

CSHL team finds evidence for the genetic basis of autism

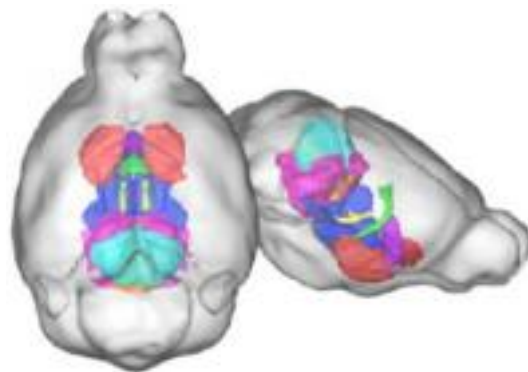
Models of autism show that gene copy number controls brain structure and behavior

Cold Spring Harbor, N.Y.- Scientists at Cold Spring Harbor Laboratory (CSHL) have discovered that one of the most common genetic alterations in autism -- deletion of a 27-gene cluster on chromosome 16 -- causes autism-like features. By generating mouse models of autism using a technique known as chromosome engineering, CSHL Professor Alea Mills and colleagues provide the first functional evidence that inheriting fewer copies of these genes leads to features resembling those used to diagnose children with autism. The study appears in the Proceedings of the National Academy of Sciences in the early online edition during the week of October 3.

"Children normally inherit one copy of a gene from each parent. We had the tools to see whether copy number changes found in kids with autism were causing the syndrome," explains Mills. In 2007, Professor Michael Wigler, also at CSHL, revealed that some children with autism have a small deletion on chromosome 16, affecting 27 genes in a region of our genomes referred to as 16p11.2. The deletion -- which causes children to inherit only a single copy of the 27-gene cluster -- is one of the most common copy number variations (CNVs) associated with autism.

"The idea that this deletion might be causing autism was exciting," says Mills. "So we asked whether clipping out the same set of genes in mice would have any effect."

After engineering mice that had a chromosome defect corresponding to the human 16p11.2 deletion found in autism, Mills and her team analyzed these models for a variety of behaviors, as the clinical features of autism often vary widely from patient to patient, even within the same family.



This three-dimensional representation of the mouse brain highlights eight regions (shown with different colors) affected by 16.p11.2 deletion. Image courtesy of Mills@CSHL

"Mice with the deletion acted completely different from normal mice," explains Guy Horev, a Postdoctoral Fellow in the Mills laboratory and first author of the study. These mice had a number of behaviors characteristic of autism: hyperactivity, difficulty adapting to a new environment, sleeping deficits, and restricted, repetitive behaviors.

Interestingly, mice that had been engineered to carry an extra copy, or duplication, of the 16p11.2 region did not have these characteristics, but instead, had the reciprocal behaviors. For each behavior, the deletion had a more dire consequence than the duplication, indicating that gene loss was more severe. This might explain why 16p11.2 duplications are detected much more frequently than deletions within the human population, and why patients with 16p11.2 deletions tend to be diagnosed earlier than those with duplications.

The mouse models also revealed a potential link between 16p11.2 deletion and survival, as about half the mice died following birth. Whether these findings extend to the human population might be answered by future studies that investigate the link between this deletion and unexplained cases of infant death.

The researchers also used MRI to identify specific regions of the brain that were altered in the autism models, revealing that eight different parts of the brain were affected. The group is now working to identify which gene or group of genes among the 27 that are located within the deleted region is responsible for the behaviors and brain alterations observed.

"Alea Mills has created a valuable resource for everyone engaged in autism research. The technical skill is extraordinary in creating mouse models bearing a human genetic variant that has been associated with autism," says Dr. Gerald Fischbach, Director of Life Sciences and Simons Foundation Autism Research Initiative (SFARI).

These mice will be invaluable for pinpointing the genetic basis of autism and for elucidating how these alterations affect the brain. They could also be used for inventing ways to diagnose children with autism before they develop the full-blown syndrome, as well as for designing clinical interventions.

