For gunshot and stab victims, on-scene spine immobilization may do more harm than good

Johns Hopkins study says patients twice as likely to die if treated this way instead of being taken to the hospital immediately

Immobilizing the spines of shooting and stabbing victims before they are taken to the hospital - standard procedure in Maryland and some other parts of the country - appears to double the risk of death compared to transporting patients to a trauma center without this time-consuming, on-scene medical intervention, according to a new study by Johns Hopkins researchers.

The findings, published in January issue of the Journal of Trauma, suggest that prehospital spine immobilization for these kinds of patients provides little benefit and may lethally delay proven treatments for what are often life-threatening injuries. Wounds from guns and knives are often far from the spine, yet patients are routinely put in a cervical collar and secured to a board, the investigators say.

"If you're twice as likely to die, that seems like a bad thing to do," says Elliott R. Haut, M.D., an assistant professor of surgery at the Johns Hopkins University School of Medicine and the study leader. "We like to use interventions that preserve life."

Haut says he hopes that as a result of his study, Maryland will consider changing its protocol, which encourages spine immobilization for nearly all shooting and stabbing victims.

The researchers caution that spine immobilization has been shown to be well worth the time and quite effective in saving lives and reducing disability from injuries sustained in car crashes and similar events.

One finding that Haut says startled his team: Some of the least injured gunshot or stab wound victims appear to be at greater risk of death if time is spent on prehospital immobilization.

"The patients who are very, very severely injured from their penetrating trauma are going to die no matter what you do," says Haut, a trauma surgeon at The Johns Hopkins Hospital. "But if someone is stabbed in the lung or shot in the liver, what we do for them and how fast we do it make a huge difference. That time difference in getting them to the hospital for treatment may make the difference between life and death."

EMTs and others who immobilize gunshot and stab wound patients don't intend to do harm, Haut emphasizes, but a cervical collar may, for example, conceal an injury to the trachea or make inserting a needed breathing tube more difficult.

The merits of other prehospital protocols, such as the need for universal intravenous fluid administration, have also been called into question in recent studies.

Haut and his colleagues looked at records from more than 45,000 patients with penetrating trauma included in the National Trauma Data Bank from 2001 to 2004. They calculated that the chance of benefiting from spine immobilization in those cases was 1 in 1,000, while 15 additional people potentially died for every 1,000 shooting or stabbing victims immobilized before being taken to the hospital.

"The idea of putting a board and collar on everybody is probably not the way to go," Haut says.
While standard protocol in Maryland requires spine immobilization for nearly all patients with bullet and knife wounds, there is more flexibility in other jurisdictions, Haut says. In the national data used by his group, only 4.3 percent of shooting and stabbing victims were immobilized before being taken to the emergency department.

Other Johns Hopkins authors on the study include David T. Efron, M.D.; Adil H. Haider, M.D., M.P.H.; Kent A. Stevens, M.D., M.P.H.; and David C. Chang, M.B.A., M.P.H., Ph.D.

Sedentary TV time may cut life short

A study found that every hour spent in front of the television per day brings with it an 11 percent greater risk of premature death from all causes, and an 18 percent greater risk of dying from cardiovascular disease. The findings apply to both obese and overweight people as well as people with a healthy weight because prolonged periods of sitting have an unhealthy influence on blood sugar and blood fat levels.

DALLAS, - Couch potatoes beware: every hour of television watched per day may increase the risk of dying earlier from cardiovascular disease, according to research reported in Circulation: Journal of the American Heart Association.

Australian researchers tracked the lifestyle habits of 8,800 adults and found that each hour spent in front of the television daily was associated with:

- an 11 percent increased risk of death from all causes,
- a 9 percent increased risk of cancer death; and
- an 18 percent increased risk of cardiovascular disease (CVD)-related death.

Compared with people who watched less than two hours of television daily, those who watched more than four hours a day had a 46 percent higher risk of death from all causes and an 80 percent increased risk for CVD-related death. This association held regardless of other independent and common cardiovascular disease risk factors, including smoking, high blood pressure, high blood cholesterol, unhealthy diet, excessive waist circumference, and leisure-time exercises.

While the study focused specifically on television watching, the findings suggest that any prolonged sedentary behavior, such as sitting at a desk or in front of a computer, may pose a risk to one's health. The human body was designed to move, not sit for extended periods of time, said David Dunstan, Ph.D., the study's lead author and professor and Head of the Physical Activity Laboratory in the Division of Metabolism and Obesity at the Baker IDI Heart and Diabetes Institute in Victoria, Australia.

"What has happened is that a lot of the normal activities of daily living that involved standing up and moving the muscles in the body have been converted to sitting," Dunstan said. "Technological, social, and economic changes mean that people don't move their muscles as much as they used to - consequently the levels of energy expenditure as people go about their lives continue to shrink. For many people, on a daily basis they simply shift from one chair to another – from the chair in the car to the chair in the office to the chair in front of the television."

Dunstan said the findings apply not only to individuals who are overweight and obese, but also those who have a healthy weight. "Even if someone has a healthy body weight, sitting for long periods of time still has an unhealthy influence on their blood sugar and blood fats," he said.

Although the study was conducted in Australia, Dunstan said the findings are certainly applicable to Americans. Average daily television watching is approximately three hours in Australia and the United Kingdom, and up to eight hours in the United States, where two-thirds of all adults are either overweight or obese.

The benefits of exercise have been long established, but researchers wanted to know what happens when people sit too much. Television-watching is the most common sedentary activity carried out in the home.

Researchers interviewed 3,846 men and 4,954 women age 25 and older who underwent oral glucose-tolerance tests and provided blood samples so researchers could measure biomarkers such as cholesterol and blood sugar levels.

Participants were enrolled from 1999–2000 and followed through 2006. They reported their television-viewing habits for the previous seven days and were grouped into one of three categories: those who watched less than two hours per day; those who watched between two and four hours daily; and those who watched more than four hours.

People with a history of CVD were excluded from the study. During the more than six-year follow-up, there were 284 deaths - 87 due to CVD and 125 due to cancer.

The association between cancer and television viewing was only modest, researchers reported. However, there was a direct association between the amount of television watched and elevated CVD death as well as death from all causes even after accounting for typical CVD risk factors and other lifestyle factors. The implications are simple, Dunstan said. "In addition to doing regular exercise, avoid sitting for prolonged periods and keep in mind to 'move more, more often'. Too much sitting is bad for health."

Co-authors are: E. L. M. Barr, Ph.D.; G. N. Healy, Ph.D.; J. Salmon, Ph.D.; J. E. Shaw, M.D.; B. Balkau, Ph.D.; D. J. Magliano, Ph.D.; A. J. Cameron, Ph.D.; P. Z. Zimmet, Ph.D. and N. Owen, Ph.D. Author disclosures and funding sources are on the manuscript.

Ongoing human evolution could explain recent rise in certain disorders

Scientists call for integrating evolutionary perspectives into medical curricula

Cambridge, Mass. The subtle but ongoing pressures of human evolution could explain the seeming rise of disorders such as autism, autoimmune diseases, and reproductive cancers, researchers write in the Proceedings of the National Academy of Sciences. Certain adaptations that once benefited humans may now be helping such ailments persist in spite of – or perhaps because of – advancements in modern culture and medicine.

"This work points out linkages within the plethora of new information in human genetics and the implications for human biology and public health, and also illustrates how one could teach these perspectives in medical and premedical curricula," says author Peter Ellison, John Cowles Professor of Anthropology at Harvard University.

Ellison's co-authors are Stephen Stearns of Yale University, Randolph Nesse of the University of Michigan, and Diddahally Govindaraju of the Boston University School of Medicine. The research was first presented at the Arthur M. Sackler Colloquium, co-sponsored by the National Academy of Science and the Institute of Medicine.

Colloquium presentations described in the current paper include research suggesting that:

* Autism and schizophrenia may be associated with the over-expression of paternally or maternally derived genes and influences, a hypothesis advanced by Bernard Crespi of Simon Fraser University.

* Maternal and paternal genes engage in a subtle tug-of-war well into childhood with consequences for childhood development, as posited by David Haig, George Putnam Professor of Organismic and Evolutionary Biology at Harvard.

* Humans may be susceptible to allergies, asthma, and autoimmune diseases because of increased hygiene, according to Kathleen Barnes of Johns Hopkins University. Without being exposed to intestinal worms and parasites, as our ancestors were, our immune systems are hypersensitive.

* Natural selection still influences our biology, despite advances in modern culture and medicine. Stearns found that natural selection favors heavier women and reduces the age at which a woman has her first child.

In the final presentation of the colloquium, researchers called for the integration of evolutionary perspectives into medical school curricula, to help future physicians consider health problems from an evolutionary perspective.

"We're trying to design ways to educate physicians who will have a broader perspective and not think of the human body as a perfectly designed machine," says Ellison. "Our biology is the result of many of evolutionary trade-offs, and understanding these histories and conflicts can really help the physician understand why we get sick and what we might do to stay healthy."

Previous work in evolutionary medicine helped explain why disease is so prevalent and difficult to prevent – because natural selection favors reproduction over health, biology evolves more slowly than culture, and pathogens evolve more quickly than humans.

"I think that the main take-home point is that evolution and medicine really do have things to say to each other, and some of these insights actually reduce suffering and save lives," says Stearns.

Study Reveals How One Form Of Natural Vitamin E Protects Brain After Stroke

Columbus, Ohio – Blocking the function of an enzyme in the brain with a specific kind of vitamin E can prevent nerve cells from dying after a stroke, new research suggests.

In a study using mouse brain cells, scientists found that the tocotrienol form of vitamin E, an alternative to the popular drugstore supplement, stopped the enzyme from releasing fatty acids that eventually kill neurons.

The Ohio State University researchers have been studying how this form of vitamin E protects the brain in animal and cell models for a decade, and intend to pursue tests of its potential to both prevent and treat strokes in humans.

“Our research suggests that the different forms of natural vitamin E have distinct functions. The relatively poorly studied tocotrienol form of natural vitamin E targets specific pathways to protect against neural cell death and rescues the brain after stroke injury,” said Chandan Sen, professor and vice chair for research in Ohio State’s Department of Surgery and senior author of the study. “Here, we identify a novel target for tocotrienol that explains how neural cells are protected.”

The research appears online and is scheduled for later print publication in the Journal of Neurochemistry.

Vitamin E occurs naturally in eight different forms. The best-known form of vitamin E belongs to a variety called tocopherols. The form of vitamin E in this study, tocotrienol or TCT, is not abundant in the American diet but is available as a nutritional supplement. It is a common component of a typical Southeast Asian diet.

Sen’s lab discovered tocotrienol vitamin E’s ability to protect the brain 10 years ago. But this current study offers the most specific details about how that protection works, said Sen, who is also a deputy director of Ohio State’s Heart and Lung Research Institute.

“We have studied an enzyme that is present all the time, but one that is activated after a stroke in a way that causes neurodegeneration. We found that it can be put in check by very low levels of tocotrienol,” he said. “So what we have here is a naturally derived nutrient, rather than a drug, that provides this beneficial impact.”

Sen and colleagues had linked TCT’s effects to various substances that are activated in the brain after a stroke before they concluded that this enzyme could serve as an important therapeutic target. The enzyme is called cystolic calcium-dependent phospholipase A2, or cPLA2.

Following the trauma of blocked blood flow associated with a stroke, an excessive amount of glutamate is released in the brain. Glutamate is a neurotransmitter that, in tiny amounts, has important roles in learning and memory. Too much of it triggers a sequence of reactions that lead to the death of brain cells, or neurons – the most damaging effects of a stroke.

Sen and colleagues used cells from the hippocampus region of developing mouse brains for the study. They introduced excess glutamate to the cells to mimic the brain’s environment after a stroke.

With that extra glutamate present, the cPLA2 enzyme releases a fatty acid called arachidonic acid into the brain. Under normal conditions, this fatty acid is housed within lipids that help maintain cell membrane stability.

But when it is free-roaming, arachidonic acid undergoes an enzymatic chemical reaction that makes it toxic – the final step before brain cells are poisoned in this environment and start to die. Activation of the cPLA2 enzyme is required to release the damaging fatty acid in response to insult caused by high levels of glutamate.

Sen and colleagues introduced the tocotrienol vitamin E to the cells that had already been exposed to excess glutamate. The presence of the vitamin decreased the release of fatty acids by 60 percent when compared to cells exposed to glutamate alone.

Brain cells exposed to excess glutamate followed by tocotrienol fared much better, too, compared to those exposed to only the damaging levels of glutamate. Cells treated with TCT were almost four times more likely to survive than were cells exposed to glutamate alone.

Though cPLA2 exists naturally in the body, blocking excessive function of this enzyme is not harmful, Sen explained. Scientists have already determined that mice genetically altered so they cannot activate the enzyme achieve their normal life expectancy and carry a lower risk for stroke.

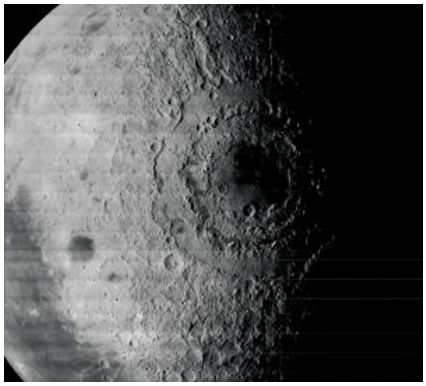
Sen also noted that the amount of tocotrienol needed to achieve these effects is quite small – just 250 nanomolar, a concentration about 10 times lower than the average amount of tocotrienol circulating in humans who consume the vitamin regularly.

“So you don’t have to gobble up a lot of the nutrient to see these effects,” he said.

The National Institutes of Health supported this work. The study was co-authored by Savita Khanna, Sashwati Roy and Cameron Rink of the Department of Surgery and Narasimham Parinandi and Sainath Kotha of the Department of Internal Medicine, all at Ohio State; and Douglas Bibus of the University of Minnesota.

Crystal mountains speak of moon's molten past

* 11 January 2010 **by Rachel Courtland**



The moon's crystal basin **(Image: Lunar Orbit 4/NASA)**

SUPERMAN'S sparkling Fortress of Solitude they're not, but giant outcrops of crystals, found on the moon by India's Chandrayaan-1 probe, prove that a roiling ocean of magma once engulfed the rocky body of our satellite.

The moon is thought to have coalesced more than 4 billion years ago from the molten debris of an impact between the Earth and a Mars-sized object. Models suggest that heat from that impact, as well as from material compressing to form the moon, created a sea of magma that lasted for a few hundred million years. Heavy, iron-bearing minerals should have sunk through this magma to form the moon's mantle, while lighter, iron-poor minerals called plagioclases should have crystallised and floated to the surface.

But it has been difficult to find direct evidence of the moon's primordial crystalline crust, as it was likely jumbled by meteoroid impacts and paved over by lava flows early in the moon's history. Until recently, the only evidence came from lunar samples collected at a few sites by the Apollo astronauts.

Last year, however, Japan's Kaguya probe spotted patches of the stuff inside a number of craters (Nature, DOI: 10.1038/nature08317). Now, it seems Chandrayaan-1, which orbited the moon for almost 10 months until it failed in August, found the mother lode - vast outcrops of plagioclase crystal along a mountain range inside the moon's 930-kilometre-wide Orientale basin (below). Lava has resurfaced less of Orientale than other craters of its size.

In 1994, the US orbiter Clementine found regions inside Orientale that seemed to be virtually iron-free, hinting at plagioclase. But Chandrayaan-1 was able to detect the light absorbed by the crystal itself. It found that the rock containing the crystal spans at least 40 kilometres and is quite pure - less than 5 per cent of it is composed of iron-rich minerals.

