings, or four and a half cups a day, according to the Harvard School of Public Health. But how should they be served?

Surprisingly, raw and plain vegetables are not always best. In The British Journal of Nutrition next month, researchers will report a study involving 198 Germans who strictly adhered to a raw food diet, meaning that 95 percent of their total food intake came from raw food. They had normal levels of vitamin A and relatively high levels of beta carotene.



Stuart Bradford

But they fell short when it came to lycopene, a carotenoid found in tomatoes and other red-pigmented vegetables that is one of the most potent antioxidants. Nearly 80 percent of them had plasma lycopene levels below average.

"There is a misperception that raw foods are always going to be better," says Steven K. Clinton, a nutrition researcher and professor of internal medicine in the medical oncology division at Ohio State University. "For fruits and vegetables, a lot of times a little bit of cooking and a little bit of processing actually can be helpful."

The amount and type of nutrients that eventually end up in the vegetables are affected by a number of factors before they reach the plate, including where and how they were grown, processed and stored before being bought. Then, it's up to you. No single cooking or preparation method is best. Water-soluble nutrients like vitamins C and B and a group of nutrients called polyphenolics are often lost in processing. For instance, studies show that after six months, frozen cherries have lost as much as 50 percent of anthocyanins, the healthful compounds found in the pigment of red and blue fruits and vegetables. Fresh spinach loses 64 percent of its vitamin C after cooking. Canned peas and carrots lose 85 percent to 95 percent of their vitamin C, according to data compiled by the University of California, Davis.

Fat-soluble compounds like vitamins A, D, E and K and the antioxidant compounds called carotenoids are less likely to leach out in water. Cooking also breaks down the thick cell walls of plants, releasing the contents for the body to use. That is why processed tomato products have higher lycopene content than fresh tomatoes.

In January, a report in The Journal of Agriculture and Food Chemistry concluded that over all, boiling was better for carrots, zucchini and broccoli than steaming, frying or serving them raw. Frying was by far the worst.

Still, there were tradeoffs. Boiling carrots, for instance, significantly increased measurable carotenoid levels, but resulted in the complete loss of polyphenols compared with raw carrots.

That report did not look at the effects of microwaving, but a March 2007 study in The Journal of Food Science looked at the effects of boiling, steaming, microwaving and pressure cooking on the nutrients in broccoli. Steaming and boiling caused a 22 percent to 34 percent loss of vitamin C. Microwaved and pressure-cooked vegetables retained 90 percent of their vitamin C.

What accompanies the vegetables can also be important. Studies at Ohio State measured blood levels of subjects who ate servings of salsa and salads. When the salsa or salad was served with fat-rich avocados or full-fat salad dressing, the diners absorbed as much as 4 times more lycopene, 7 times more lutein and 18 times the beta carotene than those who had their vegetables plain or with low-fat dressing.

Fat can also improve the taste of vegetables, meaning that people will eat more of them. This month, The American Journal of Preventive Medicine reported on 1,500 teenagers interviewed in high school and about four years later on their eating habits. In the teenage years, many factors influenced the intake of fruits and vegetables. By the time the study subjects were 20, the sole factor that influenced fruit and vegetable consumption was taste. Young adults were not eating vegetables simply because they didn't like the taste.

"Putting on things that make it taste better — spices, a little salt — can enhance your eating experience and make the food taste better, so you're more likely to eat vegetables more often," Dr. Clinton said.

Because nutrient content and taste can vary so widely depending on the cooking method and how a vegetable is prepared, the main lesson is to eat a variety of vegetables prepared in a variety of ways.

As Susan B. Roberts, director of the energy metabolism laboratory at the Tufts University Friedman School of Nutrition, put it, "Eating a variety of veggies is especially important so you like them enough to eat more."

Regimens Aspirin More Beneficial if Taken at Night By ERIC NAGOURNEY

People who take aspirin to keep their blood pressure down will get more benefit if they take it at bedtime, researchers say.

The hormones and other chemicals the aspirin acts on are most active at night, they say.

Though blood pressure tends to drop at night, that is the time when the body is setting everything in motion for the pressure to go up the next day, during waking hours, said Ramón C. Hermida of the University of Vigo in Spain.

"If you take the aspirin in the morning, it is not going to be effective because aspirin basically has an effect for fours hours or so," Dr. Hermida said.

While doctors often advise patients to take aspirin to help control their blood pressure, he said, they generally do not give any advice about the time of the day.

For the study, presented at a conference of the American Society of Hypertension, researchers looked at more than 240 people with a condition known as prehypertension over three months. Some took aspirin in the morning, others at night and some not at all. Their blood pressure was taken regularly during the study, and the researchers also kept track of physical activity.

Older Brain Really May Be a Wiser Brain

By SARA REISTAD-LONG

When older people can no longer remember names at a cocktail party, they tend to think that their brainpower is declining. But a growing number of studies suggest that this assumption is often wrong.

Instead, the research finds, the aging brain is simply taking in more data and trying to sift through a clutter of information, often to its longterm benefit.

The studies are analyzed in a new edition of a neurology book, "Progress in Brain Research."



Yarek Waszul

Some brains do deteriorate with age. Alzheimer's disease, for example, strikes 13 percent of Americans 65 and older. But for most aging adults, the authors say, much of what occurs is a gradually widening focus of attention that makes it more difficult to latch onto just one fact, like a name or a telephone number. Although that can be frustrating, it is often useful.

"It may be that distractibility is not, in fact, a bad thing," said Shelley H. Carson, a psychology researcher at Harvard whose work was cited in the book. "It may increase the amount of information available to the conscious mind."

For example, in studies where subjects are asked to read passages that are interrupted with unexpected words or phrases, adults 60 and older work much more slowly than college students. Although the students plow through the texts at a consistent speed regardless of what the out-of-place words mean, older people slow down even more when the words are related to the topic at hand. That indicates that they are not just stumbling over the extra information, but are taking it in and processing it.

When both groups were later asked questions for which the out-of-place words might be answers, the older adults responded much better than the students.

"For the young people, it's as if the distraction never happened," said an author of the review, Lynn Hasher, a professor of psychology at the University of Toronto and a senior scientist at the Rotman Research Institute.

"But for older adults, because they've retained all this extra data, they're now suddenly the better problem solvers. They can transfer the information they've soaked up from one situation to another."

Such tendencies can yield big advantages in the real world, where it is not always clear what information is important, or will become important. A seemingly irrelevant point or suggestion in a memo can take on new meaning if the original plan changes. Or extra details that stole your attention, like others' yawning and fidgeting, may help you assess the speaker's real impact.

"A broad attention span may enable older adults to ultimately know more about a situation and the indirect message of what's going on than their younger peers," Dr. Hasher said. "We believe that this characteristic may play a significant role in why we think of older people as wiser."

In a 2003 study at Harvard, Dr. Carson and other researchers tested students' ability to tune out irrelevant information when exposed to a barrage of stimuli. The more creative the students were thought to be, determined by a questionnaire on past achievements, the more trouble they had ignoring the unwanted data. A reduced ability to filter and set priorities, the scientists concluded, could contribute to original thinking.

This phenomenon, Dr. Carson said, is often linked to a decreased activity in the prefrontal cortex. Studies have found that people who suffered an injury or disease that lowered activity in that region became more interested in creative pursuits.

Jacqui Smith, a professor of psychology and research professor at the Institute for Social Research at the University of Michigan, who was not involved in the current research, said there was a word for what results when the mind is able to assimilate data and put it in its proper place — wisdom.

"These findings are all very consistent with the context we're building for what wisdom is," she said. "If older people are taking in more information from a situation, and they're then able to combine it with their comparatively greater store of general knowledge, they're going to have a nice advantage."

Findings Comfort Food, for Monkeys By JOHN TIERNEY

The ladies who lunch do not obsess about their weight in the rhesus monkey compound at the Yerkes National Primate Research Center in Atlanta. Food is freely available, and the high-status females do not pride themselves on passing it up. They don't seem to

stigmatize obesity — there is no equivalent of a Kirstie Alley joke — and they certainly don't turn themselves into Social X-Rays.

In fact, the dominant females ordinarily eat a little more than the subordinates. The lower status monkeys can get as much food as they want but seem to have less of a desire to eat, perhaps because of the higher level of stress hormones in their brain. The anxiety of constantly toadying to their social superiors seems to curb their appetite, researchers suspect, at least when their regular high-fiber, low-fat chow is on the menu.



Viktor Koen

But suppose you tempted them with the equivalent of chocolate and potato chips and ice cream? Mark Wilson, a neuroscientist at Emory University, and a team tried that experiment at Yerkes by installing feeders with a constant supply of banana-flavored pellets — not exactly Dove bars, but they had enough sugar and fat to appeal even to human palates. (In the interest of science, I sampled a few pellets.)

Once these foods were available, the low-status monkeys promptly developed an appetite. They began eating significantly more calories than their social superiors. While the dominant monkeys dabbled in the sweet, fatty pellets just during the daytime, the subordinate monkeys kept scarfing them down after dark.

These results may not surprise any stressed-out wage slave who has polished off a quart of Häagen-Dazs at midnight while contemplating the day's humiliations. But the experiment intrigues scientists studying human junk-food binges, which are hard to understand because there are so many confounding factors.