Collaborators on this work include a group of MRI specialists led by Dr. Mark Henkelman at the Hospital of Sick Children in Toronto. This study was funded by the Simons Foundation Autism Research Initiative (SFARI).

"Dosage-dependent phenotypes in models of 16p11.2 lesions found in autism," which appears in Proceedings of the National Academy of Sciences, is embargoed for release until 3pm on October 3. The full citation is: Guy Horev, Jacob Ellegood, Jason P. Lerch, Young-Eun E. Son, Lakshmi Muthuswamy, Hannes Vogel, Abba M. Krieger, Andreas Buja, R. Mark Henkelman, Michael Wigler, and Alea A. Mills.

Researchers call for more awareness of male breast cancer as cases rise
Awareness of male breast cancer is low and most men do not even know they are at risk despite an increase in cases, reveals new research from the University of Leeds.

Breast cancer is very much seen as a female disease with around 48,000 diagnoses in women in the UK each year. However around 340 men, equivalent to 30 football teams will be diagnosed with breast cancer each year and around 70 men will die.

Funded by Breast Cancer Campaign and Yorkshire Cancer Research, University of Leeds researchers reviewed male breast cancer cases in four Western countries; England, Scotland, Canada and Australia. In England, the incidence of male breast cancer was seen to rise over a 20 year period: from 185 cases in 1986 to 277 cases in 2006. This corresponds to a rise of one third from 0.5 to 0.7 cases per 100,000 of the population.

Pinpointing an exact cause for this increase is difficult, according to Dr Valerie Speirs, who led the study. "Lifestyle changes over the latter decades of the 20th century, leading to increased obesity, physical inactivity and development of a binge drinking culture may be contributing factors. Some of the same inherited genetic changes that increase the risk of women developing breast cancer are also thought to influence risk in men," she said.

Most of the information used to diagnose and treat men with breast cancer comes from studies of female breast cancer. The new data pointing towards a rise in cases, published in the on-line journal Breast Cancer Research, provides impetus to study the biology of male breast cancer in more detail. Men need to get the right information, treatment and emotional support, the researchers concluded.

Dr Speirs and her colleagues now plan to examine the genes and proteins involved in male breast cancers to determine whether there are similarities or differences with female breast cancer. This may help pinpoint gender-specific differences which can be exploited to improve and develop treatments specifically targeted at men. University of Leeds researchers are collecting and storing male breast tissue samples in the groundbreaking Breast Cancer Campaign Tissue Bank. Dr Speirs' ongoing work is also being supported by a new grant from Yorkshire Cancer Research.

"Many men are unaware they can be affected by breast cancer but this work has highlighted that the number of cases is gradually increasing. It must be stressed that the numbers are still extremely small - 150 times less than in women so we are certainly not talking about an epidemic. However better awareness is needed," Dr Speirs said. "Symptoms include discharge from the nipple that may be blood stained, swelling of the breast, a sore or ulcer in the skin of the breast, a nipple that is pulled or retracted into the breast or a lump under the arm. If you have any of these symptoms contact your GP straight away," she added.

Baroness Delyth Morgan, Chief Executive, Breast Cancer Campaign said, "The study of breast cancer in men has been difficult in the past because of the relatively small number of cases. As early diagnosis and treatment is vital to increase the chances of survival, we need to raise awareness.

"The new Breast Cancer Campaign Tissue Bank, with a core centre in Leeds, will be invaluable to researchers to enable them to understand the molecular causes, similarities and differences between male and female breast cancer, as well as testing the effectiveness of existing and new treatments."

Dr Kathryn Scott, Research Liaison Officer with Yorkshire Cancer Research said "This is a fantastic example of two charities working together to advance the knowledge into this relatively unknown disease in men. Many men do not realise they can get breast cancer and, although still rare, the incidence has risen. It is important to raise awareness because early detection is often linked to a more successful outcome for cancer patients."