That is purer than a number of Apollo samples, which until now have been the primary source of information on the moon's ancient crust. "This is a game-changer," says Paul Warren of the University of California, Los Angeles. "We now have to rethink a lot of lunar science; issues such as the way the crust originally floated over the denser melt of the magma ocean [and] the extent to which the crust was jumbled by large impacts."

In an alternative to the magma theory, the moon formed with much less energy, and its surface solidified quickly. In that case, plagioclase would have reached the surface in a series of volcanic events. But finding widespread, pure plagioclase suggests a more global process. "It really pretty much ties up the magma ocean part of the story," says Carle Pieters of Brown University in Providence, Rhode Island, who presented the Chandrayaan-1 results at the American Geophysical Union meeting in December in San Francisco.

Laminated Linen Protected Alexander the Great

Alexander's men wore linothorax, a highly effective type of body armor created by laminating together layers of linen, research finds.

By Rossella Lorenzi

A Kevlar-like armor might have helped Alexander the Great (356–323 B.C.) conquer nearly the entirety of the known world in little more than two decades, according to new reconstructive archaeology research.

Presented at the annual meeting of the Archaeological Institute of America in Anaheim, Calif., the study suggests that Alexander and his soldiers protected themselves with linothorax, a type of body armor made by laminating together layers of linen.

"While we know quite a lot about ancient armor made from metal, linothorax remains something of a mystery since no examples have survived, due to the perishable nature of the material," Gregory Aldrete, professor of history and humanistic studies at the University of Wisconsin-Green Bay, told Discovery News.

This mosaic of Alexander the Great shows the king wearing linothorax -- an armor made from laminated linen

Martin Beckmann

"Nevertheless, we have managed to show that this linen armor thrived as a form of body protection for nearly 1,000 years, and was used by a wide variety of ancient Mediterranean civilizations," Aldrete said. Indeed, Aldrede and co-investigator Scott Bartell discovered that linothorax was widely mentioned in ancient records.

"Currently we have 27 descriptions by 18 different ancient authors and nearly 700 visual images on objects ranging from Greek vases to Etruscan temple reliefs," Aldrete said.

The main visual evidence for Alexander wearing linothorax is the famous "Alexander Mosaic" from Pompeii, in which the Macedonian king is depicted with this sort of armor.

Indeed, in his "Life of Alexander," the Greek historian Plutarch states that Alexander wore "a breastplate of folded (or doubled) linen" at the Battle of Gaugamela in 331 B.C. This battle a was a huge victory for the Greeks and led to the fall of the Achaemenid Empire.

According to the researchers, there is further evidence that linen breastplates were standard equipment in the Macedonian army. "When Alexander was in India, and received 25,000 new suits of armor for his army, he is described as having ordered the old worn-out suits of armor to be burned. This would only make sense if they had been made of fabric rather than metal," Aldrete said.

In order to determine how wearable this armor was, and how effective it would have been in protecting its wearer from arrows and other battlefield hazards, Aldrete and Bartell reconstructed several complete sets of linen armor using only material that were only available in the ancient world.

"The hardest part of the project was finding truly authentic linen. It had to be made from flax plants that were grown, harvested and processed, spun and woven by hand," Aldrete said.

The other key ingredient was glue, which was placed over various layers of linen. The researchers chose to work with two simpler glues that would have been available everywhere: a glue made from the skins of rabbits and another from flax seeds.

Tests included shooting the resulting patches with arrows and hitting them with a variety of weapons including swords, axes and spears.

"Our controlled experiments basically dispelled the myth that armor made out of cloth must have been inferior to other available types. Indeed, the laminated layers function like an ancient version of modern Kevlar armor, using the flexibility of the fabric to disperse the force of the incoming arrow," Aldrete said.

According to Heidi Sherman, linen expert and professor of history at the University of Wisconsin-Green Bay, the researchers have achieved some very convincing results.

"One cannot know with complete certainty how close the model is to the linen armor used by Alexander the Great's army, but several layers of fused linen can indeed withstand quite a rigorous battering. They would have provided ample protection under rather extreme conditions," Sherman told Discovery News.

US war on salt begins

* 16:11 12 January 2010 **by Ewen Callaway**

Already a leader in the charge against unhealthy fats, New York City has now declared war on salt. The aim is to cut the nationwide incidence of high blood pressure, which can lead to heart attacks and strokes.

"There's been a shot across the bow," says Marion Nestle, a nutrition and public health specialist at New York University. "I think salt is a huge issue that's coming."

Unlike the city's bans on smoking in the workplace and the use of artificial trans-fats, using large amounts of salt won't be illegal.

Instead, the city's health department has launched the National Salt Reduction Initiative, which asks restaurant chains and food manufacturers across the US to pledge to slash their use of salt by specific amounts.

Within five years, the NSRI aims to cut by a quarter the amount of sodium in processed foods, which account for four-fifths of an average American's salt intake.

Public health enemy

Nestle believes the NSRI is a good way to start, but says that there are challenges to painting salt as a public health enemy. For one, salt use is ubiquitous, making it difficult to examine its effects in clinical studies.

Michael Alderman, an epidemiologist and hypertension specialist at Albert Einstein College of Medicine in New York, warns that cutting salt consumption across the board could have unintended consequences. As well as reducing blood pressure, lowering salt levels can increase insulin resistance – a risk factor for diabetes – and cause heart problems, he says.

Analysis of new data confirms bisphenol A link to disease in adults

New findings confirm those of 2008 study

Researchers from the Peninsula Medical School and the University of Exeter, UK, have found more evidence for a link between Bisphenol A exposure (BPA, a chemical commonly used in plastic food containers) and cardiovascular disease. The team analysed new US population data and their results are published by the online journal, PLoS ONE.

The new study uses data from NHANES 2006-2006 US population study. While the new study found that urinary BPA concentrations were one third lower than in 2003-2004, higher BPA concentrations in urine samples were still associated with heart disease in 2005-2006. Associations with some liver enzymes were also present. Their original paper in 2008 was the first to find evidence of associations between BPA and heart disease, and this new data confirms their earlier findings.

In 2008 the team believed that higher urinary BPA concentrations might be associated with adverse health effects in adults, especially in relation to liver function, insulin, diabetes and obesity. By using data from the US government's National Health and Nutrition Examination Survey (NHANES) 2004-2004, which for the first time measured urinary BPA concentrations, the research team found that a quarter of the population with the highest levels of BPA were more than twice as likely to report having heart disease or diabetes, compared to the quarter with the lowest BPA levels. They also found that higher BPA levels were associated with clinically abnormal liver enzyme concentrations.

Professor David Melzer, Professor of Epidemiology and Public Health at the Peninsula Medical School (Exeter, UK), who led the team, commented: "This is only the second analysis of BPA in a large human population sample. It has allowed us to largely confirm our original analysis and exclude the possibility that our original findings were a statistical 'blip'"

Professor Tamara Galloway, Professor of Ecotoxicology at the University of Exeter and senior author of the paper added: "We now need to investigate what causes these health risk associations in more detail and to clarify whether they are caused by BPA itself or by some other factor linked to BPA exposure. The risks associated with exposure to BPA may be small, but they are relevant to very large numbers of people. This information is important since it provides a great opportunity for intervention to reduce the risks."

BPA is a controversial chemical commonly used in food and drink containers. It has previously caused concerns over health risks to babies, as it is present in some baby's bottles. Several nations have moved to ban BPA from the manufacture of baby's bottles and other feeding equipment.

BPA is used in polycarbonate plastic products such as refillable drinks containers, some plastic eating utensils and many other products in everyday use. It is one of the world's highest production volume chemicals, with over 2.2 million tonnes (6.4 billion pounds) produced annually, and it is detectable in the bodies of more than 90% of the population.

Scientists find 'missing link' between heart failure and environment

Scientists have found what they believe is the "missing link" between heart failure, our genes and our environment. The study could open up completely new ways of managing and treating heart disease.

The Cambridge team compared heart tissue from two groups – patients with end-stage heart failure and those with healthy hearts. The diseased tissue came from men who had undergone heart transplants at Papworth Hospital, Cambridge, and the healthy hearts from age-matched victims of road traffic accidents.

They found that specific regions of the DNA in the diseased hearts contained "marks" known as DNA methylation, whereas the healthy hearts did not. This is the first study linking DNA methylation with human heart failure.

DNA methylation is already known to play a key part in development of most cancers, and its role in other complex diseases such as schizophrenia and diabetes is being investigated.

This study, funded by the British Heart Foundation, suggests the process also underlies development of different types of heart disease.

According to lead author Dr Roger Foo of the University of Cambridge: "DNA methylation leaves 'marks' on the genome, and there is already good evidence that these marks are strongly influenced by environment and diet. We found that this process is different in diseased and normal hearts. Linking all these things together suggests this may be the 'missing link' between environmental factors and heart failure."

The findings deepen our understanding of the genetic changes that can lead to heart disease, and how these can be caused by diet and the environment. As a result, Foo's findings should open up new ways of managing and treating heart disease.

"The next stage of our research is to find hotspots in the genome. This should help us identify people at risk of heart disease, and pinpoint patients whose disease will progress fastest. This would radically alter how we manage patients with heart disease, allowing us to target treatments and tailor monitoring," Foo explains.

The DNA that makes up our genes comprises four "bases" or nucleotides – cytosine, guanine, adenine and thymine, commonly abbreviated to C, G, A and T. DNA methylation is the addition of a methyl group (CH3) to cytosine.

When bound to cytosine, the methyl group sticks out. This means it looks different and is recognised differently by proteins. As a result, methylation alters how genes are expressed, ie which are turned on and off.

Foo likens DNA methlyation to a fifth nucleotide: "We often think of DNA as being composed of four nucleotides. Now, we are beginning to think there is a fifth – the methylated C."

DNA methylation is a crucial part of normal development, allowing different cells to become different tissues despite having the same genes. As well as happening during development, DNA methlyation continues throughout our lives in response to environmental changes and can lead to disease.

According to the study's first author, Dr Mehregan Movassagh of the University of Cambridge: "DNA methylation is a mechanism by which the environment and diet alters the expression of certain human genes, and has been the explanation for why, for instance, identical twins may have differing features and differ in their susceptibility to disease, despite having an identical set of genes."

It is also a very widespread process, occurring in plants and insects as well as vertebrates. In honey bees, for example, it is the reduction in DNA methylation that occurs as a result of feeding royal jelly which causes genetically identical larvae to develop into a queen, rather than a worker.

Epigenetic factors, such as DNA methylation, are currently the focus of much medical research because they offer further insight into disease than simply looking at our genes.

"We already know that several genes play an important role in heart failure. Researchers have looked at mutations in these genes and sometimes don't see any, so it could be methylation, not mutation, which is responsible for the altered expression that leads to disease. This opens a new window on the link between genome and disease," Movassagh says.

Professor Jeremy Pearson, Associate Medical Director at the British Heart Foundation (BHF), which funded the research, said: "By detecting these molecular changes in failing hearts, this research suggests that previously unsuspected mechanisms contribute to the development of heart failure. The findings open up the possibility of identifying new ways to treat this debilitating condition, which affects more than 700,000 people in the UK. We're supporting these researchers and others around the country to help us turn these vital discoveries into treatments for patients." *The research is published today in PLoS ONE.*

Notes to editors: Mehregan Movassagh et al, 'Differential DNA methylation correlates with differential expression of angiogenic factors in human heart failure' is published in PLoS ONE on 13 January 2010.

Angiotensin receptor blockers associated with lower risk of Alzheimer's disease

Boston, MA - Researchers from Boston University School of Medicine (BUSM) have found that angiotensin receptor blockers (ARBs) - a particular class of anti-hypertensive medicines - are associated with a striking decrease in the occurrence and progression of dementia. These findings appear in the January issue of the British Medical Journal.

Using data from the Decision Support System Database of the U.S. Department of Health System Veterans Affairs (with information on more than 5 million people), the BUSM researchers looked at records from patients who used ARBs, and compared them with subjects who had a similar health status, but were taking

different medications. They found patients taking ARBs had up to a 50 percent lower chance of getting Alzheimer's disease or dementia. Patients taking two forms of medications targeting the angiotensin system, ARBs and Angiotensin Converting Enzyme (ACE) inhibitors, had a 55 percent lower risk of dementia.

The researchers also examined patients who were already suffering from Alzheimer's disease or dementia, and found those subjects had up to a 67 percent lower chance of being admitted to nursing homes or dying if they were taking both ARBs and ACE inhibitors. Patients who appeared to benefit particularly well from use of ARBs were those who had experienced strokes before or during the course of their illness.

According to the BUSM researchers these results suggest that ARBs might protect against developing Alzheimer's disease and dementia. "For those who already have dementia, use of ARBs might delay deterioration of brain function and help keep patients out of nursing homes," said senior author Benjamin Wolozin, MD, PhD, a professor of pharmacology at BUSM. "The study is particularly interesting because we compared the effects of ARBs to other medications used for treating blood pressure or cardiovascular disease. This suggests that ARBs are more effective than other blood pressure and cardiovascular medications for preventing Alzheimer's disease or dementia," he added.

Although the researchers are unsure why ARBs might be so beneficial, they believe one possibility suggested by prior studies on animal models is that ARBs help prevent nerve cell injury from blood vessel damage or help promote nerve cell recovery after blood vessel damage. The authors also speculate that ARBs might help protect the blood vessels in the brain against damage related to cardiovascular disease. Damage to blood vessels is thought to reduce brain capacity and promote dementia, so reducing this damage might prevent the occurrence or progression of dementia.

Funding for this study was provided by the Retirement Research Foundation and from the Casten Foundation.

Carnegie Mellon scientists crack brain's codes for noun meanings

Identifying thoughts through brain codes leads to deciphering the brain's dictionary

Two hundred years ago, archaeologists used the Rosetta Stone to understand the ancient Egyptian scrolls. Now, a team of Carnegie Mellon University scientists has discovered the beginnings of a neural Rosetta Stone. By combining brain imaging and machine learning techniques, neuroscientists Marcel Just and Vladimir Cherkassky and computer scientists Tom Mitchell and Sandesh Aryal determined how the brain arranges noun representations. Understanding how the brain codes nouns is important for treating psychiatric and neurological illnesses.

"In effect, we discovered how the brain's dictionary is organized," said Just, the D.O. Hebb Professor of Psychology and director of the Center for Cognitive Brain Imaging. "It isn't alphabetical or ordered by the sizes of objects or their colors. It's through the three basic features that the brain uses to define common nouns like apartment, hammer and carrot."

As the researchers report today in the journal PLoS One, the three codes or factors concern basic human fundamentals: (1) how you physically interact with the object (how you hold it, kick it, twist it, etc.); (2) how it is related to eating (biting, sipping, tasting, swallowing); and (3) how it is related to shelter or enclosure. The three factors, each coded in three to five different locations in the brain, were found by a computer algorithm that searched for commonalities among brain areas in how participants responded to 60 different nouns describing physical objects. For example, the word apartment evoked high activation in the five areas that code shelter-related words.

In the case of hammer, the motor cortex was the brain area activated to code the physical interaction. "To the brain, a key part of the meaning of hammer is how you hold it, and it is the sensory-motor cortex that represents 'hammer holding,'" said Cherkassky, who has a background in both computer science and neuroscience.

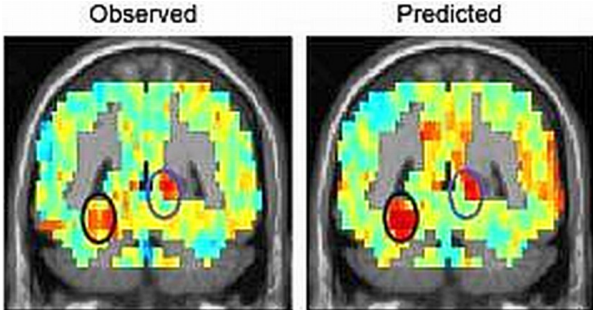
The research also showed that the noun meanings were coded similarly in all of the participants' brains. "This result demonstrates that when two people think about the word 'hammer' or 'house,' their brain activation patterns are very similar. But beyond that, our results show that these three discovered brain codes capture key building blocks also shared across people," said Mitchell, head of the Machine Learning Department in the School of Computer Science.