Monkeys' cravings aren't so complicated. The female monkeys weren't dieters who tasted one forbidden food and then couldn't stop themselves from binging. They were not rebelling against the thin mandate from tyrannical fashion magazines. They weren't choosing junk food because they couldn't find healthier fare. They weren't seduced by commercials telling them they deserved a break today.

For the monkeys the situation seems simple. They get some sort of comfort that is particularly appealing to the subordinate monkeys. One possibility is that the fatty foods help block the monkeys' stress responses. Studies with rodents have shown that high-calorie foods cause a metabolic change that tamps the release of stress hormones like cortisol.

Another possible explanation, the one favored by the Yerkes researchers, is that the snacks activated the reward pathways in the brain. They may have provided the same sort of dopamine reward as cocaine, which was studied in a previous experiment with monkeys by researchers at Wake Forest University.

In that experiment, the dominant monkeys didn't show much interest in pressing a lever that administered an intravenous dose of cocaine. But the subordinate monkeys, who started off with compromised dopamine receptors, kept pushing the lever to get more cocaine, just as the subordinates in the new study kept munching on the fatty pellets. Dr. Wilson suggests that the snackers are reinforcing the dopamine systems that had been diminished by stress.

"Essentially, eating high-calorie foods becomes a coping strategy to deal with daily life events for an individual in a difficult social situation," Dr. Wilson said. "The subordinates don't get beat up, but they get harassed by high-ranking monkeys. If they're sitting somewhere and a dominant monkey comes over, they give up their seat and move away. They're always looking over their shoulders."

These results seem to jibe with the famous Whitehall study of British civil servants, which found that lowerranking workers were more obese than higher-status workers. Even though the subordinate workers were neither poor nor lacked health care, their lower status correlated with more health problems.

The new monkey data also jibe with an American study that looked at women's snacking tendencies. After they worked on puzzles and recorded a speech, the women were tempted with an array of chocolate granola bars, potato chips, rice cakes and pretzels provided by the research team, led by Elissa Epel, a psychologist at the University of California, San Francisco.

The women who seemed most stressed by the tasks, as measured by their levels of cortisol, ate more of the sweet, high-fat snacks, the same pattern observed in the subordinate monkeys with high cortisol levels. But as Dr. Wilson and others caution, there are plenty of other factors besides status and stress that affect humans' diets and waistlines.

Debra A. Zellner, a psychologist at Montclair State University, tested both men and women by putting bowls of potato chips, M&Ms, peanuts and red grapes on a table as the participants in the study worked on solving anagrams. Some of the people were given unsolvable anagrams, and they understandably reported being more stressed than the ones given easy anagrams.

The stress seemed to affect snacking in different ways for each sex. The women given solvable puzzles ate more grapes than M&Ms, while the women under stress preferred M&Ms. The men ate more of the high-fat snacks when they were not under stress, apparently because the ones who got the easy anagrams had more time to relax and have a treat.

Dr. Zellner says these gender patterns are probably because of a simple difference between the sexes: more of the women were on diets. Previous studies have shown that such "restrained eaters" are more likely than nondieters to keep scarfing snacks once they yield to temptation. This might be because they're hungrier, but it might also be because all restraint disappears once a diet is broken — the "what the hell" theory of binging.

Humans are not as lucky as monkeys in one way. "Female humans report that they eat high-calorie foods to make themselves feel better when stressed," Dr. Zellner says, "but they actually don't feel better after eating them. Instead, because they are restrained eaters, they feel guilt and actually feel worse. Female monkeys don't have that cognitive baggage."

Only the monkeys, it seems, find comfort in comfort foods.

Cat brain could provide bionic eye firmware

* 18:08 21 May 2008 * NewScientist.com news service

* Barbara Axt

It may not be able to catch mice yet, but software developed in the US can perceive moving images in much the same way a cat's brain does. The researchers hope the work will one day lead to implants that make it possible for people to see without an optic nerve.

Researchers at the Smith-Kettlewell Eye Research Institute, San Francisco, were motivated by the fact that, until now, models of the way brains respond to visual input used simple images like dots, bars and grids. They are typically unable to cope with the complex scenes a human would usually see.

To try and develop a more sophisticated model, the team recorded the responses of 49 individual neurons in a part of a cat's brain called the lateral geniculate nucleus (LGN). The LGN receives and processes visual information from the retina, via the optic nerve, before sending it on to the cerebral cortex.

Using a mixture of simple stimuli, like dots and bars, and building up to more complex moving artificial scenes, the team tried to work out the basics of the LGN's response to visual features.

Call in the catcam

The data made it possible to build a software model of the LGN that can approximate how the neurons would respond to real scenes. The model was tested against scenes recorded from a "catcam" camera attached to a cat's head.

"We chose the catcam because it was the most natural stimulus we could think of, the closest to what a cat would see when walking around," Matteo Carandini told New Scientist. Because the catcam footage lacked elements moving independently from the rest of the scene, the researchers also used a scene from Disney's animated film Tarzan.

The model's predictions proved to be 80% accurate when shown artificial scenes, but this figure fell to 60% with the natural scenes or the Tarzan movie.

"This is still impressive, but shows a way to go," says Stephen Hicks, a neuroscientist at Imperial College London, UK.

Predicting LGN activity from moving images at all is significant, he says. "[The researchers] recognise that the perceptual world is not a single frame at a time but a constant stream of data," he told New Scientist. **Bionic eyes**

The ultimate goal of the research, still years distant, is to develop an implant that uses visual data to directly stimulate the LGN of blind people whose optic nerve or retina has degenerated from lack of use.

"For these people, a prosthesis in the eye doesn't help," Carandini explains. Only people who have recently become blind can benefit from such implants - currently being tested in humans - that stimulate the retina or optic nerve,.

Work on monkeys last year showed it is possible to stimulate the LGN using electrodes to alter their vision, something previously thought impossible. Software models like that developed by Carandini and colleagues would be vital for an implant to stimulate the right neurons to create a mental impression of vision. Journal reference: Neuron (DOI: 10.1016/j.neuron.2008.03.011)

Smoking is addictive, but quitting is contagious

BOSTON, Mass. (May 21, 2008)-Over the last 30 years, the number of smokers in the U.S. has steadily decreased-a tribute to the efforts of public-health workers everywhere. And while this fact is unarguable, less obvious are the social and cultural forces that lead an individual to kick the habit. In fact, when someone crumbles that last empty pack of their favorite unfiltered brand and vows to never buy another, he might not realize that he is less like the heroic individual grasping his own boot straps and more like a single bird whose sudden left turn is just one speck in the larger flock.

These are the findings of a massive longitudinal study spanning 32 years: people quit smoking in droves. Through reconstructing the social network of 12,067 individuals, researchers from Harvard Medical School and the University of California, San Diego have discovered that smoking cessation occurs in network clusters and is hardly the isolated decision it might feel like to the individual quitter.

"We've found that when you analyze large social networks, entire pockets of people who might not know each other all quit smoking at once," says Nicholas Christakis, a professor in Harvard Medical School's Department of Health Care Policy, who, along with U.C. San Diego researcher James Fowler, authored the study. "So if there's a change in the zeitgeist of this social network, like a cultural shift, a whole group of people who are connected but who might not know each other all quit together."

The study, which was funded primarily by the National Institute on Aging, appears in the May 22 issue of the New England Journal of Medicine.

Over the last few years, Christakis, who is also a professor of sociology in the Faculty of Arts and Sciences at Harvard University, and Fowler have been analyzing data from the Framingham Heart Study (an ongoing cardiovascular study begun in 1948), recreating the social patterns contained within the study data to see how health correlates with an individual's social network.

The researchers derived information from archived, handwritten administrative tracking sheets dating back to 1971. All family changes for each study participant, such as birth, marriage, death, and divorce, were recorded. In addition, participants had also listed contact information for their closest friends, as well as coworkers and neighbors. Coincidentally, many of these friends and coworkers were also study participants. 2008/05/26 21

Focusing on 5,124 individuals, Christakis and Fowler observed a total of 53,228 social, familial, and professional ties.

Last year, they reported on how obesity spreads through social networks. Using the same data, they decided to analyze smoking cessation trends within that same population. The first and most striking finding was the discovery that, from the larger network perspective, people quit smoking as groups and not as individuals.

"When you look at the entire network over this 30-year period, you see that the average size of each particular cluster of smokers remains roughly the same," says Fowler. "It's just that there are fewer and fewer of these clusters as time goes on."

They were able to quantify the person-to-person effects of smoking cessation among married couples, siblings, friends, and coworkers. In addition, they also discovered "quitting cascades" that advanced from person-to-person-to-person. (See end of release for statistical chart.)

Christakis illustrates this point by describing a small network containing three individual smokers, persons A, B, and C. The first person, A, is friends with B, and B is friends with C, but A and C do not know each other. If C quits smoking, A's chances of not smoking spike 30 percent, regardless of whether or not B smokes. The middle individual, it would appear, might act as a kind of "carrier" for a social norm.

Education also seems to matter. We are more influenced by the quitting behavior of others if those people are highly educated. To add a further twist, we are also more influenced by others if we ourselves are more educated.