Notes to editors 1. The paper: Male breast carcinoma: increased awareness needed, White J, et al, is published in Breast Cancer Care [doi:10.1186/bcr2930].

<http://www.newscientist.com/article/mg21128324.000-inside-of-nose-reveals-time-of-death.html>

Inside of nose reveals time of death

TINY finger-like projections lining the nose continue to beat after death. Since the beating of these cilia slows at a predictable rate, forensic teams should be able to estimate time of death more accurately.

Pinpointing precisely when someone died can be a challenge for investigators. They can look at body temperature or decomposition rate, but these indicators can be confounded by temperature, or whether the person was involved in a struggle, say, shortly before death. The beating rate of cilia could provide an additional tool to help decide time of death, especially if it was within the previous 24 hours.

Nasal cilia are tiny projections that waft mucous, dust and bacteria out of the nose and into the throat. Biagio Solarino of the University of Bari in Italy and his colleagues suspected that cilia continue to beat after death. So they took a scraping of the inside of the nose from 100 cadavers to examine the cilia.

"Motility was observed as long as 20 hours after death," says Solarino, who will present his results at the International Symposium on Advances in Legal Medicine in Frankfurt, Germany, this week. They hope to use the cilia to judge time of death since not only does the beating slow gradually but it also seems relatively immune to environmental factors.

<http://medicalxpress.com/news/2011-10-lancet-hormonal-contraception-hiv.html>

Study in Lancet finds use of hormonal contraception doubles HIV risk

Women using hormonal contraception --such as a birth control pill or a shot like Depo-Provera – are at double the risk of acquiring HIV

Women using hormonal contraception --such as a birth control pill or a shot like Depo-Provera – are at double the risk of acquiring HIV, and HIV-infected women who use hormonal contraception have twice the risk of transmitting the virus to their HIV-uninfected male partners, according to a University of Washington-led study in Africa of nearly 3,800 couples. The study was published in *The Lancet Infectious Diseases*.

The research, first presented in July in Rome at the meeting of the International AIDS Society, emphasizes the need for couples to use condoms in addition to other forms of contraception in order to prevent pregnancy and HIV, said lead study author Renee Heffron, an epidemiology doctoral student working with the International Clinical Research Center at UW. "Women should be counseled about potentially increased risk of HIV acquisition and transmission with hormonal contraception, particularly injectable methods, and about the importance of dual protection with condoms to decrease HIV risk," said Heffron.

Jared Baeten, an associate professor of global health with the International Clinical Research Center, said to his knowledge this is the first prospective study to show increased HIV risk to male partners of HIV-infected women using hormonal contraception. More than 140 million women worldwide use hormonal contraception, including daily oral pills and long-acting injectables, like Depo-Provera. "The benefits of effective hormonal contraception are unequivocal and must be balanced with the risk for HIV infection," said Baeten.

This study was designed to establish whether hormonal contraception increases the risk of women acquiring HIV and transmitting the virus to their male partners. The study included 3,790 heterosexual HIV serodiscordant couples (i.e. one partner with HIV infection and the other without) who were participating in two long-term studies of HIV in couples in seven African countries (Botswana, Kenya, Rwanda, South Africa, Tanzania, Uganda, and Zimbabwe).

Findings showed that using hormonal contraceptives doubled an HIV uninfected woman's chances of becoming infected with HIV. The risk was increased for both injectable (mainly depot medroxyprogesterone acetate: DMPA) and oral contraceptives, although it was not statistically significant for oral contraceptives.

Additionally, women who were HIV-positive at the beginning of the study and using hormonal contraception were twice as likely to transmit the virus to their male partner compared to women who did not use hormonal contraception. *Provided by University of Washington*

http://www.eurekalert.org/pub_releases/2011-10/uoth-uam100311.php

University of Texas Health Science Center: Alzheimer's might be transmissible in similar way as infectious prion diseases

The brain damage that characterizes Alzheimer's disease may originate in a form similar to that of infectious prion diseases such as bovine spongiform encephalopathy (mad cow) and Creutzfeldt-Jakob, according to newly published research by The University of Texas Health Science Center at Houston (UTHealth).