This study marked the first time that the thoughts stimulated by words alone were accurately identified using brain imaging, in contrast to earlier studies that used picture stimuli or pictures together with words. The programs were able to identify the thought without benefit of a picture representation in the visual area of the brain, focusing instead on the semantic or conceptual representation of the objects.

Additionally, the team was able to predict where the activation would be for a previously unseen noun. A computer program assigned a score to each word for each of the three dimensions, and that score predicted how much brain activation there would be in each of 12 specified brain locations. The theory generated a prediction of the activation for apartment based only on the patterns derived from the other 59 words. As one slice of the

observed brain image from a human participant (left) and the theory (right) shows, the theory makes precise predictions, particularly about the two shelter-related coding areas in this slice (circled), where brighter red indicates more activation.

To test the theory, the team used the word scores to identify which word a participant was thinking about, just by analyzing the person's brain activation patterns for that word. The program was able to tell which of the 60 words a participant was thinking about, with a rank accuracy as high as 84 percent for two of the participants, and an average rank accuracy of 72 percent across all 10 participants (where pure guessing would be accurate 50 percent of the time).



Carnegie Mellon University

One absent code in the study that is essential for the human species concerns sex or love or reproduction. "Our vocabulary of 60 test nouns lacked any words related to the missing dimension, such as 'spouse' or 'boyfriend' or even 'person,'" Just said. "We certainly expect some human dimension to be part of the brain's coding of nouns, in addition to the three dimensions we found."

"With psychiatric and neurological illnesses, the meanings of certain concepts are sometimes distorted," Just said. "These new techniques make it possible to measure those distortions and point toward a way to 'undistort' them. For example, a person with agoraphobia, the fear of open spaces, might have an exaggerated coding of the shelter dimension. A person with autism might have a weaker coding of social contact."

Another implication is in developing and testing domain expertise at the neural level. "We teach to the mind but we are shaping the brain, and now we can give the brain a test of how well it has learned a concept," says Just. "If an instructor knows how an advanced concept is represented in the brains of experts in that area, she will be able to teach to the brain test. We can do it for hammers and carrots right now. In the near future isotope and telomere may soon be on some brain researcher's agenda."

The research was funded by grants from the W.M. Keck Foundation and the National Science Foundation. To download the article, visit http://dx.plos.org/10.1371/journal.pone.0008622. For more information about the group's discoveries, visit www.ccbi.cmu.edu.

18 and Under

To Treat Bed-Wetting, Healthy Doses of Patience

By PERRI KLASS, M.D.

A couple of weeks ago, I saw a 5-year-old girl who was still wetting the bed every night. It's a common complaint: at least 15 percent of healthy 5-year-olds are not reliably "dry" at night. And bed-wetting is quite common even in older children.

But what may be most surprising about primary nocturnal enuresis, to use the clinical term for urinary incontinence in a child who does fine by day but has never been reliably dry through the night, is that it is often genetically based.

In other words, it is not about emotional problems, or mistakes a parent made during potty training, or laziness, which some still attribute to the bed-wetter himself. (The problem is about three times as common in boys as in girls.)

Indeed, one of the worst things about bed-wetting is the stigma. Sufferers and their families have been accused of everything from poor parenting to latent criminality. (In 1945, The New York Times reported on a psychological study of the backgrounds of 500 men who got into disciplinary trouble in the wartime Navy. The most powerful predictor of failure in the Navy, the article reported, was a combination of three factors: expulsion from school, civilian arrest and enuresis beyond age 5.)

Enuresis can have a number of physiological causes. Some children lack a hormone that decreases urine production at night. Others wet the bed simply because their bladder capacity is small.

"Here's the encounter I usually have when I see children in my clinic," Dr. Jennifer Abidari, chief of pediatric urology at the Santa Clara Valley Medical Center in California, told me. "I draw a bunch of bladders, and three of them are big and one of them is very small. "I ask them which one was wetting and they'll usually guess the smaller one, and I'll say, 'You're right — you have a bladder that's smaller than your age, and it's not your fault.' And I'll see the child glance over to the parent and I'll know there's been a lot of conflict."

In 1995, the first news of a genetic basis for bed-wetting made headlines, after Danish researchers reported a link to Chromosome 13. "It's very clear that there is a strong hereditary component in the course of enuresis," said Dr. Soren Rittig, a professor of pediatric nephrology at Aarhus University Hospital in Denmark.

Dr. Rittig is one of a group of researchers who have published new findings on the genetics of nocturnal enuresis, which turn out to be far from simple; linkage to three other chromosomes has been found in other families.

The researchers identified several large families in which enuresis was inherited following an autosomal dominant pattern - that is, if either parent has a history of bed-wetting, a child has a 50 percent chance of inheriting it.

As children grow older than my patient, behavioral and other treatments can make a big difference. Children whose bladders tend to spasm can be treated with anticholinergic drugs, and children who lack an antidiuretic hormone can take a synthetic version. But these drugs treat the symptom, not the underlying problem. “I consider enuresis to be a developmental delay which will improve by itself,” Dr. Abidari said, adding that if the medication is stopped and development has not progressed, “they will wet again.”

In such cases an effective treatment is a bed alarm, which vibrates and makes a noise when a child starts to urinate. Dr. Abidari says the alarms can cure the problem but can be hard on families, especially if the child is a sound sleeper. “The alarm goes off, everybody in the household wakes up but the child is still asleep,” she said. Success, she said, requires motivation on everyone’s part.

The doctors, nurse practitioners and counselors who treat enuresis can be almost messianic about the relief they can offer children and families. “The physician has to have an enthusiasm for wanting to treat wetters,” said Dr. Kenneth I. Glassberg, director of pediatric urology at Morgan Stanley Children’s Hospital of New York-Presbyterian. There must also be a committed staff, he added, to handle the frequent visits, phone calls and long-term support the children and their families may need.

All children with wetting problems should be checked for urinary tract infections. Children who develop secondary enuresis — that is, they are fully dry for six months, then begin wetting again — may have infections, constipation (an overly full bowel can put pressure on the bladder) or a variety of other problems, including behavioral and psychological issues.

My patient was also having some daytime accidents, and many specialists would want to address those even before age 5. The same bladder problems may be at work, but there can also be behavioral components.

In addition to anatomical and hormonal factors, “developing continence day and night is a combination of neurological readiness, developmental readiness and the interplay between a child and his environment, whether that’s day care, parents, sibling, preschool,” said Dr. Alison D. Schonwald, an assistant professor of pediatrics at Harvard Medical School and the co-author of “The Pocket Idiot’s Guide to Potty Training Problems” (Alpha, 2006).

My plan was to check the 5-year-old’s urine, just to make sure she didn’t have an infection, and to offer a referral to a pediatric urologist. Although the patient’s mother felt that the daytime problems were improving, she was happy to see a specialist. And the child herself demonstrated her bladder control by flatly refusing to urinate in a plastic cup.

New stroke therapy successful in rats

Protein completely restores motor function; scientists hope it will help humans

People with impaired mobility after a stroke soon may have a therapy that restores limb function long after the injury, if a supplemental protein works as well in humans as it does in paralyzed rats.

Two new studies by UC Irvine biologists have found that a protein naturally occurring in humans restores motor function in rats after a stroke. Administered directly to the brain, the protein restores 99 percent of lost movement; if it’s given through the nose, 70 percent of lost movement is regained. Untreated rats improve by only 30 percent.

“No drugs exist that will help a stroke after a few days. If you have a stroke, you don’t have many treatment options,” said James Fallon, psychiatry & human behavior professor and senior co-author of the studies. “Now we have evidence there may be therapies that can repair damage to a significant degree long after the stroke. It’s a completely unexpected and remarkable finding, and it’s worth trying in humans.”

The studies, carried out by UCI postdoctoral researcher Magda Guerra-Crespo, chronicle the success of a small protein called transforming growth factor alpha, which plays critical tissue-forming and developmental roles in humans from just after conception through birth and into old age.

“TGF alpha has been studied for two decades in other organ systems but never before has been shown to reverse the symptoms of a stroke,” Guerra-Crespo said. No lasting side effects were observed.

In the first study, published in the journal Neuroscience, scientists sought to learn whether TGF alpha administered directly to the brain could help rats with stroke-induced loss of limb function, typically on one side – as is seen in humans. When put inside a cylinder, healthy rats will jump up with both front legs, but

stroke-impaired rats will use just one leg, favoring the injured side. When given a choice of directions to walk, impaired rats will move toward their good side.

One month after the study rats suffered an induced stroke (equal to about a year for humans), some were injected with TGF alpha. Within a month, they had regained nearly all their motor function, hopping up with both legs in the cylinder exercise and not favoring a side in the directional test. Rats that did not receive treatment improved just 30 percent.

Scientists examined the rats' brains and found that TGF alpha was stimulating neuron growth. First, it prompted adult stem cells in the brain to divide, creating more cells. Those cells then turned into brain cells and moved to the injured part of the brain, replacing neurons lost to the stroke. These new neurons, the scientists believe, helped restore motor function.

"It's becoming more and more clear that the brain is like any other organ: It has a lot of potential to regenerate," said Darius Gleason, a developmental & cell biology graduate student who worked on the study. "We are just emulating nature by giving a little nudge to what the brain is trying to do itself."

In the second study, appearing online Jan. 11 in the Journal of Stroke & Cerebrovascular Diseases, scientists placed TGF alpha in the rats' noses, simulating a nasal spray. They used a slightly different chemical version of the protein to render it more stable on its journey to the brain. After a month, the injured rats had regained 70 percent of their function, indicating that the intranasal method also works well.

"We saw the same phenomena," Fallon said. "It wasn't as profound, but we still ended up with very significant behavioral improvements and the same regenerative anatomical process."

UCI researchers Andres Sistos, Tina Toosky, Ihsan Solaroglu, John Zhang and Peter Bryant also worked on the intracranial study. Guerra-Crespo was supported by a UC MEXUS postdoctoral fellowship, Gleason was supported by a California Institute for Regenerative Medicine fellowship, and the research was funded by unrestricted gifts to Fallon.

UW-Madison scientists create super-strong collagen

MADISON — A team of University of Wisconsin-Madison researchers has created the strongest form of collagen known to science, a stable alternative to human collagen that could one day be used to treat arthritis and other conditions that result from collagen defects.

"It's by far the most stable collagen ever made," says Ron Raines, a University of Wisconsin-Madison professor of chemistry and biochemistry who led the study, published in the Jan. 12 issue of the Proceedings of the National Academy of Sciences.

Collagen is the most abundant protein in the human body, forming strong sheets and cables that support the structure of skin, internal organs, cartilage and bones, as well as all the connective tissue in between. For decades, doctors have used collagen from cows to treat serious burns and other wounds in humans despite the risk of tissue rejection associated with cross-species transplants.

In 2006, Raines' team figured out how to make human collagen in the lab, creating collagen molecules longer than any found in nature. Now, with funding from the National Institutes of Health, the researchers have taken this line of inquiry one step further, creating a form of super-strong collagen that may one day help millions. Raines says this artificial collagen holds promise as a therapy for conditions such as arthritis, which is caused by a breakdown of the body's natural collagen and affects more than 46 million Americans.

To make the new form of collagen, Raines' team substituted two-thirds of the protein's regular amino acids with less-flexible versions that stiffened the overall structure of the protein and helped it hold its form. "The breakthrough of this approach was the use of rigid analogues that have shapes similar to [the shapes the natural amino acids take] in the folded, functional form of the protein," explains Raines.

The resulting collagen holds together at temperatures far above what it takes for natural collagen to fall apart. And although it's built largely from amino acids that aren't found in nature, X-ray crystallography confirms that the three-dimensional structure of the lab-made collagen is indistinguishable from that of natural collagen, according to UW-Madison bacteriologist Katrina Forest, a co-author of the study.

"This hyper-stable collagen is really a testament to the power of modern protein chemistry," says Raines.

Mosquito hunters invent better, cheaper, DIY disease weapon

Emory University researchers believe they have come up with the cheapest, most efficient way yet to monitor adult mosquitoes and the deadly diseases they carry, from malaria to West Nile Virus. Emory has filed a provisional patent on the Prokopack mosquito aspirator, but the inventors have provided simple instructions for how to make it in the Journal of Medical Entomology.

"This device has broad potential, not only for getting more accurate counts of mosquito populations, but for better understanding mosquito ecology," said Gonzalo Vazquez-Prokopec, the invention's namesake and a post-doctoral in environmental studies.

"There is a great need for effective and affordable mosquito sampling methods. Use of the Prokopack can increase the coverage area, and the quality of the data received, especially for blood-fed mosquitoes. Ultimately, it can help us develop better health intervention strategies."

In both field and lab tests, the Prokopack outperformed the current gold standard for resting mosquito surveillance – the Centers for Disease Control and Prevention Backpack Aspirator (CDC-BP). In addition to having a longer reach, enabling it to collect more mosquitoes than the CDC-BP, the Prokopack is significantly smaller, lighter, cheaper and easier to build.

Anyone with access to a hardware store, and about $45 to $70, can make the Prokopack, which uses a battery-powered motor to suck up live mosquitoes for analysis. Mosquito-borne diseases rank among the world's top killers, and Vazquez-Prokopec hopes that more affordable and efficient surveillance methods will help save lives.

"I come from a developing country," says the Argentine native. "I understand what it feels like to know that there is a health technology available, and to not have the money to access it."

For decades, public health officials have struggled to conduct mosquito surveillance. One early method, with obvious drawbacks, was to expose a bit of skin and count the bites. Another low-tech method is to spray inside a home with insecticide, and gather the bugs that fall onto on a drop cloth.

Mosquito traps baited with a chemical that mimics human sweat are sometimes used to catch live adult insects. But these traps capture only females who are looking for a meal.

The CDC-BP can quickly vacuum up samples of live specimens, which can be analyzed in a lab to determine the source of blood they recently consumed. The drawbacks to the CDC-BP, however, include its heavy weight (26 pounds), its bulk and its price – about $450 to $750 in the United States.

Emory researchers used a CDC-BP in their study of West Nile Virus and urban mosquito ecology in Atlanta. They wanted to learn if mosquitoes that harbor the virus were overwintering in nooks near the ceilings of sewer tunnels. But the CDC-BP only reaches six feet, and the tunnels are 15-feet high.

With a bit of ingenuity and a few trips to the hardware store, the research team put together a solution: a plastic container, a wire screen, a plumbing pipe coupler, a battery-powered blower motor and painter extension poles. After some experimentation with these components, the Prokopack was born.

"It's not like we woke up one day and said, 'Let's invent a mosquito aspirator,'" Vazquez-Prokopec explains. "It grew out of our needs during field research."

Comparative tests with the Prokopack and the CDC-BP were conducted outdoors and in sewer tunnels during the Emory lab's Atlanta research projects. Additional field tests were done during a dengue fever study in Iquitos, Peru, where public health technicians are trying to control mosquitoes in homes. The Prokopack, which weighs less than two pounds, collected more mosquitoes than the CDC-BP, and reached higher into ceilings and into foliage.

Collecting more mosquitoes in higher locations can give researchers more insights into their behaviors. Upper foliage, for instance, can yield more mosquitoes resting after feeding on birds. And upper walls and ceilings of homes may harbor more mosquitoes resting after a meal on humans.

Deciphering the Chatter of Monkeys and Chimps

By NICHOLAS WADE

Walking through the Tai forest of Ivory Coast, Klaus Zuberbühler could hear the calls of the Diana monkeys, but the babble held no meaning for him.