Says Christakis, "We see by this that the educated are not only more influential, but they are also more easily influenced."

And finally, Christakis and Fowler discovered that smokers are increasingly marginalized throughout social networks.

"If you look back at 1971, smokers and non-smokers alike were at the centers of social networks," says Fowler. "For people running companies and having parties, smoking was irrelevant. But during the '80s and '90s we saw a dramatic shift of smokers to the periphery of the social network. Contrary to what we might have thought in high school, smoking has become a supremely bad strategy for getting popular."

This marginalization of smokers appears to occur across all educational and economic demographics.

According to the researchers, this is an additional concern. Social marginalization leads to poor health. Smoking then is not only bad for your physical health but for your social health as well.

"What people need to understand is that because our lives are connected, our health is connected," says Christakis.

"Policy makers have an understandable tendency to treat people as atomized individuals, and to anticipate the impact of their policies accordingly," says Duncan Watts, professor of sociology at Columbia University, who was not involved with this study. "What this study—like the authors' previous study on obesity—points out clearly, however, is that individuals do not behave as atoms, but as part of a network. Although simple to state, the consequences of that observation are profound, and will require us to fundamentally rethink our intuition about the world."

"The culture of individualism is so strong that we sometimes forget how powerfully and silently social networks and those around us influence our health," said Richard Suzman, director of National Institute on Aging's Division of Behavioral and Social Research. "If decisions to quit cascade through social networks, then this study has provided public health campaigns a powerful new methodology with which to influence behaviors."

Written by David Cameron

SMOKING CESSATION, RANKED BY RELATIONSHIP:

- * When one spouse quits smoking, the other spouse's chances of continuing smoking decrease 67 percent.
- * When a friend quits, a person's chances of continuing decrease by 36 percent.
- * Among co-workers in small firms, 34 percent. (Data for larger firms was insignificant.)
- * Among siblings, 25 percent

rinong storings, 20 percent.		
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Amy Lavoie	"Dynamics of Smoking Behavior in a Large Social Network"	
amy_lavoie@harvard.edu	Nicholas Christakis(1,2) and James Fowler(3)	
617.496.9982	1-Harvard Medical School, Department of Healthcare Policy, Boston, MA	
National Institute on Aging	2-Harvard University, Department of Sociology, Cambridge, MA	
Margaret Vaughn	3-University of California, San Diego, Department of Political Science, San	
vaughnms@mail.nih.gov	Diego, CA	
301.451.8408		

A missing link settles debate over the origin of frogs and salamanders

The description of an ancient amphibian that millions of years ago swam in quiet pools and caught mayflies on the surrounding land in Texas has set to rest one of the greatest current controversies in vertebrate evolution. The discovery was made by a research team led by scientists at the University of Calgary.

The examination and detailed description of the fossil, Gerobatrachus hottoni (meaning Hotton's elder frog), proves the previously disputed fact that some modern amphibians, frogs and salamanders evolved from one ancient amphibian group called temnospondyls.

The discovery is described for the first time in the prestigious international research journal Nature.

"The dispute arose because of a lack of transitional forms. This fossil seals the gap," says Jason Anderson, assistant professor, University of Calgary Faculty of Veterinary Medicine and lead scientist in the study.

An Early Permian landscape, with Gerobatrachus hottoni lunging at the mayfly Protoreisma between stands of Calamites and under a fallen Walchia conifer. Michael Skrepnick

The Gerobatrachus fossil provides a much fuller understanding of the origin and evolution of modern amphibians. The skull, backbone and teeth of Gerobatrachus have a mixture of frog and salamander features—the fossil has two fused bones in the ankle, which is normally only seen in salamanders, and a very large tympanic ear (ear drum). It also has a lightly built and wide skull similar to that of a frog. Its backbone is exactly intermediate in number between the modern frogs and salamanders and more primitive amphibians.

The new fossil also addresses a controversy over molecular clock estimates, or the general time salamanders and frogs evolved into two distinct groups.

"With this new data our best estimate indicates that frogs and salamanders separated from each other sometime between 240 and 275 million years ago, much more recently than previous molecular data had suggested," says Robert Reisz, professor, University of Toronto Mississauga and second author on the paper.

Gerobatrachus was originally discovered in Texas in 1995 by a field party from the Smithsonian Institution that included the late Nicholas Hotton, for whom the fossil is named. It remained unstudied until it was "rediscovered" by Anderson's team. It took countless hours of work on the small, extremely delicate fossil to remove the overlying layers of rock and uncover the bones to reveal the anatomy of the spectacular looking skeleton.

"It is bittersweet to learn about frog origins in this Year of the Frog, dedicated to informing the public about the current global amphibian decline," continues Anderson. "Hopefully we won't ever learn about their extinction."

Virtual biopsy can tell whether colon polyp is benign without removal, Mayo researchers say

JACKSONVILLE, Fla. – A probe so sensitive that it can tell whether or not a cell living within the human body is veering towards cancer development may revolutionize how future colonoscopies are done, say researchers from the Mayo Clinic in Jacksonville, Fla.

Investigators have found that technology known as a high resolution confocal endomicroscopy probe system can determine whether a colon polyp is benign (not precancerous) - without having to remove it for examination by a pathologist.

Their study, to be presented at the Digestive Disease Week, a scientific meeting of gastrointestinal specialists and researchers held in San Diego, shows that using the probe system was 89 percent accurate in identifying whether polyps were either precancerous or benign. But more importantly, it was correct 98 percent of the time in flagging polyps that were benign, which would then not need to be removed for biopsy. The Mayo researchers, who are the first in the U.S. to comprehensively test the system in the colon, believe they can push accuracy close to 100 percent with more research.

What this means is that the probe system can be used to during a colonoscopy to rule out removal of polyps that are not harmful, says the study's senior author, Michael Wallace, M.D., M.P.H., Professor of Medicine at Mayo Clinic.

"Today, half of all polyps surgically removed during colonoscopy procedures are benign, and so this virtual biopsy will save time and expense, and reduce complications that can occur," he says.



The device is a tiny imaging tool, only 1/16th of an inch in diameter, which can be attached to a variety of endoscopes that are already being used during colonoscopies, Dr. Wallace says. When a suspicious polyp is seen during a colonoscopy, a physician can use the probe to look closely at the lesion. To do this, a small amount of fluorescent contrast is used to illuminate the area, and the probe magnifies it by 1,000 times – enough to see a single red blood cell as it moves through a blood vessel.

In this study, the researchers first tested 10 precancerous ("adenomatous") lesions as well as 10 benign ("hyperplastic") lesions using the probe system in order to understand the differences in appearance between the two. (The status of the polyps was later verified by pathologists.) Among other things, they looked at changes in cell color and size, how nuclei within the cells looked, and whether cells were crowed within tissue, or fused.

They then, without knowledge of the pathologists' diagnosis, used their new grading system to determine the status of 37 polyps within 25 patients, which were then removed. The most important clinical result is that the probe was 98 percent accurate in identifying lesions that were not cancerous. "That is what you want in a device like this," says the project's lead research fellow, Anna M. Buchner, M.D., who will be presenting the findings. "Removing a polyp that looks precancerous, but turns out to be benign, is okay, but you don't want to leave polyps intact in the colon that are actually cancerous," she says. "This probe is almost perfectly reliable in that regard and with more experience I am sure we can improve accuracy to nearly 100 percent."

Wallace says the technology, which is also being tested in the esophagus, has the capacity to fundamentally change how many different endoscopy procedures are done. "This will shift our role from one of going in and getting tissue for a pathologist to examine to one in which we can do the pathology ourselves," Dr. Wallace says. "This is instantaneous, real time pathology."

The study was supported by the American Society for Gastrointestinal Endoscopy.

Earth may hide a lethal carbon cache

CARBON buried in the Earth could ultimately determine the fate of our planet's atmosphere. So concluded a pioneering meeting last week about the Earth's long-neglected "deep" carbon cycle.

Carbon is locked away down in the Earth's crust: in magma and old carbonate rocks buried by plate tectonics, in fossil fuels like coal and oil, and in ice lattices beneath the ocean bed. It has long been assumed that this carbon was largely cut off from the surface, and could safely be ignored when analysing the effect of greenhouse gases on climate.

Now it seems there may be much more "deep carbon" ready to spew out than we thought.

This realisation could have profound implications for our climate, argues Robert Hazen of the Carnegie Institution, who organised the meeting at the institution's Geophysical Laboratory in Washington DC. "We may be on the verge of a transformational moment…a glimpse of new, unexplored scientific territory," he says.

Perhaps the greatest threat of an unexpected release of carbon from the deep comes from an indirect effect of human-made CO2. Global warming could destabilise some deep carbon reserves, notably in clathrates - ice lattices which are found beneath the ocean floor and continental permafrost, and even under freshwater lakes like Lake Baikal in Siberia (pictured). These ice structures may hold trillions of tonnes of methane.

"We are extremely concerned that clathrates are the largest single source of greenhouse gases that could be added to the atmosphere," says Hazen. "If you raise temperatures even slightly, they could be released." According to Ronald Cohen, a geophysicist at the Carnegie Institution, natural warming caused large releases of methane around 55 million years ago.