HOUSTON -- "Our findings open the possibility that some of the sporadic Alzheimer's cases may arise from an infectious process, which occurs with other neurological diseases such as mad cow and its human form, Creutzfeldt-Jakob disease," said Claudio Soto, Ph.D., professor of neurology at The University of Texas Medical School at Houston, part of UTHealth. "The underlying mechanism of Alzheimer's disease is very similar to the prion diseases. It involves a normal protein that becomes misshapen and is able to spread by transforming good proteins to bad ones. The bad proteins accumulate in the brain, forming plaque deposits that are believed to kill neuron cells in Alzheimer's."

The results showing a potentially infectious spreading of Alzheimer's disease in animal models were published in the Oct. 4, 2011 online issue of *Molecular Psychiatry*, part of the Nature Publishing Group. The research was funded by The George P. and Cynthia W. Mitchell Center for Research in Alzheimer's Disease and Related Brain Disorders at UTHealth.

Alzheimer's disease is a form of progressive dementia that affects memory, thinking and behavior. Of the estimated 5.4 million cases of Alzheimer's in the United States, 90 percent are sporadic. The plaques caused by misshapen aggregates of beta amyloid protein, along with twisted fibers of the protein tau, are the two major hallmarks associated with the disease. Alzheimer's is the sixth leading cause of death in the United States, according to the Alzheimer's Association.

Researchers injected the brain tissue of a confirmed Alzheimer's patient into mice and compared the results to those from injected tissue of a control without the disease. None of the mice injected with the control showed signs of Alzheimer's, whereas all of those injected with Alzheimer's brain extracts developed plaques and other brain alterations typical of the disease.

"We took a normal mouse model that spontaneously does not develop any brain damage and injected a small amount of Alzheimer's human brain tissue into the animal's brain," said Soto, who is director of the Mitchell Center. "The mouse developed Alzheimer's over time and it spread to other portions of the brain. We are currently working on whether disease transmission can happen in real life under more natural routes of exposure."

UTHealth co-authors of the paper, "De novo Induction of amyloid-B Deposition in vivo," are Rodrigo Morales, Ph.D, postdoctoral fellow, and Claudia Duran-Aniotz, research assistant. Other co-authors are Joaquín Castilla, Ph.D., Basque Foundation for Science, Bilbao, Spain; and Lisbell D. Estrada, Ph.D., Universidad Catolica de Chile, Santiago, Chile. Duran-Anioitz is also a doctoral student at the Universidad de los Andes in Santiago, Chile. Soto, Morales, Castilla and Estrada did a portion of the research at The University of Texas Medical Branch at Galveston.

http://www.eurekalert.org/pub_releases/2011-10/mali-ppa100411.php

Pumice proposed as home to the first life forms: A new hypothesis in Astrobiology journal

The glassy, porous, and once gas-rich rock called pumice may have given rise to early life forms, according to a provocative new hypothesis on the origin of life

New Rochelle –The glassy, porous, and once gas-rich rock called pumice may have given rise to early life forms, according to a provocative new hypothesis on the origin of life published in *Astrobiology*, a peer-reviewed journal from Mary Ann Liebert, Inc.. The article is available free online at www.liebertpub.com/ast for the next week.

Martin Brasier, Richard Matthewman, and Sean McMahon, University of Oxford (U.K.), and David Wacey, University of Western Australia (Crawley), contend that pumice has "four remarkable properties" that would enable it to have had "a significant role in the origin of life and provided an important habitat for the earliest communities of microorganisms." They describe those four properties in detail in the article "Pumice as a Remarkable Substrate for the Origin of Life."

To validate their hypothesis, the authors call for laboratory research to test the ability of pumice rock to adsorb organic compounds from water and create catalysts and new compounds by simulating the thermal cycles, UV light, and other conditions that existed when the first organic polymers and microbes co-existed.