That was in 1990. Today, after nearly 20 years of studying animal communication, he can translate the forest’s sounds. This call means a Diana monkey has seen a leopard. That one means it has sighted another predator, the crowned eagle. “In our experience time and again, it’s a humbling experience to realize there is so much more information being passed in ways which hadn’t been noticed before,” said Dr. Zuberbühler, a psychologist at the University of St. Andrews in Scotland.

Do apes and monkeys have a secret language that has not yet been decrypted? And if so, will it resolve the mystery of how the human faculty for language evolved? Biologists have approached the issue in two ways, by trying to teach human language to chimpanzees and other species, and by listening to animals in the wild.

The first approach has been propelled by people’s intense desire — perhaps reinforced by childhood exposure to the loquacious animals in cartoons — to communicate with other species. Scientists have invested enormous effort in teaching chimpanzees language, whether in the form of speech or signs. A New York Times reporter who understands sign language, Boyce Rensberger, was able in 1974 to conduct what may be the first newspaper interview with another species when he conversed with Lucy, a signing chimp. She invited him up her tree, a proposal he declined, said Mr. Rensberger, who is now at M.I.T.

But with a few exceptions, teaching animals human language has proved to be a dead end. They should speak, perhaps, but they do not. They can communicate very expressively — think how definitely dogs can make their desires known — but they do not link symbolic sounds together in sentences or have anything close to language.

Better insights have come from listening to the sounds made by animals in the wild. Vervet monkeys were found in 1980 to have specific alarm calls for their most serious predators. If the calls were recorded and played back to them, the monkeys would respond appropriately. They jumped into bushes on hearing the leopard call, scanned the ground at the snake call, and looked up when played the eagle call.

It is tempting to think of the vervet calls as words for "leopard," "snake" or "eagle," but that is not really so. The vervets do not combine the calls with other sounds to make new meanings. They do not modulate them, so far as is known, to convey that a leopard is 10, or 100, feet away. Their alarm calls seem less like words and more like a person saying "Ouch!" — a vocal representation of an inner mental state rather than an attempt to convey exact information.

But the calls do have specific meaning, which is a start. And the biologists who analyzed the vervet calls, Robert Seyfarth and Dorothy Cheney of the University of Pennsylvania, detected another significant element in primates' communication when they moved on to study baboons. Baboons are very sensitive to who stands where in their society's hierarchy. If played a recording of a superior baboon threatening an inferior, and the latter screaming in terror, baboons will pay no attention — this is business as usual in baboon affairs. But when researchers concoct a recording in which an inferior's threat grunt precedes a superior's scream, baboons will look in amazement toward the loudspeaker broadcasting this apparent revolution in their social order.

Baboons evidently recognize the order in which two sounds are heard, and attach different meanings to each sequence. They and other species thus seem much closer to people in their understanding of sound sequences than in their production of them. "The ability to think in sentences does not lead them to speak in sentences," Drs. Seyfarth and Cheney wrote in their book "Baboon Metaphysics."

Some species may be able to produce sounds in ways that are a step or two closer to human language. Dr. Zuberbühler reported last month that Campbell's monkeys, which live in the forests of the Ivory Coast, can vary individual calls by adding suffixes, just as a speaker of English changes a verb's present tense to past by adding an "-ed."

The Campbell's monkeys give a "krak" alarm call when they see a leopard. But adding an "-oo" changes it to a generic warning of predators. One context for the krak-oo sound is when they hear the leopard alarm calls of another species, the Diana monkey. The Campbell's monkeys would evidently make good reporters since they distinguish between leopards they have observed directly (krak) and those they have heard others observe (krak-oo).

Even more remarkably, the Campbell's monkeys can combine two calls to generate a third with a different meaning. The males have a "Boom boom" call, which means "I'm here, come to me." When booms are followed by a series of krak-oos, the meaning is quite different, Dr. Zuberbühler says. The sequence means "Timber! Falling tree!"

Dr. Zuberbühler has observed a similar achievement among putty-nosed monkeys that combine their "pyow" call (warning of a leopard) with their "hack" call (warning of a crowned eagle) into a sequence that means "Let's get out of here in a real hurry."

Apes have larger brains than monkeys and might be expected to produce more calls. But if there is an elaborate code of chimpanzee communication, their human cousins have not yet cracked it. Chimps make a food call that seems to have a lot of variation, perhaps depending on the perceived quality of the food. How many different meanings can the call assume? "You would need the animals themselves to decide how many meaningful calls they can discriminate," Dr. Zuberbühler said. Such a project, he estimates, could take a lifetime of research.

Monkeys and apes possess many of the faculties that underlie language. They hear and interpret sequences of sounds much like people do. They have good control over their vocal tract and could produce much the same range of sounds as humans. But they cannot bring it all together.

This is particularly surprising because language is so useful to a social species. Once the infrastructure of language is in place, as is almost the case with monkeys and apes, the faculty might be expected to develop very quickly by evolutionary standards. Yet monkeys have been around for 30 million years without saying a single sentence. Chimps, too, have nothing resembling language, though they shared a common ancestor with humans just five million years ago. What is it that has kept all other primates locked in the prison of their own thoughts?

Drs. Seyfarth and Cheney believe that one reason may be that they lack a “theory of mind”; the recognition that others have thoughts. Since a baboon does not know or worry about what another baboon knows, it has no urge to share its knowledge. Dr. Zuberbühler stresses an intention to communicate as the missing factor. Children from the youngest ages have a great desire to share information with others, even though they gain no immediate benefit in doing so. Not so with other primates.

“In principle, a chimp could produce all the sounds a human produces, but they don’t do so because there has been no evolutionary pressure in this direction,” Dr. Zuberbühler said. “There is nothing to talk about for a chimp because he has no interest in talking about it.” At some point in human evolution, on the other hand, people developed the desire to share thoughts, Dr. Zuberbühler notes. Luckily for them, all the underlying systems of perceiving and producing sounds were already in place as part of the primate heritage, and natural selection had only to find a way of connecting these systems with thought.

Yet it is this step that seems the most mysterious of all. Marc D. Hauser, an expert on animal communication at Harvard, sees the uninhibited interaction between different neural systems as critical to the development of language. “For whatever reason, maybe accident, our brains are promiscuous in a way that animal brains are not, and once this emerges it’s explosive,” he said.

In animal brains, by contrast, each neural system seems to be locked in place and cannot interact freely with others. “Chimps have tons to say but can’t say it,” Dr. Hauser said. Chimpanzees can read each other’s goals and intentions, and do lots of political strategizing, for which language would be very useful. But the neural systems that compute these complex social interactions have not been married to language.

Dr. Hauser is trying to find out whether animals can appreciate some of the critical aspects of language, even if they cannot produce it. He and Ansgar Endress reported last year that cotton-top tamarins can distinguish a word added in front of another word from the same word added at the end. This may seem like the syntactical ability to recognize a suffix or prefix, but Dr. Hauser thinks it is just the ability to recognize when one thing comes before another and has little to do with real syntax.

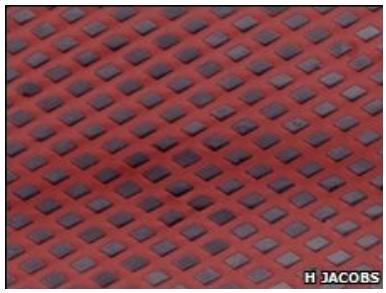
“I’m becoming pessimistic,” he said of the efforts to exp lore whether animals have a form of language. “I conclude that the methods we have are just impoverished and won’t get us to where we want to be as far as demonstrating anything like semantics or syntax.”

Yet, as is evident from Dr. Zuberbühler’s research, there are many seemingly meaningless sounds in the forest that convey information in ways perhaps akin to language.

The solar cell that builds itself

By Jason Palmer Science and technology reporter, BBC News

Researchers have demonstrated a simple, cheap way to create self-assembling electronic devices using a property crucial to salad dressings.



The approach made a device of 64,000 parts in three minutes

It uses the fact that oil- and water-based liquids do not mix, forming devices from components that align along the boundary between the two.

The idea joins a raft of approaches toward self-assembly, but lends itself particularly well to small components. Crucially, it could allow the large-scale assembly of high-quality electronic components on materials of just about any type, in contrast to "inkjet printed" electronics or some previous self-assembly techniques. The work is reported in Proceedings of the National Academy of Sciences.

Specific gravity

Such efforts have until now exploited the effect of gravity, assembling devices through so-called "sedimentation".

In this approach, "blank" devices are etched with depressions to match precisely-shaped components. Simply dumped into a liquid, the components should settle down into the blank device like sand onto a riverbed, in just the right places.

"That's what we tried for at least two years and we were never able to assemble these components with high yield - gravity wasn't working," said Heiko Jacobs of the University of Minnesota, who led the research.
"Then we thought if we could concentrate them into a two-dimensional sheet and then have some kind of conveyor belt-like system we could assemble them with high yields and high speed," he told BBC News.
To do that, the team borrowed an idea familiar to fans of vinaigrette: they built their two-dimensional sheets at the border between oil and water.
They first built a device blank as before, with depressions lined with low-temperature solder, designed for individual solar cell elements.

They then prepared the elements - each a silicon and gold stack a few tens of millionths of a metre across - and put different coatings on each side.

On the silicon side, they put a hydrophobic molecule, one that has a strong tendency to evade contact with water. On the gold side, they put a hydrophilic molecule, which has the converse tendency to seek out water.

By getting the densities of the oil- and water-based parts of the experiment just right, a "sheet" of the elements could be made to "float" between the two, pointing in the right direction thanks to their coatings.

The conveyor belt process is to simply dunk the device blank through the boundary and draw it back slowly; the sheet of elements rides up along behind it, each one popping neatly into place as the solder attracts its gold contact.

The team made a working device comprising 64,000 elements in just three minutes.

Bendy future

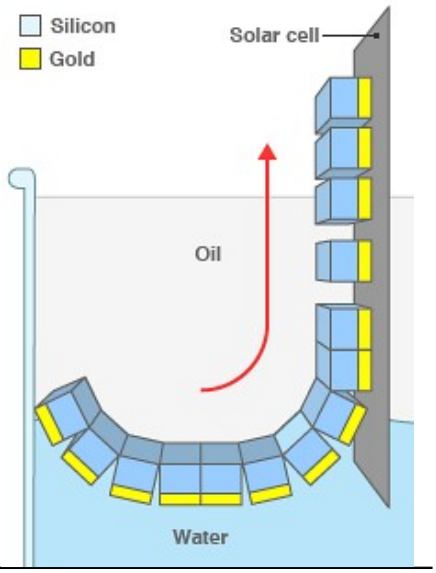
Having proved that the concept works, the team is now investigating just how small they can go in terms of individual elements, or how large they can go in finished devices. The approach should also work for almost any material, stiff or flexible, plastic, metal or semiconductor - a promising fact for future display and imaging applications.

Babak Parviz, a nano-engineering professor at the University of Washington in Seattle, said the technique is a "clear demonstration that self-assembly is applicable across size scales". "Self-assembly is probably the best method for integrating high-performance materials onto unconventional substrates," he told BBC News.

The method tackles what Dr Parviz said is the most challenging problem - the proper alignment of thousands of parts, each thinner than a human hair. But it also works with the highest-performance materials, he said.

"For example, this method allows one to use single-crystal silicon, which is far superior to other types of silicon for making solar cells."

SELF-ASSEMBLY EXPLAINED



The oil/water mix contains a number of individual solar cell elements

Each is coated with a "water-loving" molecule on the bottom and a "water-hating" one on top

The elements align neatly at the oil/water boundary in a two-dimensional sheet

The "blank" solar cell has pre-cut places for the elements and is dipped through the boundary

As it is slowly drawn upwards, the elements pop into place

Jurassic tree survives big chill

What is believed to be the world's most northerly grove of a Jurassic tree has so far survived freezing temperatures.

Wollemi Pine - thought to have died out two million years ago before being discovered in Australia - were planted at Inverewe Garden last June.

National Trust for Scotland gardener Kevin Ball said the Highlands site had experienced its coldest temperatures in more than 30 years.

He said -7C was the lowest recorded at the garden so far this winter.

Mr Ball added: "The Wollemi Pine was only discovered in 1994, so we're learning about it all the time.

"However, evidence at the moment suggests it can tolerate the cold more effectively than its Australian origins would suggest and can survive temperatures as low as -12C. "Wollemi Pine can live up to 1,000 years and we're hoping this will be the case for our sturdy little saplings."

The Wollemi Pine was thought to have died out millions of years ago

Isolated grove

The trees at Inverewe were cultivated from those found to have survived in a single isolated grove in Australia.

The discovery of the pine in 1994 caused a scientific sensation, and prompted the Australian government to protect the site where it was growing. Park ranger David Noble found the trees in the Blue Mountains, west of Sydney. The species was thought to have been extinct for at least two million years. The only previously known examples were fossils which were 175 million years old. Eight Wollemi Pines were planted at Inverewe.

Duke scientists map brain pathway for vocal learning

DURHAM, N.C. – Scientists at Duke University Medical Center have identified neurons in the songbird brain that convey the auditory feedback needed to learn a song.

Their research lays the foundation for improving human speech, for example, in people whose auditory nerves are damaged and who must learn to speak without the benefit of hearing their own voices.

"This work is the first study to identify an auditory feedback pathway in the brain that is harnessed for learned vocal control," said Richard Mooney, Ph.D., Duke professor of neurobiology and senior author of the study. The researchers also devised an elegant way to carefully alter the activity of these neurons to prove that they interact with the motor networks that control singing.

The study, supported by an NIH grant, was published online in Neuron on Jan. 13.

Vocal learning isn't a simple process. "One challenge the brain faces when trying to learn a new behavior is that it only receives feedback about performance tens or even hundreds of milliseconds after it has generated the motor commands controlling that performance," Mooney said. "The challenge is pushed to an extreme if the brain has to use this sensory information in a retrospective way and still make corrections with millisecond precision, as humans and songbirds do when they learn to vocalize."

The problems that juvenile birds solve when they learn a song from a tutor bird are similar to the problems humans solve when we learn to speak, and birds and humans exploit similar neural systems to reach this solution, Mooney said.

The major question of this research was how the brain encodes and harnesses auditory feedback to shape the vocal performance in juvenile birds that are learning to sing.

In a painstaking experiment, lead author Huimeng Lei, Ph.D., used fine microelectrodes to locate neurons that become active in the pupil's brain when it hears its own song, Mooney said. "This was a very difficult procedure that had to be exquisitely accurate. Huimeng was able to get the recordings working just right to locate the feedback-sensing neurons."

Once the scientists knew they had located the correct set of neurons, they passed a brief pulse of electricity through the implanted electrodes to alter neural activity associated with one of the notes that the pupil was learning to sing.

"We think that the stimulation alters what the pupil bird perceives, and it is this altered perception that results in the note becoming distorted (as it sings the song back)," Mooney said. "In contrast, if we stimulated directly in the motor network (which produces the note) we would trigger an immediate distortion of the targeted song syllable."

Because birds sing their song with millisecond precision, the scientists could determine how precisely the brain learned to assign perceived error to the part of the song where the stimulation occurred. "The acoustical features of the stimulated region of the song grew distorted over time," Mooney said.

Three findings of interest emerged. First, the distortion in the bird's singing was delayed and showed up anywhere from hours to weeks after the bird first heard the electrical noise pulse in its song.

Second, the distortion always came in the same place in the pupil bird's song. This means the distortion was temporally precise and occurred at the exact point in the song where the electrical "noise" was introduced. "The brain somehow is learning to associate the stimulation with a certain part of the performance, and then alter the performance accordingly," Mooney said.