Though the deep carbon cycle could theoretically absorb human-made emissions, Hazen points out that this would take millions of years. Catastrophic methane emissions could happen over just a few decades.

Natural processes such as volcanism are also known to bring carbon to the surface, but there may be other mechanisms to release buried carbon that have not been considered by mainstream climate science. For example, there is growing evidence that microbes living deep in the crust may be converting carbon into forms that can migrate to the surface - notably methane.

Vladimir Kutcherov of the Royal Institute of Technology in Stockholm, Sweden, speculates that unknown non-biological chemical reactions may also be able to produce methane or hydrocarbons that seep up through the crust. For example, methane or petroleum might be produced when carbonate rocks react with water and iron upon being subducted into the mantle. Kutcherov and colleagues say hydrocarbon deposits from Kidd Creek in Ontario, Canada, have an isotopic signature suggesting they are not organic in origin - though this claim was disputed by others at the meeting.

Halting methane squanderlust

Researchers determine structure of catalyst that converts methane to more useful compounds RICHLAND, Wash. -- The pipes that rise from oil fields, topped with burning flames of natural gas, waste fossil fuels and dump carbon dioxide into the air. In new work, researchers have identified the structure of a catalytic material that can turn methane into a safe and easy-to-transport liquid. The insight lays the foundation for converting excess methane into a variety of useful fuels and chemicals.

"There's a big interest in doing something with this 'stranded' methane other than flaring it off," said chemist Chuck Peden of the Department of Energy's Pacific Northwest National Laboratory. "An important thing researchers have struggled with is determining the structure of the active catalyst."

That catalyst -- molybdenum oxide sitting on a zeolite mineral -- converts methane gas into the more tractable liquid benzene. But the process is not yet commercially viable. Scientists don't understand enough about the molecular details to improve the catalyst. Now, researchers at PNNL and the Chinese Academy of Sciences' Dalian Institute of Chemical Physics in Dalian have worked out some of the details that will help researchers zoom in on an efficient catalyst.

They reported their results March 26 in the Journal of the American Chemical Society. This work is the first publication to come out of the International Consortium for Clean Energy, a collaboration between PNNL, the DICP and China's Institute of Coal Chemistry.

To get these results, the chemists -- led by Peden at PNNL and Xinhe Bao at DICP -- used the world's largest instrument of its kind -- a 900-megahertz nuclear magnetic resonance (NMR) spectrometer. The NMR is armed with one of the strongest magnets constructed and can be outfitted to investigate solid samples, a step above its smaller cousins.

The combination of molybdenum oxide and a zeolite mineral had been shown in 1993 to convert methane, but the catalyst has been difficult to analyse. Researchers know that the zeolite anchors molybdenum oxide in place so methane and molybdenum oxide can react chemically, either on or in the zeolite channels. But no one could tell which comprised the reactive form: a small nugget of one or two molecules, or a larger cluster of many molybdenum oxide molecules.

"This uncertainty has led to a controversy in the scientific literature about the active phase and reaction mechanism of methane activation on these promising catalyst materials," said DICP's Bao.

Enter the world's largest NMR, uniquely capable of addressing this issue. The technological problem lay in the molybdenum oxide itself. To study this particular oxide with NMR, the chemists needed to pick up the signal from one variant of molybdenum, 95Mo; the ultra-high field of the NMR, housed at the DOE's Environmental Molecular Sciences Laboratory on the PNNL campus, allowed them to do so.

"The higher magnetic field improves the signal to noise," said Peden. "And its large sample volume allowed us to put enough catalyst into the spectrometer to overcome the poor sensitivity of 95Mo NMR."

The researchers painstakingly prepared catalysts with increasing concentrations of molybdenum in the zeolite scaffold and focused the 900 MHz NMR on the samples. The data revealed two different forms of the catalyst, as expected. One form contained the smaller nugget and the other form comprised the much larger clusters. When the concentration of molybdenum rose, more of these large clusters formed.

Then the team added methane and measured how much got converted into benzene by the catalysts. They found that when more smaller nuggets were present, more benzene was made, indicating the variety of one or two molybdenum oxide molecules was the reactive one.

Now, said Peden, the challenge is to design and produce the active form of the catalyst that could be used for large-scale benzene production, research that Bao and his group are already working on.

"We need to figure out how to get that structure and keep it that way," Bao said.

Reference: H. Zheng, D. Ma, X. Bao, J.Z. Hu, J.H. Kwak, Y. Wang, and C.H.F. Peden, Direct Observation of the Active Center for Methane Dehydroaromatization Using an Ultra-High Field 95Mo NMR Spectroscopy, J. Am. Chem. Soc., 130 (12), 3722 - 3723, 2008, DOI: 10.1021/ja7110916.

This work was supported by the Department of Energy's Office of Basic Energy Sciences and the National Science Foundation of China.

Urge to kill doctors increased by pain

* 18:14 21 May 2008

* NewScientist.com news service

* Jim Giles

Been patronised or fobbed off by your doctor? It may have made you angry, but hopefully not angry enough to want to kill them.

Yet it turns out that the urge is not uncommon, especially among patients who are in pain, undergoing physical rehabilitation or seeking legal compensation for disability.

David Fishbain and colleagues at the University of Miami, Florida, found that just over 1 in 20 (5%) of roughly 800 physical rehabilitation patients admitted feeling like they wanted to murder their physician.

Even amongst a control group, who were not being treated for any condition, slightly fewer than 1 in 50 (2%) said they had previously had the same urge.

Few doctors are actually killed by their patients, but many are attacked and injured. Understanding who is likely to have a wish to harm, and why, could help reduce attacks.

Fishbain says that distrust of doctors often underlies the problem. Involvement in a disability compensation case is, for example, an important predictor of what he calls the "kill-MD" urge. He says that patients often become angry because they feel that their doctor will not support their compensation claim.

Being in pain, perhaps not surprisingly, was another factor influencing whether patients felt murderous desire.

The work was presented at the American Pain Society meeting this month in Tampa, Florida.

Oregano oil works as well as synthetic insecticides to tackle common beetle pest

New research in the Society of Chemical Industry's Journal of the Science of Food and Agriculture shows that oregano oil works as well as synthetic insecticides to combat infestation by a common beetle, Rhizoppertha dominica. found in stored cereals.

Not only does oregano oil work as well as synthetic versions but it has none of the associated side effects of synthetic insecticides on the environment.

Growing resistance to synthetic insecticides combined with potential environmental damage and new government directives on changes to the way chemicals are registered means that scientists are increasingly looking at natural alternatives that can be produced in the large scale quantities needed for agricultural industry use.

Oregano, a member of the Lamiaceae family of plants, has long been renowned as a natural insecticide. It appears to work by inhibiting egg laying and larval development but this is the first time it has been looked at as a viable alternative for synthetic insecticides.

Dr Chahrazed Boutekedjiret and her team from the National Polytechnic in Algeria identified 18 components in oregano oil that combat pests and found that the greater the concentration of the oil used, the more effective it was.

She says: "It is feasible that, in the near future, these natural insecticides will replace synthetic insecticides and add considerably to more environmentally friendly insecticides on a large scale."

Dr Alan Baylis, the honorary secretary of the Society of Chemical Industry's Bioresources Group said: "Just because something is natural does not mean it is harmless to humans - some of the most toxic compounds lethal to humans and other mammals are natural products. However, there will be markets for natural insecticides which have been rigorously tested for safety and efficacy, but as they are difficult to produce on a large scale for agricultural use, then the scope for them is rather limited."

For more information or a full copy of the paper, contact: Meral Nugent, Press and Public Relations Manager, T: +44 (0)20 7598 1533, F: +44 (0) 20 7598 1545, Mob: 07931 315077

E: meral.nugent@soci.org

Scientists See Supernova in Action BV DENNIS OVERBYE

A star trembled on the brink of eternity. Outwardly all was serene, but its inside was falling into chaos. Far away on the day of Jan. 9, Earth time, a satellite telescope by the name of Swift, which happened to be gazing at the star's galaxy, a smudge of stars 88 million light-years away in the constellation Lynx, recorded an unexpected burst of invisible X-rays 100 billion times as bright as the Sun.

Alicia Soderberg, a Princeton astronomer who had been using the NASA satellite to study the fading remains of a previous supernova explosion, received the startling results of that observation by e-mail while giving a talk in Michigan. Recognizing that this was something extraordinary, she sounded a worldwide alert. 2008/05/26 26

In the following hours and days, as most of the big telescopes on Earth, and the Hubble Space Telescope and the Chandra X-ray Observatory watched from space, the star erupted into cataclysmic explosion known as a supernova, lighting up its galaxy and delighting astronomers who



had never been able to catch an exploding star before it exploded.

Supernova 2007uy in the galaxy NGC2770 was already several weeks old on January 7, 2008 when NASA's Swift satellite took the image at left. The image on the right was taken two days later and shows Supernova 2008D as well. NASA Swift Team

"We caught the whole thing on tape, so to speak," Dr. Soderberg said in an interview. "I truly won the astronomy lottery. A star in the galaxy exploded right in front of my eyes."