The context for the emergence of life on Earth sometime prior to 3.5 billion years ago is almost as big a puzzle as the definition of life itself. Hitherto, the problem has largely been addressed in terms of theoretical and experimental chemistry plus evidence from extremophile habitats like modern hydrothermal vents and meteorite impact structures.

Here, we argue that extensive rafts of glassy, porous, and gas-rich pumice could have had a significant role in the origin of life and provided an important habitat for the earliest communities of microorganisms. This is because pumice has four remarkable properties. First, during eruption it develops the highest surface-area-to-volume ratio known for any rock type. Second, it is the only known rock type that floats as rafts at the air-water interface and then becomes beached in the tidal zone for long periods of time. Third, it is exposed to an unusually wide variety of conditions, including dehydration. Finally, from rafting to burial, it has a remarkable ability to adsorb metals, organics, and phosphates as well as to host organic catalysts such as zeolites and titanium oxides.

"The hypothesis that pumice provided a unique physical substrate in which life got its start is exciting and testable," says Sherry L. Cady, PhD, Editor-in-Chief of *Astrobiology* and Professor in the Department of Geology at Portland State University. "Key for astrobiology is whether such rock types preserved evidence of prebiotic reactions or ancient life forms in the rock record."

These remarkable properties now deserve to be rigorously explored in the laboratory and the early rock record.

Part of placebo effect ascribed to cannabinoids

Study suggests that cannabinoids are playing an important role in nonopioid preconditioned placebo effects

By Jonathan M. Gitlin

In clinical trials, new drugs are often compared to older treatments, but sometimes they're also compared to placebos - inert treatments that ought to have no effect. Except that's not what happens. The placebo effect can actually be pretty strong, and even more strangely, placebos can work even when the patient knows they're being given one.

Most of what we know about placebos results from studies on how we process pain, since it's more ethical to give someone a placebo instead of a painkiller than it would be to replace an anti-cancer drug or insulin. Some of the analgesic (painkilling) effect of placebo treatment is due to endogenous opioids, ones made by the body. Now, evidence has emerged that suggests an additional effect results from the cannabinoid pathway, according to a publication in *Nature Medicine*.

Placebo-activated opioid analgesia doesn't work all the time. Experimentally, researchers can induce it by preconditioning a research subject with an actual opioid analgesic. Or, to explain that in plain English, you give the subject a painful stimulus then give them an opioid to treat it. You do this several times then, instead of giving them a real drug, you give them a placebo, which will block the pain. What's more, you can actually inhibit the action of the placebo by giving the subject an opioid antagonist like naloxone, which blocks the effect of opioids. Still with me? Good.

Here's where things get more complicated. You can also use a nonsteroidal anti-inflammatory (NSAID), like ibuprofen, to create a placebo analgesic effect. But this time, it can't be blocked with naloxone. So there's more than one biochemical pathway responsible for the analgesic effects of sugar pills. The new paper involves an attempt to look for alternate pathways.

The *Nature Medicine* study involved several test groups, and measured their pain response to a tourniquet on five non-consecutive days. The first group receive no treatment at all during the study, and they showed no variation in pain threshold across its duration. A second group was given morphine on days 2 and 3, and a placebo on day 4, which had the same analgesic effect as morphine. The normal placebo effect worked.

A third group were given, without their knowledge (beyond general informed consent) a drug called rimbonant (marketed as Accomplia and also know as SR141716A). Rimbonant largely works by blocking a receptor called CB1. CB1 is activated in the body by a molecule called anandamide, and it's also the same receptor that cannabinoids activate. Rimbonant didn't have any effect on pain tolerance in this group, which had very similar responses to the subjects who received no drugs at all in the study. From this we can infer that blocking cannabinoid signaling through CB1 has no effect on the type of pain being measured.

Another group got the morphine treatment described above, but also got rimbonant with the placebo. Again, in this group, rimbonant had no effect, meaning that the opioid placebo effect isn't working through the body's cannabinoid pathway.