Third, by disrupting neural activity at different stages of the learning process, they determined that the distortion effects were strongly age-dependent. The target portion of the song degraded very quickly in the younger birds, sometimes within an hour. The older birds who experienced electrical interference kept singing properly for a while, but slowly their singing degraded, over a period of weeks.

"Because we are directly injecting an electrical pulse into the auditory feedback pathway, the changing ability of the brain to respond to the perceived error in performance likely reflects changes in the motor network itself," Mooney said.

Song precision is vital to songbirds because females select mates based in part on the temporal precision with which they sing. Temporal precision is also highly important in human speech, because acoustical features of two speech sounds may differ on the millisecond level.

This study lays the groundwork for scientists to improve human speech. For example, people whose auditory nerves are damaged may benefit as scientists explore how to stimulate auditory feedback pathways in the human brain that are important for speech learning. This is especially true for older children and adults who have been deaf and who need to learn speech well past the prime time for vocal learning, Mooney said.

This study also opens the door to exploring how the brain compares performance-related feedback to a sensory model, which is the basis of imitation, Mooney said.

"Imitation is the wellspring for much of human culture," he noted. "Because it would be impossible to use humans in experiments about initial vocal learning, songbird tutors and students provide a beautiful substitute system so that we can study the detailed brain mechanisms that underlie this relatively complex type of learning."

Chimp and human Y chromosomes evolving faster than expected

CAMBRIDGE, Mass. – Contrary to a widely held scientific theory that the mammalian Y chromosome is slowly decaying or stagnating, new evidence suggests that in fact the Y is actually evolving quite rapidly through continuous, wholesale renovation.

By conducting the first comprehensive interspecies comparison of Y chromosomes, Whitehead Institute researchers have found considerable differences in the genetic sequences of the human and chimpanzee Ys - an indication that these chromosomes have evolved more quickly than the rest of their respective genomes over the 6 million years since they emerged from a common ancestor. The findings are published online this week in the journal Nature.

"The region of the Y that is evolving the fastest is the part that plays a role in sperm production," say Jennifer Hughes, first author on the Nature paper and a postdoctoral researcher in Whitehead Institute Director David Page's lab. "The rest of the Y is evolving more like the rest of the genome, only a little bit faster."

The chimp Y chromosome is only the second Y chromosome to be comprehensively sequenced. The original chimp genome sequencing completed in 2005 largely excluded the Y chromosome because its hundreds of repetitive sections typically confound standard sequencing techniques. Working closely with the Genome Center at Washington University, the Page lab managed to painstakingly sequence the chimp Y chromosome, allowing for comparison with the human Y, which the Page lab and the Genome Center at Washington University had sequenced successfully back in 2003.

The results overturned the expectation that the chimp and human Y chromosomes would be highly similar. Instead, they differ remarkably in their structure and gene content. The chimp Y, for example, has lost one third to one half of the human Y chromosome genes--a significant change in a relatively short period of time. Page points out that this is not all about gene decay or loss. He likens the Y chromosome changes to a home undergoing continual renovation.

"People are living in the house, but there's always some room that's being demolished and reconstructed," says Page, who is also a Howard Hughes Medical Institute investigator. "And this is not the norm for the genome as a whole."

Wes Warren, Assistant Director of the Washington University Genome Center, agrees. "This work clearly shows that the Y is pretty ingenious at using different tools than the rest of the genome to maintain diversity of genes," he says. "These findings demonstrate that our knowledge of the Y chromosome is still advancing."

Hughes and Page theorize that the divergent evolution of the chimp and human Y chromosomes may be due to several factors, including traits specific to Y chromosomes and differences in mating behaviors.

Because multiple male chimpanzees may mate with a single female in rapid succession, the males' sperm wind up in heated reproductive competition. If a given male produces more sperm, that male would theoretically be more likely to impregnate the female, thereby passing on his superior sperm production genes, some of which may be residing on the Y chromosome, to the next generation.

Because selective pressure to pass on advantageous sperm production genes is so high, those genes may also drag along detrimental genetic traits to the next generation. Such transmission is allowed to occur because, unlike other chromosomes, the Y has no partner with which to swap genes during cell division. Swapping genes between chromosomal partners can eventually associate positive gene versions with each other and eliminate detrimental gene versions. Without this ability, the Y chromosome is treated by evolution as one large entity. Either the entire chromosome is advantageous, or it is not.

In chimps, this potent combination of intense selective pressure on sperm production genes and the inability to swap genes may have fueled the Y chromosome's rapid evolution. Disadvantages from a less-than-ideal gene version or even the deletion of a section of the chromosome may have been outweighed by the advantage of improved sperm production, resulting in a Y chromosome with far fewer genes than its human counterpart.

To determine whether this rapid rate of evolution affects Y chromosomes beyond those of chimps and humans, the Page lab and the Washington University Genome Center are now sequencing and examining the Y chromosomes of several other mammals.

This research was funded by the National Institutes of Health (NIH) and the Howard Hughes Medical Institute (HHMI).
Written by Nicole Giese

David Page's primary affiliation is with Whitehead Institute for Biomedical Research, where his laboratory is located and all his research is conducted. He is also a Howard Hughes Medical Institute Investigator and a Professor of Biology at Massachusetts Institute of Technology.

Full Citation: *"Chimpanzee and human Y chromosomes are remarkably divergent in structure and gene content" Nature, online January 13, 2010.*

Jennifer F. Hughes (1), Helen Skaletsky (1), Tatyana Pyntikova (1), Tina A. Graves (2), Saskia K. M. van Daalen (3), Patrick J. Minx (2), Robert S. Fulton (2), Sean D. McGrath (2), Devin P. Locke (2), Cynthia Friedman (4), Barbara J. Trask (4), Elaine R. Mardis (2), Wesley C. Warren (2), Sjoerd Repping (3), Steve Rozen (1), Richard K. Wilson (2), David C. Page (1).

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Nursing students twice as likely to smoke as the general population

Public health experts are calling for urgent steps to reduce the number of healthcare professionals who smoke, after a survey of over 800 new nursing students found that more than half were current or former smokers.

The Italian study, published in the January issue of the Journal of Advanced Nursing, surveyed 812 students who were just starting their University course. They found that 44% of them were still smoking – twice as many as in the general population – and a further 12% were former smokers.

Three-quarters of the smoking students had at least one parent who smoked and almost half had at least one brother or sister who smoked.

"Smoking prevention is an important issue and healthcare professionals, especially physicians and nurses, can play a major role in helping people to understand the consequences that smoking can have on their health and their lives" says Professor Anna Maria Tortorano from the Department of Public Health at the University of Milan, Italy.

"However when health professionals smoke it makes it more difficult for them to encourage patients to stop."

Key findings of the study included:

* 87% of the students agreed to take part in the survey. 63% were female and 85% were native Italians, with the rest coming from developing countries like Peru, Albania and Ecuador.

* The Italian students were much younger than the immigrant students – averaging 23 and 31 respectively for the males and 23 and 28 for the females.

* 39% of the female students and 53% of the male students smoked, giving an overall average of 44%. 37% smoked up to five cigarettes a day and 4% smoked more than 20.

* Students were much more likely to be current or former smokers if their parents smoked. 75% of smokers had a least one smoking parent, compared with 54% of those who had never smoked and 22% came from homes where both parents smoked, compared with 14% of those who had never smoked.

* The smoking habits of the fathers made little difference, with 33% of smokers having just a father who smoked, compared with 31% of non-smokers. However, smokers were twice as likely to have just a mother who smoked (20%) than non-smokers (10%).

* 47% of current and former smokers had siblings who smoked, compared to 25% of those who have never smoked.

"Figures from the World Health Organization show that approximately 35% of men and 22% of women in developed countries are daily smokers, together with 50% of men and 9% of women in developing countries" says Professor Tortorano, who carried out the study with research associate Dr Emanuela Biraghi.

"Figures for the general Italian population show that 22% of people over the age of 14 smoked in 2007.

"However the figure of 44% reported by nursing students who took part in our study is much higher than the 25% observed for medical students at the same University. It is also twice as high as the general Italian population.

"We believe that smoking cessation programmes should be incorporated into nursing studies as high levels of smoking among healthcare professionals undermine the credibility of non-smoking campaigns aimed at the general public."

Notes to Editors *Tobacco smoking habits among nursing students and the influence of family and peer smoking behaviour. Biraghi E and Tortorano A M. Journal of Advanced Nursing. 66.1, pp 33-39. (January 2010). DOI: 10.1111/j.1365-2648.2009.05135.x*

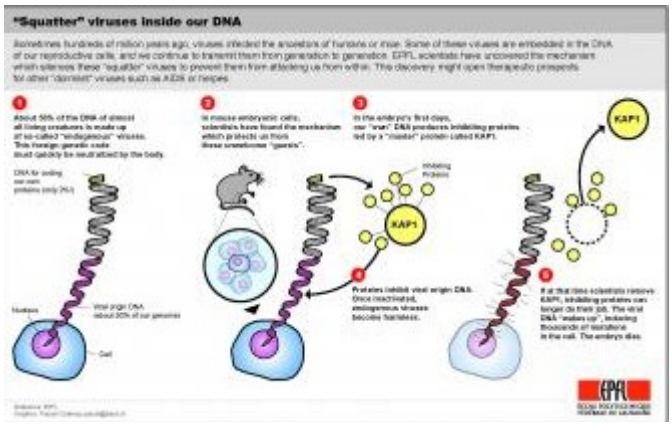
The viruses within -- and what keeps them there

Biologists wake dormant viruses and uncover mechanism for survival

It is known that viral "squatters" comprise nearly half of our genetic code. These genomic invaders inserted their DNA into our own millions of years ago when they infected our ancestors. But just how we keep them quiet and prevent them from attack was more of a mystery until EPFL researchers revived them.

The reason we survive the presence of these endogenous retroviruses—viruses that attack and are passed on through germ cells, the cells that give rise to eggs and sperm—is because something keeps the killers silent. Now, publishing in the journal Nature, Didier Trono and his team from EPFL, in Switzerland, describe the mechanism. Their results provide insights into evolution and suggest potential new therapies in fighting another retrovirus—HIV.

By analysing embryonic stem cells in mice within the first few days of life, Trono and team discovered that mouse DNA codes for an army of auxiliary proteins that recognize the numerous viral sequences littering the genome. The researchers also demonstrated that a master regulatory protein called KAP1 appears to orchestrate these inhibitory proteins in silencing would-be viruses. When KAP1 is removed, for example, the viral DNA "wakes up," multiplies, induces innumerable mutations, and the embryo soon dies.



This shows the functioning of Kap1 protein in mouse embrocation cells. **Pascal Coderay, pascal@salut.ch**

Because retroviruses tend to mutate their host's DNA, they have an immense power and potential to alter genes. And during ancient pandemics, some individuals managed to silence the retrovirus involved and therefore survived to pass on the ability. Trono explains that the great waves of endogenous retrovirus appearance coincide with times when evolution seemed to leap ahead.

"In our genome we find traces of the last two major waves. The first took place 100 million years ago, at the time when mammals started to develop, and the second about fifty million years ago, just before the first anthropoid primates," he says.

The discovery of the KAP1 mechanism could be of interest in the search for new therapeutic approaches to combat AIDS. The virus that causes AIDS can lie dormant in the red blood cells it infects, keeping it hidden from potential treatments. Waking the virus up could expose it to attack.

Co-authors include Helen M. Rowe, School of Life Sciences, École Polytechnique Fédérale de Lausanne (EPFL), Switzerland; Johan Jakobsson, EPFL and Wallenberg Neuroscience Center, Department of Experimental Medical Sciences, Lund University, Sweden; Daniel Mesnard, EPFL; Jacques Rougemont, EPFL; Séverine Reynard, EPFL; Tugce Aktas, EMBL Heidelberg, Germany; Pierre V. Maillard, EPFL; Hillary Layard-Liesching, EPFL; Sonia Verp, EPFL; Julien Marquis, EPFL; François Spitz, EMBL Heidelberg, Germany; Daniel B. Constam, EPFL; and Didier Trono, EPFL.

To view a YouTube video related to this release, please visit http://www.youtube.com/watch?v=4cGIRRidqa8.

Thyme oil can inhibit COX2 and suppress inflammation

For those who do not drink, researchers have found that six essential oils –from thyme, clove, rose, eucalyptus, fennel and bergamot—can suppress the inflammatory COX-2 enzyme, in a manner similar to resveratrol, the chemical linked with the health benefits of red wine. They also identified that the chemical carvacrol was primarily responsible for this suppressive activity.

These findings, appearing in the January issue of Journal of Lipid Research, provide more understanding of the health benefits of many botanical oils and provide a new avenue for anti-inflammatory drugs.

Essential oils from plants have long been a component of home remedies, and even today are used for their aromatherapy, analgesic (e.g. cough drops), or antibacterial properties. Of course, the exact way they work is not completely understood. However, Hiroyasu Inoue and colleagues in Japan believed that many essential oils might target COX-2 much like compounds in wine and tea.

So, they screened a wide range of commercially available oils and identified six (thyme, clove, rose, eucalyptus, fennel and bergamot) that reduced COX-2 expression in cells by at least 25%. Of these, thyme oil proved the most active, reducing COX-2 levels by almost 75%.

When Inoue and colleagues analyzed thyme oil, they found that the major component –carvacrol– was the primary active agent; in fact when they use pure carvacrol extracts in their tests COX-2 levels decreased by over 80%.

From the article: "Carvacrol, a component of thyme oil, activates PPAR-gamma and suppresses COX-2 expression" by Mariko Hotta, Rieko Nakata, Michiko Katsukawa, Kazuyuki Hori, Saori Takahashi, and Hiroyasu Inoue

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Scent of a Woman: Men's Testosterone Responses to Olfactory Ovulation Cues

Women around the world spend billions of dollars each year on exotic smelling perfumes and lotions in the hopes of attracting a mate. However, according to a new study in Psychological Science, a journal of the Association for Psychological Science, going "au natural" may be the best way to capture a potential mate's attention.

Smells are known to be critical to animal mating habits: Animal studies have shown that male testosterone levels are influenced by odor signals emitted by females, particularly when they are ovulating (that is, when they are the most fertile). Psychological scientists Saul L. Miller and Jon K. Maner from Florida State University wanted to see if a similar response occurs in humans. In two studies, women wore tee shirts for 3 nights during various phases of their menstrual cycles. Male volunteers smelled one of the tee shirts that had been worn by a female participant. In addition, some of the male volunteers smelled control tee shirts that had not been worn by anyone. Saliva samples for testosterone analysis were collected before and after the men smelled the shirts.

Results revealed that men who smelled tee shirts of ovulating women subsequently had higher levels of testosterone than men who smelled tee shirts worn by non-ovulating women or men who smelled the control shirts. In addition, after smelling the shirts, the men rated the odors on pleasantness and rated the shirts worn by ovulating women as the most pleasant smelling.

The authors note that "the present research is the first to provide direct evidence that olfactory cues to female ovulation influence biological responses in men." In other words, this study suggests that testosterone levels may be responsive to smells indicating when a woman is fertile. The authors conclude that this biological response may promote mating-related behavior by males.

For more information about this study, please contact: Saul Miller (smiller@psy.fsu.edu).

New study raises the possibility that some antiviral drugs could make diseases worse

Research published in the journal Genetics suggests that mutagenic drugs designed to kill viruses may make them stronger

As the flu season continues in full-swing, most people can appreciate the need for drugs that stop viruses after they take hold in the body. Despite this serious need for new drugs, a team of researchers from the University of Texas at Austin raise serious concerns about an emerging strategy for stopping viral infections. According to their research report appearing in the January 2010 issue of the journal GENETICS, medications that cause viruses to die off by forcing their nucleic acid to mutate rapidly might actually, in some instances, cause them to emerge from the process stronger, perhaps even more virulent than before drug treatment. "This work questions whether the practice of 'lethal mutagenesis' of viruses works as predicted," said Jim Bull, Ph.D., a researcher involved in the study from the Institute for Cellular and Molecular Biology at the University of Texas at Austin. "It remains to be seen whether an elevated mutation rate that does not cause rapid viral extinction enhances treatment or may instead thwart treatment by enhancing viral evolution." Bull's research collaborators included Rachael Springman, Thomas Keller, and Ian Molineux from the same institution.