She and 42 colleagues from around the world have now told the tale of this discovery in a paper in Nature to be published Thursday and in a telephone news conference Wednesday. The observations, they say, provide a new window into the process by which the most massive stars end their lives and give astronomers new clues on how to look for these rare events and catch them while they are still in their most explosive, formative stages.

Most supernovas, Dr. Soderberg explained, are discovered and classified by their visible light, but that typically does not happen until the explosion is a month or more old and has brightened enough to be seen over intergalactic distances.

The true fireworks, she said, happen much earlier when a shock wave from the imploding core hits the star's surface, producing so-called breakout light, which lasts only a few minutes.

"The physics of the explosion is encoded in the breakout light," Dr. Soderberg said, adding that the chance that the Swift telescope was observing during those moments was "unfathomable." Astronomers now know, however, that X-rays from the breakout can be an early alert. "Supernova 2008D was the first to be found from its X-ray emission," said Robert Kirshner, a supernova expert at the Harvard-Smithsonian Center for Astrophysics, referring to the supernova by its official name, "but if we build the right type of X-ray satellites, it won't be the last supernova we find this way."

"That is really what is so wonderful here," he said.

So new were the X-rays, said Dr. Soderberg, that she and her collaborators did not know they were looking at an incipient supernova until a day or two later and ground-based telescopes had seen it grow in visible light.

"It was a baby supernova in that sense," Dr. Soderberg said. "Here was an object brand new. At first we didn't recognize it."

The supernova was of a sort known as Type Ibc, the rarest and most luminous of the explosions caused by the collapse of the cores of massive stars, the astronomers have concluded. Another kind, known as Type Ia supernovas, are believed to result from the destruction of much smaller stars and are beloved of cosmologists who use them to track the expansion of the universe and effects of dark energy.

The star that died last January could have been 20 times as massive as the Sun or even bigger, Dr. Soderberg said. It was probably a type called a Wolf-Rayet star. They are very hot stars with surface temperatures of 50,000 degrees Fahrenheit or more and are often blowing gas away in strong winds. Dr. Soderberg described them as "very violent stars, very massive."

Because it is gravity that stokes the thermonuclear furnace at the centers of stars, the more massive they are, the younger they die. In the case of a star 10 or 20 times as massive as the Sun, it could be only a few million years. "These stars live fast and die young. We don't know if they leave a beautiful corpse," Dr. Kirshner said.

Many of the elements necessary for life and its accessories, like carbon, oxygen, iron and gold, are produced in a thermonuclear frenzy during the final stages of these explosions, which then fling them into space to be incorporated into new stars, new planets, new creatures.

"If you're wearing gold jewelry," Dr. Kirshner said, "it came from a supernova explosion." Or as Joni Mitchell sang poetically and accurately, "We are stardust."

<u>News to May, 22, 2008</u>

Licorice extract provides new treatment option for canker sores

CHICAGO (May 22, 2008) - What common oral condition appears as shallow ulcers of different sizes, affects one in five Americans, can be caused by food allergies and hormonal changes, and also can cause severe mouth pain? Commonly referred to as "canker sores," recurrent aphthous ulcers (RAU) now can be treated by an extract in licorice root herbal extract, according to a study published in the March/April 2008 issue of General Dentistry, the Academy of General Dentistry's (AGD) clinical, peer-reviewed journal.

The authors examined the effects of an over-the-counter medicated adhesive patch (with extract from the licorice root) for treatment of RAU versus no treatment. After seven days of treatment, ulcer size in the group who received the adhesive patch with licorice extract was significantly lower, while ulcer size in the no-treatment group had increased 13 percent.

Licorice root extract was used as a prescribed treatment for gastric ulcers until the 1970s, according to the study. In its original form, licorice root extract has a very strong taste. However, when combined with a self-adhering, time-release, dissolving oral patch, the taste is mild and pleasant.

Among the causes of canker sores, a genetic predisposition might be the biggest cause, says Michael Martin, DMD, PhD, lead author of the study. "When both parents have a history of canker sores, the likelihood of their children developing them can be as high as 90 percent," he says.

The most serious side effect of canker sores is sharp pain in the mouth, which can interfere with an individual's quality of life and affect their eating, drinking or speech. Dr. Martin revealed that "in addition to speeding healing of the canker sores, the adhesive patch helped to reduce pain after just three days of treatment."

Those who experience canker sores on a regular basis can visit their dentist for treatment techniques. "Dentists can give patients the proper medication and treatment options to seal the lesions, which will prevent further infection," says Eric Shapira, DDS, MAGD, AGD spokesperson and expert on alternative medicine. "Also, increasing vitamins and other herbs, such as Vitamin C and zinc, can help treat canker sores because they help to regenerate tissue cells," Dr. Shapira adds.

Common causes of canker sores:

- * Local trauma and stress
- * Diet and food allergies
- * Hormonal changes
- * Use of certain medications

Common treatments of canker sores:

- * Antimicrobial mouthwashes
- * Local painkillers

* Over-the-counter remedies (oral adhesive patches, liquids and gels)

Sun's properties not 'fine-tuned' for life

* 14:42 22 May 2008 * NewScientist.com news service * Hazel Muir

There's nothing special about the Sun that makes it more likely than other stars to host life, a new study shows. The finding adds weight to the idea that alien life should be common throughout the universe.

"The Sun's properties are consistent with it being pulled out at random from the bag of all stars," says Charles Lineweaver from the Australian National University (ANU) in Canberra. "Life does not seem to require anything special in its host star, other than it be close."

Some previous studies of the Sun's vital statistics have concluded that it is unusual among stars, for instance, by having a higher mass than average. Such atypical properties might somehow help explain why the Sun seems to be unique, as far as we know, in having an inhabited planet.

But the earlier studies only looked at a small number of solar features, such as its mass and iron content. Lineweaver suspects there was a temptation to sift through the Sun's properties, then focus on the outstanding ones while ignoring the normal ones.

Mistaken conclusion

"You can mistakenly come to the conclusion that the Sun is 'special'," Lineweaver told New Scientist.

With his ANU colleague José Robles and others, Lineweaver has now analysed 11 features of the Sun that might affect its ability to have habitable planets. They included its mass, age, rotation speed and orbital distance from the centre of the Milky Way.

Then they compared these with well-measured statistics for other stars to answer the question – overall, does the Sun stand out from the crowd any more than some other randomly chosen star would?

The Sun did stand out in two ways: it is more massive than 95% of nearby stars and its orbit around the centre of our galaxy is more circular than those of 93% of nearby stars.

It may be the only star known to have an inhabited planet, but there's really nothing special about our Sun (Image: SOHO-EIT Consortium/ESA/NASA)

Very ordinary

But when all 11 properties were taken on board, the Sun looked very ordinary. Robles's team calculates that there would be only about one chance in three that a star selected at random would be "more typical" than the Sun.

They conclude that there are probably no special attributes that a star requires to have a habitable planet, other than the obvious one – the planet must be within the star's habitable "goldilocks" zone, orbiting at a distance where the temperature is not too hot for life, nor too cold, but just right. *Journal reference: Astrophysical Journal (in press)*

Gut bugs may have guided the evolution of life

* 19:00 22 May 2008

* NewScientist.com news service

* Ewen Callaway

The history of evolution could be written in an animal's excrement. A new analysis of faeces from dozens of mammals, including humans, suggests that gut-dwelling microbes might shape animal evolution.

Trillions of mostly harmless bacteria and other microbes inhabit the guts of all mammals, outnumbering the number of mammalian cells by 10 to one.

Now, a census of the microbes living in 60 mammals, from cows to kangaroos to capybaras, has found that closely related animals and those with similar diets tend to have the same species of gut microbes.

Scientists have long known that our stomachs team up with harmless bugs, but we are only beginning to appreciate the breadth of bacterial diversity in our bellies. By reading the chemical letters of a molecule called 16s ribosomal RNA – a cousin to DNA – researchers can catalogue bacterial species and conduct a rough census of their numbers.

Distance no barrier

Jeff Gordon and Ruth Ley, microbiologists at Washington University in St. Louis, tried this approach with stool samples collected from zoos and from animals in the wild.

They found more than 20,000 different kinds of bacteria. But the closer two species were on the tree of life, the more bacterial species they had in common living in their guts.

Diet also shaped an animal's gut content. Meat eaters, such as bears and cheetahs, tended to share many of the same microbes. The same was true for omnivores, which included humans, as well as plant eaters.

Animals of the same species that lived thousands of kilometres away from each other also tended to have the same kinds of bacteria in their gut.

Gordon's team says the findings could help explain the evolutionary success of mammals, particularly plant eaters such as cattle and giraffes that flourished over the last 2 million years after a large increase in grassland habitats.

Bug buddies

"If animals from an omnivorous background have moved into a more herbivorous lifestyle they have absolutely needed bacterial partners and microbes to allow that to happen," Gordon says.



David Relman, a microbiologist at Stanford University in California agrees that microbes could have played an important part in mammalian evolutionary history.

"It's possible that our microbial makeup has guided and played a major role in defining who we are and what we do, but it could also be the flip side," he says. Gut microbe populations could passively respond to changes in host physiology and diet.