Finally, there were two more groups that were given ketorolac - an NSAID - instead of morphine on days 2 and 3. One of these groups was given a placebo on day 4, which worked just as well as ketorolac.

The other group got a placebo plus rimbonant. Normally, the placebo would block the pain but, in this case the rimbonant+placebo had no effect. This indicates that rimbonant blocked the placebo effect. This suggests that cannabinoids are playing an important role in nonopioid preconditioned placebo effects.

I should mention that this was only a fairly small study, and more work needs to be done in the area to fully flesh out this idea. Rimbonant can also have effects that are not all mediated through CB1 receptors, as I found out during the course of my Ph.D. But it is a neat little study, and one that expands our understanding of the pharmacology of placebos, to the degree such a thing is possible. *Nature Medicine*, 2011. doi: 10.1038/nm.2435

http://www.eurekalert.org/pub_releases/2011-10/smri-aht092911.php

A hormone that fights fat with fat

Sanford-Burnham scientists reveal that a hormone called orexin prevents obesity in mice by activating brown fat, a tissue that's good at burning calories

ORLANDO, Fla. The fat we typically think of as body fat is called white fat. But there's another type - known as brown fat - that does more than just store fat. It burns fat. Scientists used to think that brown fat disappeared after infancy, but recent advances in imaging technology led to its rediscovery in adult humans. Because brown fat is so full of blood vessels and mitochondria - that's what makes it brown - it's very good at converting calories into energy, a process that malfunctions in obesity. In a study published October 5 in *Cell Metabolism*,

researchers at Sanford-Burnham Medical Research Institute (Sanford-Burnham) discovered that orexin, a hormone produced in the brain, activates calorie-burning brown fat in mice. Orexin deficiency is associated with obesity, suggesting that orexin supplementation could provide a new therapeutic approach for the treatment of obesity and other metabolic disorders. Most current weight loss drugs are aimed at reducing a person's appetite. An orexin-based therapy would represent a new class of fat-fighting drugs - one that focuses on peripheral fat-burning tissue rather than the brain's appetite control center.

"Our study provides a possible reason why some people are overweight or obese despite the fact that they don't overeat - they might lack the orexin necessary to activate brown fat and increase energy expenditure," explained Devanjan Sikder, D.V.M, Ph.D., senior author of the study and assistant professor in Sanford-Burnham's Diabetes and Obesity Research Center, located in Orlando's Medical City at Lake Nona.

Since the best way to determine something's function is to see what happens when it's missing, Dr. Sikder's team, which included postdoctoral researchers Dyan Sellayah, Ph.D. and Preeti Bharaj, Ph.D., looked at mice genetically engineered to lack orexin. These mice weighed more than their normal counterparts, but they actually ate less, suggesting that overconsumption was not the cause of their obesity. Rather, the orexin-deficient mice lacked diet-induced thermogenesis (heat production); in other words, when fed a high-fat diet, the mice failed to dissipate the extra calories as heat the way that normal mice (and people) do. Instead, they stored that energy as fat.

This finding prompted the team to look at the mice's brown fat - a source of thermogenesis. What they found is that brown fat in mice lacking orexin didn't develop properly at the embryonic stage. This shortage had lasting effects on energy expenditure and weight even in adulthood.

Taking the opposite approach, the researchers then gave the defective mice more orexin. With the hormone present, brown fat developed properly before birth and continued to be active into adulthood. What's more, adding orexin to stem cells in a laboratory dish caused them to differentiate (specialize) into brown fat cells, creating more of this fat-burning engine.

"Without orexin, mice are permanently programmed to be obese. With it, brown fat is activated and they burn more calories," said Dr. Sikder. "We're now taking the next steps in determining how orexin - or a chemical that has the same effect - might be used in humans to therapeutically prevent or treat obesity."