Scientists tested the model of viral evolution at high mutation rates by growing a DNA virus in the presence of a mutagenic agent. The current accepted model predicted that the virus would not be able to handle the high mutation rates and would eventually die off. However, this study proved the model false, as the virus actually increased its fitness at elevated mutation rates. During this study, scientists found molecular evidence that rapid mutations had two effects. The first effect of most mutations, which was expected, was that they killed or weakened the virus. The second effect of some mutations, however, was that they actually helped the virus adapt and thrive. Although the researchers did not question that extremely high mutation will lead to viral extinction on the whole, this discovery raises the specter that forcing viruses to undergo rapid mutations could, if the mutation rate is not high enough, accidentally lead to well-adapted "super viruses."

"This study should raise more than a few eyebrows over this approach to stopping viruses," said Mark Johnston, Editor-in-Chief of the journal GENETICS, "because the last thing anyone wants to do is make a bad situation worse. More work must be done to determine the actual likelihood of this approach yielding a super virus, knowing that it is possible is a big help in preventing what could be a very big problem."

***DETAILS**: R. Springman, T. Keller, I. J. Molineux, and J. J. Bull Evolution at a High Imposed Mutation Rate: Adaptation Obscures the Load in Phage T7 Genetics, Jan 2010; 184: 221 - 232.*

Why we can't always find what we're looking for (and sometimes find what isn't there)

When people look for things that are rare, they aren't all that good at finding them. And it turns out that the reverse is also true: When people look for something common, they will often think they see it even when it isn't there. A new report published online on January 14th in Current Biology, a Cell Press publication, offers new insight into why this happens and may suggest some simple methods to help airport security personnel looking for weapons and radiologists looking for tumors get better at their jobs, according to the researchers.

"We know that if you don't find it often, you often don't find it," said Jeremy Wolfe of Harvard Medical School. "Rare stuff gets missed." That means that if you look for 20 guns in a stack of 40 bags, you'll find more of them than if you look for the same 20 guns in a stack of 2,000 bags.

But the lingering question was, why? Do people simply start going too fast, get careless, and say "no" too much? If that were true, then people looking for common stuff should also start going too fast, get careless, and say "yes" too much. It turns out that's not what they do, the new study shows. People do send false alarms when looking for common items, but they don't say "yes" faster, they say "no" much more slowly.

"When nothing is there, they don't give up on the response," Wolfe explained. "It's all terribly adaptive behavior for a beast in the world. If you know berries are there, you keep looking until you find them. If they are never there, you don't spend your time hunting."

But that adaptive inclination in nature can cause problems when people start looking for rare things, like guns in baggage or breast cancer. Airport screeners know there probably isn't a gun in your bag, and radiologists know that a tumor probably isn't going to be there, but they really want to catch it if there is. "We aren't well-built for that and make more errors than we'd like."

Wolfe thinks that there may be ways to solve this problem, or at least to improve upon our searching skills. He says that his team suspects error rates may be lowered by offering people in jobs like these some simple retraining at the start of every shift. If they spend a couple of minutes doing a simulated search for common weapons or tumors, they might then do a better job at really finding rare ones for the next 30 minutes or so.

The researchers plan to conduct tests at the clinic and the airport, to see whether the effects seen in the laboratory will hold true in the real world where the stakes are higher. They will also test strategies designed to make people less prone to making the wrong call.

The researchers include Jeremy M. Wolfe, Brigham and Women's Hospital, Cambridge, MA, Harvard Medical School, Boston, MA; and Michael J. Van Wert, Brigham and Women's Hospital, Cambridge, MA

Gators breathe like birds

Did dinosaurs' ancestors inhale their way to dominance?

SALT LAKE CITY – University of Utah scientists discovered that air flows in one direction as it loops through the lungs of alligators, just as it does in birds. The study suggests this breathing method may have helped the dinosaurs' ancestors dominate Earth after the planet's worst mass extinction 251 million years ago.

Before and until about 20 million years after the extinction – called "the Great Dying" or the Permian-Triassic extinction – mammal-like reptiles known as synapsids were the largest land animals on Earth.

The extinction killed 70 percent of land life and 96 percent of sea life. As the planet recovered during the next 20 million years, archosaurs (Greek for "ruling lizards") became Earth's dominant land animals. They evolved into two major branches on the tree of life: crocodilians, or ancestors of crocodiles and alligators, and a branch that produced flying pterosaurs, dinosaurs and eventually birds, which technically are archosaurs.

By demonstrating one-way or "unidirectional" airflow within the lungs of alligators, the new study – published in the Friday, Jan. 15 issue of the journal Science – means that such a breathing pattern likely evolved before 246 million years ago, when crocodilians split from the branch of the archosaur family tree that led to pterosaurs, dinosaurs and birds.

That, in turn, means one-way airflow evolved in archosaurs earlier than once thought, and may explain why those animals came to dominance in the Early Triassic Period, after the extinction and when the recovering ecosystem was warm and dry, with oxygen levels perhaps as low as 12 percent of the air compared with 21 percent today.

"The real importance of this air-flow discovery in gators is it may explain the turnover in fauna between the Permian and the Triassic, with the synapsids losing their dominance and being supplanted by these archosaurs," says C.G. Farmer, the study's principal author and an assistant professor of biology at the University of Utah. "That's the major reason this is important scientifically."

Even with much less oxygen in the atmosphere, "many archosaurs, such as pterosaurs, apparently were capable of sustaining vigorous exercise," she adds. "Lung design may have played a key role in this capacity because the lung is the first step in the cascade of oxygen from the atmosphere to the animal's tissues, where it is used to burn fuel for energy."

Farmer emphasized the discovery does not explain why dinosaurs, which first arose roughly 230 million years ago, eventually outcompeted other archosaurs.

Farmer conducted the study – funded by the National Science Foundation – with Kent Sanders, an associate professor of radiology at the University of Utah School of Medicine. They performed CT scans of a 4-foot-long, 24-pound alligator.

'The Great Dying' – Decline of the Synapsids, Rise of the Archosaurs

The synapsids – which technically include modern mammals – occupied ecological niches for large animals before the Permian-Triassic extinction.

"Some got up to be bear-sized," says Farmer. Some were meat-eaters, others ate plants. They were four-footed and had features suggesting they were endurance runners. Their limbs were directly under their body instead of sprawling outward like a lizard's legs. There is evidence they cared for their young.

The cause of the mass extinction 251 million years ago is unknown; theories include massive volcanism, an asteroid hitting Earth and upwelling of methane gas that had been frozen in seafloor ice.

"A few of the synapsids survived the mass extinction to re-establish their dominance in the early Triassic, and the lineage eventually gave rise to mammals in the Late Triassic," says Farmer. "However, the recovery of life in the aftermath of the extinction involved a gradual turnover of the dominant terrestrial vertebrate lineage, with the archosaurs supplanting the synapsids by the Late Triassic."

From then until the dinosaurs died out 65 million years ago, any land animal longer than about 3 feet was an archosaur, says Farmer, while mammal-like synapsid survivors "were teeny little things hiding in cracks. It was not until the die-off of the large dinosaurs 65 million years ago that mammals made a comeback and started occupying body sizes larger than an opossum."

No one knows much about the archosaur that was the common ancestor of crocodilians and of pterosaurs, dinosaurs and birds, Farmer says. It probably was "a small, relatively agile, insect-eating animal," Farmer says. Illustrations of early archosaurs look like large lizards.

"Our data provide evidence that unidirectional flow [of air in the lungs] predates the origin of pterosaurs, dinosaurs and birds, and evolved in the common ancestor of the crocodilian and bird [and pterosaur and dinosaur] lineages," Farmer says.

Cul-de-sacs or Loops for Airflow

In the lungs of humans and other mammals, airflow is like the tides. When we inhale, the air moves through numerous tiers of progressively smaller, branching airways, or bronchi, until dead-ending in the smallest chambers, cul-de-sacs named alveoli, where oxygen enters the blood and carbon dioxide moves from the blood into the lungs.

It long has been known that airflow in birds is unidirectional, and some scientists suggest it also was that way in dinosaurs.

In modern birds, the lungs' gas exchange units are not alveoli, but tubes known as "parabronchi," through which air flows in one direction before exiting the lung. Farmer says this lung design helps birds fly at altitudes that would "render mammals comatose."

Some researchers have argued that unidirectional airflow evolved after crocodilians split from the archosaur family tree, arising among pterosaurs and theropod dinosaurs, the primarily meat-eating group that included Tyrannosaurus rex. Others have argued it arose only among coelurosaurs, a group of dinosaurs that also includes T. rex and feathered dinosaurs.

Unidirectional air flow in birds long has been attributed to air sacs in the lungs. But Farmer disagrees, since gators don't have air sacs, and says it's due to aerodynamic "valves" within the lungs. She believes air sacs help birds redistribute weight to control their pitch and roll during flight. Farmer says many scientists simply assume air sacs are needed for unidirectional airflow, and have pooh-poohed assertions to the contrary.

"They cannot argue with this data," she says. "I have three lines of evidence. If they don't believe it, they need to get an alligator and make their own measurements."

Assessing Airflow in Alligators

Farmer did three experiments to demonstrate one-way airflow in alligators' lungs:

* She performed surgery on six anesthetized alligators and inserted flow meters called thermistors into the lungs to measure airflow speed and direction.

* Farmer pumped air in and out of lungs removed from four dead alligators sent to her by a wildlife refuge in Louisiana. The flow was monitored, showing the air kept going the same direction to loop through various tiers of bronchi and back to the trachea.

* Using lungs from another dead gator, she pushed and pulled water with tiny fluorescent beads through the lungs, making movies showing the unidirectional flow.

Farmer says the fact gator lungs still had unidirectional flow after being removed shows unidirectional airflow is caused by aerodynamic valves within the lungs, and not by some other factor, like air sacs or the liver, which acts like a piston to aid breathing.

How does air loop through an alligator's multichambered lungs?

Inhaled air enters the trachea, or windpipe, and then flows into two primary bronchi, or airways. Each of those primary bronchi enters a lung.

From those primary airways, the bronchi then branch into a second tier of narrower airways. Inflowing air jets past or bypasses the first branch in each lung because the branch makes a hairpin turn away from the direction of airflow, creating an aerodynamic valve. Instead, the air flows into other second-tier bronchi and then into numerous, tiny, third-tier airways named parabronchi, where oxygen enters the blood and carbon dioxide leaves it.

The air, still moving in one direction, then flows from the parabronchi into the bypassed second-tier bronchi and back to the first-tier bronchi, completing a one-way loop through the lungs before being exhaled through the windpipe.

Seeing a diagnosis: How an eye test could aid Alzheimer's detection

A simple and inexpensive eye test could aid detection and diagnosis of major neurological diseases such as Alzheimer's at an earlier stage than is currently possible, according to new research by UCL scientists.

The research, led by Professors Francesca Cordeiro & Stephen Moss and published today in Cell Death & Disease, demonstrates a new technique that enables retinal, and therefore brain cell death, to be directly measured in real time. The method, demonstrated in an animal model, could not only refine diagnosis of neurodegenerative disorders and help track disease progress; it could also aid the assessment and development of new treatments.

The technique uses fluorescent markers that attach themselves to the relevant cells and indicate the stage of cell death. The retina is then observed using a customised laser ophthalmoscope. Until now, this kind of technique has only been used in cells in the lab, rather than in live animals. This research is therefore the first ever in vivo demonstration of retinal nerve cell death in Alzheimer's Disease.

Professor Cordeiro, UCL Institute of Ophthalmology, said: "The death of nerve cells is the key event in all neurodegenerative disorders – but until now it has not been possible to study cell death in real time. This technique means we should be able to directly observe retinal nerve cell death in patients, which has a number of advantages in terms of effective diagnosis. This could be critically important since identification of the early stages could lead to successful reversal of the disease progression with treatment.

"Currently, the biggest obstacle to research into new treatments for neurodegenerative diseases is the lack of a technique where the brain's response to new treatments can be directly assessed – this technique could potentially help overcome that."

Although this paper outlines the technique in animal models (rats and mice), Professor Cordeiro's team are further along with work using the same technique to detect and assess glaucoma, and will be conducting their first patient trials later this year.

She added: "The equipment used for this research was customised to suit animal models but is essentially the same as is used in hospitals and clinics worldwide. It is also inexpensive and non-invasive, which makes us fairly confident that we can progress quickly to its use in patients.

"Few people realise that the retina is a direct, albeit thin, extension of the brain. It is entirely possible that in the future a visit to a high-street optician to check on your eyesight will also be a check on the state of your brain."

The research was supported by funding from The Wellcome Trust and The Foundation Fighting Blindness. The project has also been supported by UCL Business proof of concept funds and two patents have been filed around this technology.

Notes to Editors

1.) For more information or to interview the researchers quoted, please contact Ruth Howells in the UCL Media Relations Office on tel: +44 (0)20 7679 9739, mobile: +07790 675 947, email: ruth.howells@ucl.ac.uk

2.) The paper, 'Imaging multiple phases of neurodegeneration: a novel approach to assessing cell death in vivo', is published today in Cell Death & Disease. For copies of the paper, please contact UCL Media Relations. This new journal is published by the Nature Publishing Group.

3.) Images are available from UCL Media Relations. Caption: Retinal cell death in the Alzheimer Triple Transgenic model. Retinal images of a living 14-month Alzheimer Triple Transgenic (3xTg-AD (a) compared to an aged control living mouse (b). Many more retinal nerve cells are in the early phase of apoptosis (green spots) in the Alzheimer mouse.

McGill-CHUM study: 56 percent of young adults in a new sexual relationship infected with HPV

First-of-its-kind work sheds light on HPV transmission

A groundbreaking study of couples led by Professor Eduardo Franco, Director of McGill University's Cancer Epidemiology Unit, in collaboration with a team of colleagues from McGill and Université de Montréal/Centre Hospitalier de l'Université de Montréal (CHUM), found more than half (56 per cent) of young adults in a new sexual relationship were infected with human papillomavirus (HPV). Of those, nearly half (44 per cent) were infected with an HPV type that causes cancer.

Dr. Ann Burchell, the Project Coordinator and a former PhD student and post-doctoral fellow with Dr. Franco at the Cancer Epidemiology Unit, conducted the HITCH Cohort Study (HPV Infection and Transmission in Couples through Heterosexual activity) to determine the prevalence of HPV infections among recently formed couples. This is the first large-scale study of HPV infection among couples early in their sexual relationships when transmission is most likely.

The results, published in the January 2010 issues of Epidemiology and Sexually Transmitted Diseases, also indicate there is a high probability of HPV transmission between partners. When one partner had HPV, the researchers observed that in 42 per cent of couples, the other partner also had the infection. Moreover, the researchers found that the presence of HPV in one partner was the strongest predictor of finding the same HPV type in the other partner. If one partner was infected with HPV, the other partner's chance of also being infected with the same HPV type increased over 50 times.

"These results build on our knowledge that HPV infection is very common among young adults, and underline the importance of prevention programs for HPV-associated diseases such as cervical cancer screening and HPV vaccination," said Dr. Ann Burchell. "Our results also suggest that HPV is an easy virus to get and to transmit. Our estimates of the HPV transmission probability will be of use to other researchers who use modeling to project the public health and economic impact of HPV vaccination strategies."