To answer that question, researchers need a better grasp on the factors that determine an animal's gut flora – including genes and diet. To make things even more complex, other studies have shown that gut microbe populations change over the course of months and years.

"It's a daunting set of potential variables, only some of which you can control," Relman says. *Journal reference: Science (DOI: 10.1126/science.1155725)*

Huge hidden biomass lives deep beneath the oceans

* 19:00 22 May 2008

* NewScientist.com news service * Catherine Brahic

It's the basement apartment like no other. Life has been found 1.6 kilometres beneath the sea floor, at temperatures reaching 100 °C.

The discovery marks the deepest living cells ever to be found beneath the sea floor. Bacteria have been found deeper underneath the continents, but there they are rare. In comparison, the rocks beneath the sea appear to be teeming with life.

John Parkes, a geobiologist at the University of Cardiff, UK, hopes his team's discovery might one day help find life on other planets. He says it might even redefine what we understand as life, and, bizarrely, what we understand by "age".



Fluorescent staining highlights living cell in green (Image: Erwan Roussel)

Parkes has been hunting for deep life for over 20 years. Recently, he and his colleagues examined samples of a mud core extracted from between 860 metres and 1626 metres beneath the sea floor off the coast of Newfoundland.

They found simple organisms known as prokaryotes in every sample. Prokaryotes are organisms that often have just one cell. Their peculiarity is that, unlike any other form of life, their DNA is not neatly packed into a nucleus.

Gradual descent

About 60% of the cells Parkes and his team found were alive. They are related to organisms found in deepsea hydrothermal vents. Depending on the depth, between one in 20 and one in 10 of the cells were dividing, which is the normal way prokaryotes reproduce.

Where cells living so far beneath the sea floor could have come from remains a mystery. They may have been gradually buried in sediment as millions of years passed by, and adapted to the increasing temperatures and pressure, he says.

Another possibility is that they were sucked deep into the mud from the sea water above. Hydrothermal vents pulse hot water out of the seabed and into the ocean. This creates a vacuum in the sediment, which draws fresh sea water into the marine aquifer.

It is important to understand the way the cells got down there, because that has implications for their age. The cells are not very active and according to Parkes they have very few predators. "We find very few viruses, for example, down there," he says. "At the surface, if you don't divide you get eaten. But if there are no predators, the pressure to reproduce decreases and you can spend more energy on repairing your damaged molecules."

Ancient life

This means it is conceivable – but unproven – that some of the cells are as old as the sediment. At 1.6 km beneath the sea, that's 111 million years old. But in an underworld where cells divide excruciatingly slowly, if at all, age tends to lose its relevance, says Parkes.

Parkes' interest in prokaryotes goes far beyond those that are buried deep in the Earth. He thinks the cells found there could lead to life on other planets.

Previously, he has shown that the rocks beneath the oceans could be home to the largest population of prokaryotes on Earth, and account for one tenth of all living carbon. He estimates the combined undersea biomass could be equivalent to that of all the plants on Earth.

"We are all dominated by our surface existence where everything relates to photosynthesis and oxygen," he told New Scientist.

The possibility that there could be more forms of life beneath the surface than above it suggests that they have different and effective ways of surviving – ways that could be independent of light and oxygen. And if these "new" forms of life exist on Earth, they could exist on other planets too.

Dense at depth

"That's what really excites me. This is not just about the deepest, hottest, oldest – but also that we may have misunderstood life."

Life beneath the continents is very different. The temperature increases more slowly with depth in the continental crust, which allows life to go deeper.

"We have recovered living cells from depths of 3.2 km to about 5 km in South Africa," says Tullis Onstott of Princeton University. "But what I find most interesting in Parkes' samples is the high density of microbial cells. They are about 100 to 1000-fold greater than in our terrestrial environments at comparable depths or temperatures."

In 2002, Parkes had found prokaryotes at 842 metres beneath the seabed, the previous record, and it seems likely he will be finding life deeper yet in years to come. "The more you look the more you find," comments Karsten Pedersen of the Deep Biosphere Laboratory at Göteborg University, Sweden. *Journal reference: Science (DOI: 10.1126/science.1154545*)

Pacific coast turning more acidic

CORVALLIS, Ore. – An international team of scientists surveying the waters of the continental shelf off the West Coast of North America has discovered for the first time high levels of acidified ocean water within 20 miles of the shoreline, raising concern for marine ecosystems from Canada to Mexico.

Researchers aboard the Wecoma, an Oregon State University research vessel, also discovered that this corrosive, acidified water that is being "upwelled" seasonally from the deeper ocean is probably 50 years old, suggesting that future ocean acidification levels will increase since atmospheric levels of carbon dioxide have increased rapidly over the past half century.

Results of the study were published this week in Science Express.

"When the upwelled water was last at the surface, it was exposed to an atmosphere with much lower CO2 (carbon dioxide) levels than today's," pointed out Burke Hales, an associate professor in the College of Oceanic and Atmospheric Sciences at Oregon State University and an author on the Science study. "The water that will upwell off the coast in future years already is making its undersea trek toward us, with ever-increasing levels of carbon dioxide and acidity.

"The coastal ocean acidification train has left the station," Hales added, "and there not much we can do to derail it."

Scientists have become increasingly concerned about ocean acidification in recent years, as the world's oceans absorb growing levels of carbon dioxide from the atmosphere. When that CO2 mixes into the ocean water, it forms carbonic acid that has a corrosive effect on aragonite – the calcium carbonate mineral that forms the shells of many marine creatures.

Certain species of phytoplankton and zooplankton, which are critical to the marine food web, may also be susceptible, the scientists point out, although other species of open-ocean phytoplankton have calcite shells that are not as sensitive.

"There is much research that needs to be done about the biological implications of ocean acidification," Hales said. "We now have a fairly good idea of how the chemistry works."

Increasing levels of carbon dioxide in the atmosphere are a product of the industrial revolution and consumption of fossil fuels. Fifty years ago, atmospheric CO2 levels were roughly 310 parts per million – the highest level to that point that the Earth has experienced in the last million years, according to analyses of gas trapped in ice cores and other research.

During the past 50 years, atmospheric CO2 levels have gradually increased to a level of about 380 parts per million.

These atmospheric CO2 levels form the beginning baseline for carbon levels in ocean water. As water moves away from the surface toward upwelling areas, respiration increases the CO2 and nutrient levels of the water. As that nutrient-rich water is upwelled, it triggers additional phytoplankton blooms that continue the process.

There is a strong correlation between recent hypoxia events off the Northwest coast and increasing acidification, Hales said.

"The hypoxia is caused by persistent upwelling that produces an over-abundance of phytoplankton," Hales pointed out. "When the system works, the upwelling winds subside for a day or two every couple of weeks in what we call a 'relaxation event' that allows that buildup of decomposing organic matter to be washed out to the deep ocean.

"But in recent years, especially in 2002 and 2006, there were few if any of these relaxation breaks in the upwelling and the phytoplankton blooms were enormous," Hales added. "When the material produced by these blooms decomposes, it puts more CO2 into the system and increases the acidification."

The research team used OSU's R/V Wecoma to sample water off the coast from British Columbia to Mexico. The researchers found that the 50-year-old upwelled water had CO2 levels of 900 to 1,000 parts per million, making it "right on the edge of solubility" for calcium carbonate-shelled aragonites, Hales said.

"If we're right on the edge now based on a starting point of 310 parts per million," Hales said, "we may have to assume that CO2 levels will gradually increase through the next half century as the water that originally was exposed to increasing levels of atmospheric carbon dioxide is cycled through the system. Whether those elevated levels of carbon dioxide tip the scale for aragonites remains to be seen.

"But if we somehow got our atmospheric CO2 level to immediately quit increasing," Hales added, "we'd still have increasingly acidified ocean water to contend with over the next 50 years."

Hales says it is too early to predict the biological response to increasing ocean acidification off North America's West Coast. There already is a huge seasonal variation in the ocean acidity based on phytoplankton blooms, upwelling patterns, water movement and natural terrain. Upwelled water can be pushed all the way onto shore, he said, and barnacles, clams and other aragonites have likely already been exposed to corrosive waters for a period of time.

They may be adapting, he said, or they may already be suffering consequences that scientists have not yet determined.

"You can't just splash some acid on a clamshell and replicate the range of conditions the Pacific Ocean presents," Hales said. "This points out the need for cross-disciplinary research. Luckily, we have a fantastic laboratory right off the central Oregon coast that will allow us to look at the implications of ocean acidification."

The study, funded by the National Oceanic and Atmospheric Administration (NOAA) and the National Aeronautics and Space Administration (NASA), was the first in a planned series of biennial observations of the carbon cycle along the West Coast of the continent. In addition to Hales, principal investigators for the study included Richard A. Feely and Christopher Sabine of the NOAA Pacific Marine Environmental Laboratory; J. Martin Hernandez-Ayon, the University of Baja California in Mexico; and Debby Ianson, of Fisheries and Oceans Canada, Sidney, B.C.

Miracle leaves that may help protect against liver damage

Sea buckthorn (Hippophae rhamnoides) berries are well known for their cholesterol busting properties, but scientists in India say that its leaves are also rich in anti-oxidants and may help ward off liver disease, according to new research due to be published in the Society of Chemical Industry's (SCI) Journal of the Science of Food and Agriculture.