According to the Centers for Disease Control and Prevention, about one-third of U.S. adults (33.8 percent) are obese. As a person becomes overweight or obese, he or she is at increased risk for type 2 diabetes, coronary heart disease, stroke, and certain cancers.

http://www.eurekalert.org/pub_releases/2011-10/dumc-sda092911.php

Same-day discharge after coronary artery stenting safe, yet not used

Patients discharged the same day they undergo coronary artery stenting do just as well as patients hospitalized overnight for observation

DURHAM, N.C. – Patients discharged the same day they undergo coronary artery stenting do just as well as patients hospitalized overnight for observation, according to researchers at Duke University Medical Center. And yet, they say, same-day discharge is rarely used.

More than 1 million coronary stent procedures are performed each year, making the procedure, known technically as Percutaneous Coronary Intervention (PCI), one of the most common in the U.S.

The associated risks – heart attack, blood clots, bleeding and kidney failure – have been reported to occur in up to 9.5% of patients. However, the risk for these complications has dropped steadily in recent years thanks to new technology and improved drug therapy, says Sunil Rao, M.D., a Duke cardiologist and author of the study that appears today in the *Journal of the American Medical Association*.

"Physicians, in general, feel more comfortable monitoring patients overnight because they are genuinely concerned about their patients and want to ensure good outcomes," says Rao, an associate professor of medicine at Duke. "Our study shows the outcomes have significantly improved so that you can send selected, low risk patients home the same day without increased risk of death or hospital readmission."

In addition to being safe for patients, same-day discharge may create several advantages for hospitals. For one, it frees up hospital beds for patients who really need them, says Eric Peterson, M.D., associate director of the Duke Clinical Research Institute, and the paper's senior author. Same-day discharge may also become a more efficient care strategy. "While it's unclear what direction healthcare reform will take in the future, same-day discharge could result in a better financial picture for a heart center if bundled payments for PCI procedures becomes the norm," Peterson says.

Smaller, single center studies have reported similar results, however, this is the first multi-center study in the United States to support those earlier findings. The study is based on data collected from 107,018 patients aged

65 and over who underwent elective PCI at 903 sites participating in the American College of Cardiology's CathPCI Registry between November 2004 and December 2008. Only 1339 of these patients (1.25%) were discharged the day of their procedure.

Rao stresses the study should not be taken as evidence that same-day discharge should be widely implemented. Rather, such decisions should be made individually for specific patients based not only on the success of their procedure, but also on whether they have support at home and access to emergency medical care if they need it. Hospitals considering same-day discharge programs should develop protocols and a system of care for patients who are sent home the same day as their procedure.

Patients in the study who were sent home the same day were more likely to be low risk, while patients who stayed overnight ran the gamut from low risk to high risk. "Our findings point to the need for better risk assessment tools so that patients who are truly high risk can stay overnight and patients who are low risk can be sent home the same day," Rao says. "In addition, our study underscores the importance of participation in multicenter registries like the CathPCI registry so we can continue to identify more efficient processes of care that are both efficacious and safe."

Additional co-authors include: Lisa A. Kaltenbach, MS, and Matthew T. Roe, M.D. from the Duke Clinical Research Institute; William S. Weintraub, M.D., Christiana Care Hospital, Newark, DE; Ralph G. Brindis, M.D., M.P.H., Northern California Kaiser Permanente, Oakland, CA; and John S. Rumsfeld, M.D., Ph.D., Denver VA Medical Center. The authors have no disclosures to report relative to the content of this study.

http://www.eurekalert.org/pub_releases/2011-10/cp-tiy093011.php

This is your brain on estrogen

It's no secret that women often gain weight as they get older. The sex hormone estrogen has an important, if underappreciated, role to play in those burgeoning waistlines.

Now, researchers reporting in the October Cell Metabolism, a Cell Press publication, have traced those hormonal effects on metabolism to different parts of the brain. The findings may lead to the development of highly selective hormone replacement therapies that could be used to combat obesity or infertility in women without the risks for heart disease and breast cancer, the researchers say.