HITCH Cohort Study participants are young women attending university or college/CEGEP in Montreal, Quebec, and their male partners. New couples are defined as those who have been together for six months or less. Participants fill out questionnaires in which they answer questions about their sexual history and they also provide genital specimens for laboratory testing for the presence of HPV infection. Recruitment for the study is continuing.

"Our study is the first to investigate HPV transmission in a large number of new couples among young adults," says Dr. François Coutlée, a professor at the Université de Montréal Department of Microbiology and Immunology and researcher at the Centre Hospitalier de l'Université de Montréal where the HPV tests were analyzed. "The results suggest that many HPV transmissions occur at the start of new relationships, which reinforces the need for prevention."

HPV is sexually transmitted and causes cervical cancer as well as other cancers, including those of the vulva, vagina, anus, and penis. Although HPV viruses are very common – more than 70 per cent of women and men will have this type of infection at some point – the vast majority of infections are asymptomatic and last no more than one or two years. Fewer than 1 per cent of women who have HPV will get cervical cancer.

The Canadian Institutes for Health Research provided support for this study and for Dr. Franco's research program on HPV and cervical cancer, with supplementary and unconditional funding support by Merck-Frosst Canada Ltd. and Merck & Co. Ltd. Dr. Burchell was supported by a research studentship from the Canadian Cancer Society Research Institute and by a Richard H. Tomlinson doctoral fellowship to McGill University.

Weizmann Institute scientists find a burst of neural activity at the transition between not seeing and seeing, revealing a clear threshold that must be crossed for perception to occur.

How do the visual images we experience, which have no tangible existence, arise out of physical processes in the brain? New research at the Weizmann Institute of Science provided evidence, for the first time, that an 'ignition' of intense neural activity underlies the experience of seeing.

In research recently published in the journal Neuron, Prof. Rafael Malach and research student Lior Fisch of the Weizmann Institute's Neurobiology Department worked with a neurosurgeon, Dr. Itzhak Fried of Tel Aviv Sourasky Medical Center, a distinguished team of medical doctors from the Center and Weizmann Institute students. They asked a group of epileptic patients who had had electrodes clinically implanted into their brains in preparation for surgery to volunteer for some perceptual awareness tasks. The subjects looked at a computer screen, which briefly presented a 'target' image – a face, house, or man-made object. This image was followed by a 'mask' – a meaningless picture for distraction – at different time intervals after the target image had been

presented. This allowed the experimenter to control the visibility of the images – the patients sometimes recognized the targets and sometimes failed to do so. By comparing the electrode recordings to the patients' reports of whether they had correctly recognized the image or not, the scientists were able to pinpoint when, where and what was happening in the brain as transitions in perceptual awareness took place.

Malach: 'We found that there was a rapid burst of neural activity occurring in the high-order visual centers of the brain – centers that are sensitive to entire images of objects, such as faces – whenever patients had correctly recognized the target image.' The scientists also found that the transition from not seeing to seeing happens abruptly.

Fisch: 'When the mask was presented too soon after the target image, it 'killed' the visual input signals, resulting in the patients being unable to recognize the object. The patients suddenly became consciously aware of the target image at a clear threshold, suggesting that the brain needs a specific amount of time to process the input signals in order for conscious perceptual awareness to be 'ignited.''

This study is the first of its kind to uncover strong evidence linking 'ignition' of bursts of neural activity to perceptual awareness in humans. More questions remain: Is this the sole mechanism involved in the transition to perceptual awareness? To what extent is it a local phenomenon? By answering such questions, we might begin bridging the mysterious gap between mind and the brain.

Prof. Rafael Malach's research is supported by the Nella and Leon Benoziyo Center for Neurological Diseases; the Carl and Micaela Einhorn-Dominic Brain Research Institute; the S. and J. Lurje Memorial Foundation; the Benjamin and Seema Pulier Charitable Foundation, Inc; Vera Benedek, Israel; and Mary Helen Rowen, New York, NY. Prof. Malach is the incumbent of the Barbara and Morris Levinson Professorial Chair in Brain Research.

The Weizmann Institute of Science in Rehovot, Israel, is one of the world's top-ranking multidisciplinary research institutions. Noted for its wide-ranging exploration of the natural and exact sciences, the Institute is home to 2,600 scientists, students, technicians and supporting staff. Institute research efforts include the search for new ways of fighting disease and hunger, examining leading questions in mathematics and computer science, probing the physics of matter and the universe, creating novel materials and developing new strategies for protecting the environment.

Punishment important in plant-pollinator relationship

Figs and the wasps that pollinate them present one of biologists' favorite examples of a beneficial relationship between two different species. In exchange for the pollination service provided by the wasp, the fig fruit provides room and board for the wasp's developing young. However, wasps do not always pollinate the fig. Fig trees "punish" these "cheaters" by dropping unpollinated fruit, killing the wasp's offspring inside, report researchers working at the Smithsonian Tropical Research Institute.

Their results, published in the Proceedings of the Royal Society, show that sanctions against cheaters may be critical to maintain the relationship.

"Relationships require give and take. We want to know what forces maintain this 80-million-year-old arrangement between figs and their wasp pollinators." said lead author, Charlotte Jandér, graduate student in Cornell University's Department of Neurobiology and Behavior, who conducted the study as a Smithsonian pre-doctoral fellow. "What prevents the wasps from reaping the benefits of the relationship without paying the costs?"

Some wasp species passively carry pollen that sticks to their bodies. Others actively collect pollen in special pouches. Jandér evaluated the ability of six different fig tree-fig wasp species pairs to regulate cheating. She introduced either a single pollen-free wasp, or a wasp carrying pollen, into a mesh bag containing an unpollinated fig. The wasps entered the figs to lay their eggs. Jandér found that trees often dropped unpollinated figs before young wasps could mature.

"This is really about the all-too-human theme of crime and punishment. We found that in actively pollinated fig species - when wasps expend time and energy to collect and deposit pollen-- wasps that did not provide the basic service of pollination were sanctioned. However, in passively pollinated species - when the wasps do not need to make an effort to pollinate--sanctions were absent," said Allen Herre, STRI staff scientist. "Although we still need to clearly understand the costs associated with applying sanctions, it seems like sanctions were only present where needed."

"Sanctions seem to be a necessary force in keeping this, and other, mutually-beneficial relationships on track when being part of a mutualism is costly," said Jandér. "In our study, we saw less cheating when sanctions were stronger. Similar results have been found among human societies and in social insects. It is very appealing to think that the same general principles could help maintain cooperation both within and among species."

New UT Knoxville research finds new ways to understand bacteria's 'thinking'

KNOXVILLE -- It's not thinking in the way humans, dogs or even birds think, but new findings from researchers at the University of Tennessee, Knoxville, show that bacteria are more capable of complex decision-making than previously known.

The discovery sets a landmark in research to understand the way bacteria are able to respond and adapt to changes in their environment, a trait shared by nearly all living things, and it could lead to innovations in fields from medicine to agriculture.

In the long-term, the researchers think that scientists will be able to take the findings, published online this week in the Proceedings of the National Academy of Sciences, and use them to tailor medicines in new ways to fight harmful bacteria or to find enhanced ways to use bacteria in agricultural or other applications.

Biology typically looks at the common bacteria Escherichia coli as the model for bacteria's ability to move actively and independently, but Gladys Alexandre, an associate professor of biochemistry, cellular and molecular biology at UT Knoxville, decided to look at the more complex soil bacterium, Azospirillum brasilense.

"As bacteria's ability to make decisions goes, E. coli is kind of dumb, which makes it easy for researchers to study sensing and information processing -- essentially, decision making -- in this bacterium," says Alexandre.

It helps to understand the way that bacteria "think". Their cells contain a number of receptors, and each one affects a certain behavior or trait in the bacteria, for example where to move, how to function, even whether to become virulent. The advent of genetic sequencing means we know more about how many receptors bacteria have, and the more receptors, the more ways a bacterium has to sense its surroundings.

E. coli has only five receptors that direct its decision-making process about movement, while Azospirillum brasilense has 48, making it comparatively much "smarter" in its ability to detect changes in its environments and as a result, to make complex decisions regarding where to move.

What scientists have not known and have been unable to study until now is how the individual receptors, by sensing their environment, directly affect the bacteria's behavior and ability to adapt to their environment. Alexandre's study is one of the first to isolate and study a receptor in this way.

She and her colleagues focused on a receptor they suspected was related to the way bacteria convert nitrogen gas from the atmosphere into a form -- ammonium -- that can be used by all organisms. This ability is called nitrogen fixation and while it is uniquely found in bacteria, it is critically important to all living organisms, as it is the only way nitrogen can eventually be incorporated into building blocks of cells.

The process is carried out by an enzyme which is damaged in the presence of high concentrations of oxygen, which presents a dilemma for the bacterium, as the energy needed for the process is usually acquired in the presence of oxygen.

When Alexandre and her team created mutant versions of the bacteria without the receptor, the mutant bacteria were unable to detect where the right position in oxygen concentration was, affecting the nitrogen fixation reaction. In other words, the mutant bacteria were somewhat "blind" and could not detect the right position, showing them their hunch was correct about the receptor's purpose. But their curiosity expanded: if they were able to uncover the receptor's purpose, would they be able to figure out exactly how it functioned?

For that, they enlisted the help of UT-Oak Ridge National Laboratory distinguished scientist Igor Jouline, an expert in carrying out complex computations of biological systems, such as the one governing the receptor at the heart of Alexandre's research. Working with Alexandre's data, Jouline was able to generate a model of the receptor's structure and compare it to other structures on a nearly atom-by-atom basis.

This enabled them to predict which one of the more than 100 amino acids in the sensory part of the receptor is responsible for sensing the precise oxygen concentration that this bacterium needs for nitrogen fixation. It's a process that, using normal genetic techniques, would have taken a substantial commitment of hours and resources, but was made simpler and less labor-intensive by using computing.

Alexandre hopes that other scientists and researchers can use a similar technique to look at receptor sites on other bacteria of interest. She noted that the ability to work with Jouline and with the resources available through UT Knoxville's partnership with ORNL was key to her discovery.

"Partnering with Igor provided us great insight," said Alexandre. "We would not have been able to fully understand how this receptor works without him."

Alexandre says there's good long-term potential for the knowledge gained in the study.

"We see now that bacteria are, in their way, big thinkers, and by knowing how they 'feel' about the environment around them, we can look at new and different ways to work with them."

The paper, titled "A PAS-domain containing chemoreceptor couples dynamic changes in metabolism and chemotaxis," is published online this week in the Proceedings of the National Academy of Sciences.

Scientists hope to end sleeping sickness by making parasite that causes it self-destruct

New data offer an up-close look at the enzyme that protects the protozoa and how one compound obstructs those efforts

After many years of study, a team of researchers is releasing data today that it hopes will lead to new drug therapies that will kill the family of parasites that causes a deadly trio of insect-borne diseases and has afflicted inhabitants of underdeveloped and developing nations for centuries.

In an article to be published in today's issue of the Journal of Biological Chemistry, Vanderbilt University scientist Galina Lepesheva and her team are reporting their successful attempt at determining the structure of an enzyme essential to the survival of the protozoan parasites that cause sleeping sickness, Chagas disease and leishmaniasis. They say this new information provides the first up-close look at the busy enzyme and, perhaps more importantly, shows how one compound in particular prevents it from conducting business as usual.

"With human migrations, HIV co-infections and the broadening of the host reservoirs due to climate changes, sleeping sickness and other diseases caused by these protozoan pathogens are now spreading around the world, including within the United States and Europe," said Lepesheva, a research associate professor at the Vanderbilt's department of biochemistry. "It is our hope that the results of our work might be helpful for the development of an effective treatment for such protozoan infections, some of which still remain incurable."

Lepesheva and her team have set their sights on the trypanosomatidae family of parasites, which causes a trio of horrifying diseases:

· Human African Trypanosomiasis is transferred by the biting tsetse (pronounced TEE-TEE) fly in sub-Saharan Africa. Its victims suffer only flulike symptoms in the first phase of infection, but it often isn't diagnosed till after the parasite has entered the central nervous system, causing mental deterioration, mood swings, coma and death.

· Chagas disease is passed on by the reduviid, or "kissing bug," named for its tendency to bite its victims around the lips, in South and Central America. The parasite that causes Chagas is the world's leading cause of heart disease, and the life expectancy for patients with chronic symptoms decreases by an average of nine years.

· Leishmaniasis, a disease transferred by the biting female sandfly, is prevalent in four continents and comes in four varieties, all of which either disfigure or kill its hosts. One causes skin ulcers; another causes chronic lesions resembling leprosy; the third destroys the mucus membranes in the nose, mouth and throat; the fourth causes high fever, organ swelling and, if left untreated, has a fatality rate as high as 100 percent within two years.

Screening for trypanosomal diseases is challenging, because they most often affect people in remote locations with few or no medical resources, and existing treatments lack specificity and can cause severe side effects.

Lepesheva and her team sought to damage the single-celled parasite's cellular membrane, knowing that if they could weaken that barrier, the regulation of the intercellular environment would be disrupted, and the parasite would die.

"It has been known for some time that T. brucei, the parasite that causes sleeping sickness, consumes cholesterol in its human host's blood to shore up the cellular membrane, and researchers presumed there was no getting around that," Lepesheva said. "But we suspected the parasite, like plants and animals, still might need to make its own sterols for growth and development -- functional sterols – that could be targeted and inhibited."

The team chose to attack the parasite's enzyme known as 14DM, which is short for sterol 14α-demethylase. They picked 14DM because it has a counterpart in fungi, which cause athlete's foot and ringworm, and such fungal infections are commonly treated with drugs that prevent 14DM from making ergosterol, a sterol required for membrane synthesis.

"We tested hundreds of compounds as potential 14DM inhibitors. One of them, VNI, was one of the best in terms of killing the parasites that cause sleeping sickness, Chagas and Leishmaniasis," she said.

The team named the inhibitor VNI, short for Vienna Novartis Inhibitor, because it originally was synthesized at the Novartis Research Institute in Vienna. It binds with the worker enzyme, a lot like a piece fits snugly into a jigsaw puzzle, and blocks the enzyme's ability to make the critical sterol.

Lepesheva said having a clear picture of the structure of the enzyme and how VNI fits into it explains why VNI is effective, and it opens the door to structure-based new drug design.

Lepesheva, the lead author on study, works in the laboratory of professor Michael Waterman, chairman of the department of biochemistry at Vanderbilt. They collaborated with researchers at Vanderbilt, Nashville's Meharry Medical College, the University of Toronto, the Universite Libre de Bruxelles in Belgium, Northwestern University and Texas Tech University. The work was supported by funding from the American Heart Association and the National Institutes of Health.

By being named a "Paper of the Week" by the Journal of Biological Chemistry, Lepesheva's article has been categorized in the top 1 percent of papers reviewed by the editorial board in terms of significance and overall importance.

Siblings play formative, influential role as 'agents of socialization'

CHAMPAIGN, Ill. — What we learn from our siblings when we grow up has – for better or for worse – a considerable influence on our social and emotional development as adults, according to an expert in sibling, parent-child and peer relationships at the University of Illinois.

Laurie Kramer, a professor of applied family studies in the department of human and community development at Illinois, says that although a parent's influence on a child's development shouldn't be underestimated, neither should a sibling's.

"What we learn from our parents may overlap quite a bit with what we learn from our siblings, but there may be some areas in which they differ significantly," Kramer said.

Parents are better at teaching the social niceties of more formal settings – how to act in public, how not to embarrass oneself at the dinner table, for example. But siblings are better role models of the more informal behaviors – how to act at school or on the street, or, most important, how to act cool around friends – that constitute the bulk of a child's everyday experiences.

"Siblings are closer to the social environments that children find themselves in during the majority of their day, which is why it's important not to overlook the contributions that they make on who we end up being," Kramer said.