Indigineous to the mountainous regions of China and Russia, sea buckthorn has been shown to be rich in vitamin C, vitamin E, flavonoids and essential fatty acids. The leaves are also used to make a tea.

In a clinically controlled study, scientists looked at whether the leaves had any protective effects by testing a group of rats, some of

whom were given the leaf extract before being administered with a liver damage agent, carbon tetrachloride (CCI4).

Six groups were looked at in all – group 1 was given a daily dose of saline for 5 days; group 2 received saline for 4 days and on the 5th day was given CCI4; group 3 was given a daily dose of silymarin for 5 days

followed by a single dose of CCI4; groups 4, 5 and 6 were given 50, 100 and 200mg of sea buckthorn leaf extract respectively for five days followed by a single dose of CCI4 on the 5th day.

The results showed that the leaf extract appeared to confer a protective mechanism on the liver – the rats given CCI4 minus the leaf extract had sustained significant liver damage compared to the control group that did not receive CCI4. In comparison, liver damage was severely restricted in the rats given leaf extract at 100mg and 200mg and CCI4.

For more information or a full copy of the paper, contact: Meral Nugent, Press and Public Relations Manager, T: +44 (0)20 7598 1533, F: +44 (0) 20 7598 1545, Mob: 07931 315077 E: meral.nugent@soci.org

Let there be light

Photodynamic therapy breakthrough in cancer treatment

Researchers from the Peninsula Medical School in Cornwall, UK, have modified a photodynamic therapy (PDT) treatment that combines a topically applied cream with visible light to destroy cancer cells while leaving surrounding tissue unharmed.

The cream is applied directly to skin cancers and pre-cancers, which then naturally produces a photosensitive drug. A special red light is then shone on the tumour a few hours later, to activate this light sensitive compound. This results in cellular damage and the destruction of the tumour.

This technique results in reduced scarring and little or no damage to the surrounding healthy cells.

By adding the iron chelator CP94 to the cream, the research team have found that the effects of PDT are greatly improved and achieve greater reductions in tumour depth in tumours currently too thick to be treated easily by the non-enhanced form of this treatment.

This is the first time in the world that PDT trials of this modified PDT treatment have been carried out involving humans. Trials involving patients have taken place at clinics at the Royal Cornwall Hospitals NHS Trust in Truro.

PDT is achieving success in the treatment of actinic keratoses (lesions that can develop after years of exposure to UV light); Bowen's disease (the growth of abnormal calls that can turn into skin cancer, and that is partly due to long-term exposure to the sun); and basal cell carcinoma (the most common form of skin cancer).

The work of the Peninsula Medical School in this area of research is funded in part by the Duchy Health Charity in Cornwall.

Dr. Alison Curnow from the Peninsula Medical School in Cornwall, commented: "PDT is very effective non-surgical treatment for certain types of dermatological cancers and precancers. It normally destroys the tumour without scarring or damage to surrounding healthy cells."

She added: "Through years of research we have been able to develop a modified PDT treatment enabling for the first time for thicker nodular basal cell carcinomas to be treated effectively with a single PDT treatment. This is important, as this is a very common form of skin cancer."

The work of Dr. Curnow and her team are part of a developing research theme for the Peninsula Medical School, which is Environment and Human Health. Operated mainly from the Peninsula Medical School in Cornwall, but with collaboration from colleagues within the institution across the South West of England, this research theme seeks to identify and study the links between our health and well-being and the environment. *More information is available by logging on at www.pms.ac.uk*.

Care Study

Graham O'Neill, 54, is technical marketing director at Imerys Minerals in Cornwall and lives near Mevagissey.

Graham was raised in the West Indies, and although his mother was very careful about protecting him from the sun, his exposure to the sun's rays at an early age led to the discovery of melanomas on his skin in 1983.

"Back then the treatments were quite severe," said Graham. "It involved liquid nitrogen, scraping out the melanoma and cauterizing it. Not only was this very painful, but it also left scarring."

He now receives treatment with PDT, which is much better for him. He said: "The treatment is extremely good. From a personal point of view it is much less unpleasant and seems to be more effective. It also treats quite a big area in one go, which means fewer treatments in the long run. The other issue with melanomas is that they keep coming back. With PDT I have found that they do not return as frequently and, when they do, they are far less severe."

On balance Graham is delighted with the treatments, which he has been receiving at Treliske Hospital, Royal Cornwall Hospitals NHS Trust in Truro. He said: "Compared with the old way of doing things, PDT is a fantastic therapy and one which I would recommend to other patients. It is very exciting that the Peninsula Medical School is taking such a worldwide lead in research in this area."

The Peninsula Medical School is a joint entity of the University of Exeter, the University of Plymouth and the NHS in the South West of England, and a partner of the Combined Universities in Cornwall. The Peninsula Medical School has created for itself an excellent national and international reputation for groundbreaking research in the areas of diabetes and obesity, neurological disease, child development and ageing, clinical education and health technology assessment.

Knowledgeable Republicans 'less concerned' over climate

* 12:24 23 May 2008

* NewScientist.com news service

* Peter Aldhous

The more Democrats think they know about global warming, the more concerned they are. But Republicans who consider themselves well informed on the topic seem no more worried than those who profess ignorance, a study suggests.

When it comes to attitudes to global warming in the US, how knowledge translates into concern depends upon people's political views, and on whom they trust to provide information on climate change, say the political psychologists involved.

In February 2008, researchers at Texas A&M University in College Station published a survey suggesting that Americans who see themselves as well informed about global warming are actually less concerned than those who admit to knowing little Risk Analysis (DOI: 10.1111/j.1539-6924.2008.01010.x).

"Increased knowledge about global warming leads to apathy," stated a press release issued by the university at the time.

Trust in science

However, Jon Krosnick of Stanford University, California, who has previously worked with New Scientist to investigate US public attitudes towards policies to combat global warming, suspected the story may be more complicated.

So with his colleague Ariel Malka, Krosnick re-analysed polling data from Stanford surveys conducted in collaboration with ABC News, The Washington Post and Time magazine in 2006 and 2007.

Overall, Malka and Krosnick found that concern about global warming was greater among people who said they knew more about the subject. This was most marked for respondents who identified themselves as Democrats, and those who said they trusted scientists to provide reliable information on environmental issues.

For Republicans, and those who had little trust in scientists, more knowledge did not mean greater concern. Broader issues

In part, this may reflect the different ways people get information about global warming. If your sources are the Intergovernmental Panel on Climate Change and Al Gore, Krosnick suggests, the relationship between knowledge and concern is likely to be different than if your main sources are sceptical advocacy groups such as the Heartland Institute, and the conservative radio talk-show host Rush Limbaugh.

Why did the Stanford and Texas A&M teams obtain such different results? Possibly because of differences between their questionnaires, says Krosnick.

For instance, the Texas team asked a series of questions relating to respondents' own well-being, and the likely impact of global warming on the state in which they live. The Stanford researchers asked broader questions about respondents' concern about climate change.

Arnold Vedlitz, a member of the Texas A&M team, says that more work is needed to fully understand the factors driving concern about global warming in the US. "This is a difficult and complex issue," he says.

Public schools as good as private schools in raising math scores, study says

Craig Chamberlain, Education Editor

217-333-2894; cdchambe@illinois.edu

CHAMPAIGN, III. — Students in public schools learn as much or more math between kindergarten and fifth grade as similar students in private schools, according to a new University of Illinois study of multi-year, longitudinal data on nearly 10,000 students.

The results of the study appear in the May issue of the influential education journal Phi Delta Kappan.

"These data provide strong, longitudinal evidence that public schools are at least as effective as private schools in boosting student achievement," according to the authors, education professor Christopher Lubienski, doctoral student Corinna Crane and education professor Sarah Theule Lubienski.

The new study is the first published study to show that public schools are at least as effective as private schools at promoting student learning over time, they say.

Combined with other, yet-unpublished studies of the same data, which produced similar findings, "we think this effectively ends the debate about whether private schools are more effective than publics," said Christopher Lubienski, whose research has dealt with all aspects of alternative education.

This is important, he said, because many current reforms, such as No Child Left Behind, charter schools and vouchers for private schools, are based on that assumption.

The debate essentially began three years ago with the publication in Phi Delta Kappan of a previous study by the Lubienskis, which challenged the then-common wisdom – supported by well-regarded but dated research – that private schools were superior.

In that 2005 study, they found that public school students tested higher in math than their private school peers from similar social and economic backgrounds.

In another, more-extensive study in early 2006, they built on those findings, and also raised similar questions about charter schools.

Both studies were based on fourth- and eighth-grade test data from the National Assessment of Educational Progress (NAEP).

The conclusions of the husband-and-wife team seemed "crazy radical" at the time, Sarah Lubienski said, and generated significant controversy. They were supported, however, later in 2006, with similar findings in U.S. Department of Education studies comparing public schools with privates and with charters, which looked at NAEP test data on both math and reading.

(Unlike literacy, math is viewed as being less dependent on a student's home environment and more an indication of a school's effectiveness, Sarah Lubienski said.)

Critics of these previous studies, however, have cited the lack of longitudinal data showing the possible effect over time of different types of schooling. The studies of NAEP data were only snapshots, they said, showing student achievement at a single point in time. The studies did not address the possibility that some students may have entered private school at a lower level of achievement.

The new study was designed, in part, to address that issue, the authors say in their PDK article.

The data for the new study came from the database produced by the Early Childhood Longitudinal Study, Kindergarten Class of 1998-99 (or ECLS-K), administered by the National Center for Education Statistics (NCES), part of the U.S. Department of Education.

The ECLS-K database includes both student achievement and comprehensive background information drawn from a nationally representative sample of more than 21,000 students, starting with their entry into kindergarten in the fall of 1998.

The most recent data available for the U. of I. study was gathered in 2004, in the spring of the students' fifthgrade year. The sample used for the study included 9,791 students in 1,531 schools (1,273 public, 140 Catholic and 118 other private schools).

To better determine the effects of attending different types of schools, the sample included only students who had stayed in the same type of school – though not necessarily the same school – throughout the years covered.

As in the previous studies, the researchers used a statistical technique known as hierarchical linear modeling to control for demographic differences between students, as well as schools. Among the demographic variables included in looking at students were measures of socioeconomic status; race and ethnicity; gender; disability; and whether the child spoke a language other than English at home.

Among the variables included in looking at schools was the average socioeconomic level of its students, its racial or ethnic composition, and its location (urban or rural).

The NAEP data had included similar information, but its quality and controls on its collection were not as strong as for ECLS-K, according to Sarah Lubienski, who studies math education and specializes in statistical research. "It's one reason this study feels more definitive than the NAEP studies," she said.

After controlling for demographic differences among students and schools, the researchers' found that public school students began kindergarten with math scores roughly equal to those of their Catholic school peers. By fifth grade, however, they had made significantly greater gains, equal to almost an extra half year of schooling.

Part of the explanation, Sarah Lubienski said, might lie in the fact that Catholic schools have fewer certified teachers and employ fewer reform-oriented mathematics teaching practices – something they found in research for another study, accepted for publication in the American Journal of Education.

Public school students also "rivaled the performance of students in other (non-Catholic) private schools," the researchers wrote. After adjusting for demographics and initial kindergarten scores, they found that achievement gains between kindergarten and fifth grade were roughly equal.

The number of private schools in the study did not allow for drawing conclusions about other subcategories of private schools, such as Lutheran, conservative Christian or secular, Sarah Lubienski said. In their earlier NAEP research, they found that Lutheran schools, for instance, performed on par with publics, while conservative Christian schools performed lower than all other school types.

"It is worth noting," the researchers write in analyzing their results, "how little variation school type really accounts for in students' growth in achievement ... Specifically, while all of the variables in our model together explained 62 percent of the achievement differences between schools, school type alone accounted for less than 5 percent of these differences, with demographic considerations accounting for a much greater share."

Put another way by Sarah Lubienski, "school type alone doesn't explain very much of why these scores vary ... in truth, whether the school is public or private doesn't seem to make that much difference."

The researchers go on to write that they "personally see private schools as an integral part of the American system of education" and "there are many valid reasons why parents choose private schools and why policymakers may push for school choice."

Academic achievement, however, may no longer be one of those reasons, they write. "Claims that simply switching students from one type of school to another will result in higher scores appear to be unfounded."

They suggest "moving away from a simple focus on school type and instead examining what happens within schools."

New research forces U-turn in population migration theory

Research led by the University of Leeds has discovered genetic evidence that overturns existing theories about human migration into Island Southeast Asia (covering the Philippines, Indonesia and Malaysian Borneo) - taking the timeline back by nearly 10,000 years.

Prevailing theory suggests that the present-day populations of Island Southeast Asia (ISEA) originate largely from a Neolithic expansion from Taiwan driven by rice agriculture about 4,000 years ago - the so-called "Out of Taiwan" model.

However an international research team, led by the UK's first Professor of Archaeogenetics, Martin Richards, has shown that a substantial fraction of their mitochondrial DNA lineages (inherited down the female line of descent), have been evolving within ISEA for a much longer period, possibly since modern humans arrived some 50,000 years ago.

Moreover, the lineage can be shown to have actually expanded in the opposite direction - into Taiwan - within the last 10,000 years.

Says Professor Richards: "I think the study results are going to be a big surprise for many archaeologists and linguists on whose studies conventional migration theories are based. These population expansions had nothing to do with agriculture, but were most likely to have been driven by climate change - in particular, global warming and the resulting sea-level rises at the end of the Ice Age between 15,000-7,000 years ago."

At this time the ancient continent known as Sundaland – an extension of the Asian landmass as far as Borneo and Java – was flooded to create the present-day archipelago.

Although sea-level rise no doubt devastated many communities, it also opened up a huge amount of new coastal territory for those who survived(1). The present-day coastline is about twice as great as it was 15,000 years ago.

"Our genetic evidence suggests that probably from about 12,000 years ago these people began to recover from the natural catastrophes and expanded greatly in numbers, spreading out in all directions, including north to Taiwan, west to the Southeast Asian mainland, and east towards New Guinea. These migrations have not previously been recognised archaeologically, but we have been able to show that there is supporting evidence in the archaeological record too."

The interdisciplinary research team comprised colleagues from Leeds, Oxford, Glasgow, Australia and Taiwan. The study was funded by the Bradshaw Foundation and the European Union Marie Curie Early Stage Training program and is published in the current issue of Molecular Biology and Evolution (MBE).

Ancient poem found on wood strip The Yomiuri Shimbun

NARA--A wooden strip unearthed in fiscal 1997 from remains of the eighth-century Shigarakinomiya palace in Koka, Shiga Prefecture, was found to be inscribed with a pair of waka poems, one of which is included in "Manyoshu" (The Collection of Ten Thousand Leaves), Japan's oldest existing collection of poems, a board of education announced Thursday.

It is the first time that a wooden strip inscribed with a poem from the collection has been found.

On one side of the strip is a poem about Mt. Asaka, in present-day Fukushima Prefecture, while the other side bears a poem about Naniwazu, an ancient port in Osaka.

The poem on Mt. Asaka included in "Manyoshu" is described by Ki no Tsurayuki, a renowned poet of the Heian period (794-1192), as an archetypal poem in the preface of "Kokin Wakashu," a compilation of waka poems.

Since the strip is believed to have been made during the same period that "Manyoshu" was compiled, the discovery is of considerable importance to studies of the collection.

The poems were written using Chinese characters in the phonetic Manyo style. The poem on Mt. Asaka is included in volume 16 of "Manyoshu."

The characters for "asakaya" and "ruyama," written in black ink, were legible, leading to the discovery.

The poet, a court lady who served King Katsuragi, writes in the Mt. Asaka poem that her sincerity is deeper than the shallow spring that reflects Mt. Asaka. The poem was written to placate the king after he visited the Mutsu regions, straddling the current Aomori and Iwate prefectures, and was upset by the way he was entertained by a local governor. According to the legend, the poem brought the king out of his bad mood.

The "Manyoshu" collection, comprising 20 volumes, was compiled in the seventh to eight centuries and includes about 4,500 poems composed by emperors and aristocrats as well as commoners. None of the volumes from the original collection survive, but copies made in the Heian period and after remain in existence.

The wooden strip was unearthed from the Miyamachi Remains in Koka, where part of the Shigarakinomiya palace stood between 742 and 745, created by the order of Emperor Shomu.

The 1-millimeter-thick strip is torn into two pieces measuring 7.9 centimeters and 14 centimeters in length. The strip is believed to have been about 60 centimeters long originally, and was probably used as an uta mokkan--a wooden strip inscribed with a poem to be read aloud during ceremonies and parties. It was discovered in a ditch about 220 meters to 230 meters west of the main section of Shigarakinomiya Palace in an excavation in fiscal 1997. The strip is believed to have been put there between late 744 and early 745.

Towao Sakaehara, an ancient history professor of Osaka City University, and other researchers began examining the pieces of the strip with the Naniwazu poem in December, leading them to discover the other poem on the other side.

Manyoshu's 15th volume and appendix were compiled over a few years from 745. A leading hypothesis is that volume 16 was created by adding contents to the appendix of volume 15.

The poem strip is likely to have been made before the compilation of the collection was completed.

"The Asaka poem was included in the collection because it was widely known at the time," a Koka Municipal Board of Education spokesman said.

The Naniwazu poem is said to have expressed congratulations for the enthronement of Emperor Nintoku. Although it is not included in the "Manyoshu" collection, the poem was written on more than 30 unearthed items, including a wooden strip and clay pot.

In the Kokin Wakashu, the pair of poems are introduced as the first poems to be learned.

The finding shows that the tradition of pairing poems began in the Nara period (710-794), about 160 years earlier than once believed.

Susumu Nakanishi, director of the Nara Prefecture Complex of Man'yo Culture, called the wooden strips a valuable discovery, saying: "We learned the strips were used as a material for compiling 'Manyoshu,' and also that kana letters in the 'Manyoshu' collection's copies made in the Heian period and after in the handwriting of many different people matched the letters in the discovered strip. It's an important artifact in the study of 'Manyoshu.'"