Kramer, who along with Katherine J. Conger, of the University of California at Davis, co-edited a volume on this topic for a recent issue of the journal New Directions for Child and Adolescent Development, says a clearer understanding of how siblings function as "agents of socialization" will help answer critical societal questions such as why some children pursue antisocial behavior.

"We know that having a positive relationship with siblings is related to a whole host of better outcomes for teenagers and adults," Kramer said. "A lot of current research looks at how children learn undesirable behaviors like smoking, drinking and other delinquent acts, from exposure to an older sibling's antisocial behaviors as well as that of their sibling's friends. For example, a female teen is at higher risk for getting pregnant if her older sister was a teenage mother. Developing a better understanding of sibling influences can help us design effective strategies for protecting younger children in families."

According to Kramer, in order to maximize an older sibling's positive influence, one of the most important things parents can do is to help foster a supportive relationship between the siblings from the very beginning.

"We know from longitudinal studies that if kids start off their relationship with a sibling on a positive note, it's more likely to continue positively over time," she said.

Variables such as gender and age difference don't make much of a difference between siblings.

"It's not all that important whether you're spaced closer together or farther apart, or if you have a brother or a sister," Kramer said. "What's really much more important are the social behaviors that children learn in their early years that they can use to develop a positive relationship with a sibling. That's why it's important for parents to encourage siblings to be engaged with one another and develop a relationship where there is mutual respect, cooperation and the ability to manage problems."

Kramer said children who grow up as an only child are not necessarily less socially competent than children who grow up with siblings, but they are more likely to have developed social skills through friends as opposed to brothers and sisters.

"Growing up just with parents is a different environment for young people," she said. "Parents of only children might want to think about how they can help their child have social experiences with other children, whether that's through childcare, preschool or play dates."

Do single children establish surrogate siblings with cousins and friends?

"They may be encouraged by parents to develop deeper relationships, and that's a good thing because it provides them an opportunity to develop some of these social competencies that they probably won't acquire if they're limited to interacting with their parents and teachers," Kramer said.

Parents who have children who are spaced closely together in age may not see much of a need to have children over to the house once a week because their children are already having significant social experiences within the family unit, Kramer said.

But children whose siblings are spaced further apart in age are most likely to have different sets of friends and different social experiences because they may be in distinct school contexts or involved in unique activities. "It's possible that siblings who are spaced further apart are very connected within the home, but their social experiences outside the family may be pretty different," Kramer said.

And, Kramer notes, having Wally Cleaver for an older brother doesn't necessarily mean the younger sibling will turn out like Wally – they may end up like Beaver.

"We know that not all younger children turn out like their older siblings," Kramer said. "There are many cases where younger siblings work very hard to carve out their own unique path and be different from their brothers and sisters, a process researchers refer to as 'de-identification.'

They may choose a different path in which to excel or make their mark to base their own identity on. That child may choose to focus on sports, the arts or being the social one. It relieves them from the pressure to be seen or compared to their elder sibling, particularly if they're afraid that they won't be able to measure up.

"So they figure out who they are, what they believe in and what's important to them, in reaction to how they perceive their siblings."

Kramer cautions that while we don't know all of the implications of sibling influence, "we do know that growing up in a family where there is another child makes it a very different environment socially, cognitively and emotionally," Kramer said.

"Children learn things through growing up with other children in the house, just as they learn things growing up in a more adult-oriented environment if they're a single child. We need to understand that better so that we can form a more realistic understanding of child and family development."

Funding for this research was provided by the U.S. Department of Agriculture.

Genetic Risk Factor Identified for Parkinson's Disease: Gene Variant Influences Vitamin B6 Metabolism

Munich - An international team of doctors and human geneticists has identified a new genetic risk factor for Parkinson's disease. The institutions involved in the study were the Institute of Human Genetics of Helmholtz Zentrum München and Technische Universität München, the Neurological Clinic of Ludwig-Maximilians-Universität Munich (LMU) and the Mitochondrial Research Group of Newcastle University, Newcastle upon Tyne, UK.

"Our study reveals the interaction of genetic and environmental factors such as dietary habits in the pathogenesis of Parkinson's disease," explained Dr. Matthias Elstner of the Neurological Clinic of LMU and Helmholtz Zentrum München, lead author of the study. In addition, this genome-wide expression and association study confirms that vitamin B6 status and metabolism significantly influence both disease risk and therapy response (Annals of Neurology, January, 2010).

Scientists of the two Munich universities and Helmholtz Zentrum München investigated neurons in the brain to determine which genes modify their activity in Parkinson's disease. Among other findings, the research group detected increased activity of the pyridoxal kinase gene. In a subsequent international cooperation project, the researchers compared this gene in over 1,200 Parkinson patients with the genetic data of more than 2,800 healthy test subjects. In doing so, they discovered a gene variant which increases the risk for Parkinson's disease and which may lead to a modified quantity or activity of the enzyme pyridoxal kinase (PDXK) in the brain. In combination with genetic association analysis, the innovative method used here – single cell expression profiling of dopaminergic neurons – opens up new possibilities for analyzing genetic risk factors.

PDXK converts Vitamin B6 from food sources into its physiologically active form, which is the prerequisite for the production of the neurotransmitter dopamine. Parkinson's disease is linked to the accelerated aging and dying off of neurons that produce dopamine. The decreased synthesis of this neurotransmitter explains most of the disease symptoms: The gradual progression of the neurological disease is accompanied by muscle rigor and tremor and a slowing of movement (bradykinesia). Besides the constraints on daily life caused by these symptoms, the postural instability of the body can lead to dangerous falls. Moreover, in the course of the disease sensory symptoms like paresthesia, vegetative disorders (e.g. bladder dysfunction) and depression as well as other psychological changes can occur.

"Our study elucidates how genetic and environmental factors such as dietary habits interact in the pathogenesis of Parkinson's disease," explained Dr. Matthias Elstner of the Neurological Clinic of LMU and Helmholtz Zentrum München, who is lead author of the study. Dr. Holger Prokisch, head of the research team studying mitochondrial diseases at Helmholtz Zentrum München and TU München, added: "Although this variant is responsible for only a slight contribution to the overall risk for Parkinson's disease, our findings could aid in developing individualized therapies. "

Publication: *"Single cell expression profiling of dopaminergic neurons combined with association analysis identifies pyridoxal kinase as Parkinson's disease gene" Elstner et.al., Annals of Neurology, January 2010; DOI: 10.1002/ana.21780*

USF studies show link among Alzheimer's disease, Down syndrome and atherosclerosis

Studies implicate damage inflicted by amyloid protein as shared disease mechanism

Tampa, FL - Nearly 20 years ago Huntington Potter kicked up a storm of controversy with the idea that Down syndrome and Alzheimer's were the same disease. Now the evidence is in: He was right.

And that's not all. Down syndrome, artery-clogging cardiovascular disease, and possibly even diabetes, appear to share a common disease mechanism with Alzheimer's disease, Dr. Potter and colleagues at the Florida Alzheimer's Disease Research Center, USF Health Byrd Alzheimer's Institute, recently reported.

The researchers' two papers – one in Molecular Biology of the Cell and the other in PLoS ONE -- implicate the Alzheimer's-associated protein beta amyloid (amyloid protein), which damages the microtubule transport system responsible for moving chromosomes, proteins and other cargo around inside cells. Both studies were done in mice and humans cell cultures modeling Alzheimer's disease. Together, the laboratory discoveries suggest that protecting the microtubule network from this amyloid damage might be an effective way to prevent or even reverse Alzheimer's disease and associated disorders.

The first paper, by Antoneta Granic and colleagues published online Dec. 23 in Molecular Biology of the Cell, provides the mechanism behind previous work by Dr. Potter's laboratory showing that all Alzheimer's disease patients harbor some cells with three copies of chromosome 21, known as trisomy 21, instead of the usual two. Trisomy 21 is a characteristic shared by all the cells in people with the birth defect Down syndrome. This earlier work demonstrated that Alzheimer's disease could be considered a late onset form of Down syndrome.

By age 30 to 40, all people with Down syndrome develop the same brain pathology seen in Alzheimer's disease, including a nerve-killing buildup of sticky amyloid protein clumps. This contributes to accelerated nerve cell loss and dementia.

With the study reported in MBC, Dr. Potter and his colleagues now show that the Alzheimer's-associated amyloid protein is the culprit that interferes with the microtubule transport system inside cells. The microtubules are responsible for segregating newly duplicated chromosomes as cells divide. "Beta amyloid basically creates potholes in the protein highways that move cargo, including chromosomes, around inside cells," said Dr. Potter, who holds the Eric Pfeiffer Endowed Chair for Research on Alzheimer's Disease.

When the microtubule network is disrupted, chromosomes can be incorrectly transported as cells divide and the result is new cells with the wrong number of chromosomes and an abnormal assortment of genes. For example, Down syndrome cells contain three copies of the beta amyloid gene on chromosome 21 – leading to more accumulation of the "bad" amyloid protein over a lifetime, Dr. Potter says. "Alzheimer's disease probably is caused in part from the continuous development of new trisomy 21 nerve cells, which amplify the disease process by producing extra beta amyloid."

The second paper by lead author Jose Abisambra and colleagues, published Dec. 31 in the online journal PLoS ONE, describes another consequence of the damaged microtubule network caused by the amyloid protein.

Many Alzheimer's disease patients also commonly develop vascular diseases and diabetes. Whether this coincidence is bad luck or due to shared disease processes is intensely debated. Research teams have investigated the role that low-density lipoprotein (LDL), the bad cholesterol that causes atherosclerosis, cardiovascular disease and stroke, may play in the development of Alzheimer's with mixed results. However, the USF group focused on the amyloid protein's potential effects on LDL metabolism. The receptor needed to detect and use LDL is among the proteins transported by the microtubules.

As previously reported by their colleagues in the MBC paper, the second USF team found that the amyloid protein inflicts damage to the microtubule network. As a consequence, the receptor needed to pull LDL circulating throughout the bloodstream into the body's cells has trouble getting to the cell surface to retrieve this bad cholesterol. This interference with LDL metabolism may allow bad cholesterol to build up in into plaques that choke off blood supply to the brain and heart in people with Alzheimer's, Dr. Potter said.

Similarly, other key proteins – including insulin receptors and receptors for brain signaling molecules -- are also likely locked inside cells when the transport system is damaged by amyloid or other factors. "The insulin receptors are needed to get blood sugar inside the cell where it can be used for energy. The nerve cell signaling receptors help promote memory and learning," Dr. Potter said. "So, if these receptors are unable to function properly, it may lead to diabetes and problems with learning and memory."

"We're beginning to understand how conditions like cardiovascular disease and diabetes may manifest some of the same underlying disease processes as Alzheimer's disease," he said, "rather than being independent diseases that just happen to develop in the same patient."

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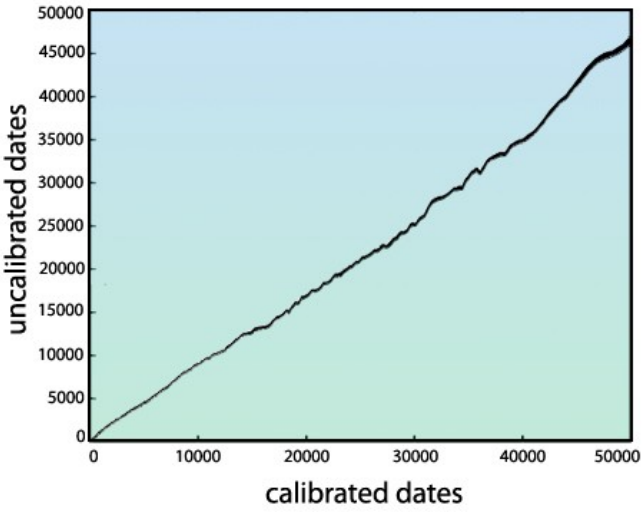
Radiocarbon Daters Tune Up Their Time Machine

By Michael Balter ScienceNOW Daily News

It took nearly 30 years and a lot of heated debate, but a team of researchers has finally produced what archaeologists, geologists, and other scientists have long been waiting for: a calibration curve that allows radiocarbon dating to achieve its full potential. The new curve, which now extends back 50,000 years, could help researchers work out key questions in human evolution, such as the effect of climate change on human adaptation and migrations.

The basic principle of radiocarbon dating is fairly simple. Plants and animals absorb trace amounts of radioactive carbon-14 from carbon dioxide (CO_2) in the atmosphere while they are alive but stop doing so when they die. The steady decay of carbon-14 from archaeological and geological samples ticks away like a clock, and the amount of radioactive carbon left in the sample gives a reproducible indication of how old it is. Most experts consider the technical limit of radiocarbon dating to be about 50,000 years, after which there is too little carbon-14 left to measure accurately.



Wiggle room. ***The radiocarbon calibration curve now extends to 50,000 years and is more accurate.*** **Credit: P. J. Reimer et al. Radiocarbon, 51 (2009)**

There is one major glitch in the approach, however: The amount of carbon-14 in the atmosphere varies with fluctuations in solar activity and Earth's magnetic field, and "raw" radiocarbon dates have to be corrected with a calibration curve that takes these fluctuations into account.

Since the early 1980s, an international working group called INTCAL has been developing and perfecting just such a curve, a process that has unfolded in several stages. To calibrate the period extending from the present to about 12,000 years ago, the team has used thousands of overlapping tree-ring segments from the Northern Hemisphere, which provide a very accurate check of raw radiocarbon dates and how much they must be corrected. But for dates older than the available tree-ring record, the researchers had to turn to several other, less-precise data sets on ancient CO_2 levels, including fossil foraminifers (single-celled organisms that secrete calcium carbonate) and corals.

By 2004, the INTCAL group was able to agree on a curve that stretched to 26,000 years ago, because the foraminifer and coral data were in reasonably close agreement up to that point. That curve, called INTCAL04, was published the same year. But hopes to extend the curve all the way to 50,000 years ago were dashed. The data sets diverged from each other by up to several thousand years after 26,000 years ago, and researchers could not agree on which ones were most accurate and how to combine the several data sets.

More recently, however, thanks to new and more accurate data from foraminifers, corals, and other sources--plus some fancy statistical treatments that help predict which way data gaps bend the curve--the INTCAL group has been able to resolve most of the discrepancies. "It took the group quite a while to come together and agree," says INTCAL team leader Paula Reimer, a geochronologist at Queen's University Belfast in Northern Ireland. But the new data, combined with what Reimer calls a "real sense of necessity" among team members to resolve the debates, won the day.

The new curve, called INTCAL09 and published this week in the journal Radiocarbon, not only extends radiocarbon calibration to 50,000 years ago but also considerably improves the earlier parts of the curve, researchers say.

Getting those dates right is critical to understanding such questions as whether humans began painting caves when the climate was colder or warmer, says Clive Gamble, an archaeologist at the University of London,

Royal Holloway. For example, the raw radiocarbon dates for the spectacular paintings of horses, lions, bison, and other animals at Chauvet Cave in southern France, the oldest known cave art, come out at 32,000 years ago, right after a major cold spell hit Europe; but the new calibration curve makes the earliest paintings at Chauvet 36,500 years old, a period of relative warmth.

And John Hoffecker, an archaeologist at the University of Colorado, Boulder, says that the data sets behind the new curve will allow a more-precise correlation between radiocarbon dates and prehistoric climate reconstructions based on Greenland ice cores and other proxy indicators of ancient weather. Even before the adoption of the new curve, Hoffecker says, those data sets were suggesting that modern humans had moved into Europe about 45,000 calibrated years ago, much earlier than previously thought--and early enough for them to have had substantial contact with Neandertals over thousands of years.

Although the new curve is a major landmark, it is "definitely not the last word" in radiocarbon calibration, Reimer says. Her team is already planning an update for 2011, "as we learn more about the Earth's carbon reservoirs and how they changed over time."