"When women approach menopause, they gain weight in fat and their energy expenditure goes down," says Deborah Clegg of the University of Texas Southwestern Medical Center. Estrogen levels decline and women grow increasingly susceptible to obesity and metabolic syndrome.

Estrogen acts on receptors found throughout the body, in fat, on ovaries and in muscle. But when it comes to the hormone's influence on metabolism, Clegg suspected receptors in the brain. Others had traced the effects of estrogen on energy balance specifically to estrogen receptor- α (ER α). When her team deleted those receptors from the entire brains of mice, "we got very, very fat mice," Clegg said. The animals consumed more calories and burned less.

The researchers showed female mice lacking ER α in one part of the brain (the hypothalamic steroidogenic factor-1 or SF1 neurons) gained weight without eating any more. Loss of ER α from another brain area (the hypothalamic pro-opiomelanocortin or POMC neurons) had the opposite effect: animals ate more without gaining weight. Loss of ER α receptors in those same neurons also led to various problems in ovulation and fertility.

The findings suggest that drugs developed to specifically target estrogen receptors in the brain might offer a useful alternative to hormone replacement therapies that hit receptors throughout the body. The researchers say they would like to continue to isolate other estrogen-related effects and symptoms, for instance, on hot flashes and cognition. "The more we know about estrogen's sites of action, the more likely it is we could develop designer hormone replacement therapies targeting tissue X, Y or Z," Clegg said.

<http://www.nytimes.com/2011/10/04/health/04vaccine.html?partner=rss&emc=rss>

An Addiction Vaccine, Tantalizingly Close

Imagine a vaccine against smoking: People trying to quit would light up a cigarette and feel nothing. Or a vaccine against cocaine, one that would prevent addicts from enjoying the drug's high.

By DOUGLAS QUENQUA

SAN DIEGO - Though neither is imminent, both are on the drawing board, as are vaccines to combat other addictions. While scientists have historically focused their vaccination efforts on diseases like polio, smallpox and diphtheria - with great success - they are now at work on shots that could one day release people from the grip of substance abuse.

“We view this as an alternative or better way for some people,” said Dr. Kim D. Janda, a professor at the Scripps Research Institute who has made this his life’s work. “Just like with nicotine patches and the gum, all those things are just systems to get people off the drugs.”

Dr. Janda, a gruff-talking chemist, has been trying for more than 25 years to create such a vaccine. Like shots against disease, these vaccines would work by spurring the immune system to produce antibodies that would shut down the narcotic before it could take root in the body, or in the brain.

Unlike preventive vaccines - like the familiar ones for mumps, measles and so on - this type of injection would be administered after someone had already succumbed to an addictive drug. For instance, cocaine addicts who had been vaccinated with one of Dr. Janda’s formulations before they snorted cocaine reported feeling like they’d used “dirty coke,” he said. “They felt like they were wasting their money.”

It’s a novel use for vaccines that has placed Dr. Janda, who is 54, in the vanguard of addiction treatment. Because addiction is now thought to cause physical changes in the brain, doctors increasingly advocate medical solutions to America’s drug problem, leading to renewed interest in his work. “It’s very fashionable now,” said Dr. Janda, seated in a black leather chair in his office. “When we started doing this 27 years ago, it wasn’t.”

In July, Dr. Janda’s lab - 25 researchers, most of graduate-school age - made headlines when it announced that it had produced a vaccine that blunted the effects of heroin in rats. Rodents given the vaccine didn’t experience the pain-deadening effects of heroin and stopped helping themselves to the drug, presumably because it ceased to have any effect.

But as has often been the case in Dr. Janda’s career, the breakthrough came on the heels of a setback: A Phase 2 clinical trial for a nicotine vaccine that was based largely on his work was declared a failure this summer when people receiving the drug quit smoking at the same rate as people receiving a placebo.

To this day, despite many promising breakthroughs, not one of Dr. Janda’s vaccines has won approval from the Food and Drug Administration. For despite many successes in the lab - including promising animal tests - the vaccines have yet to produce consistent results in humans during clinical trials. “It’s like having the carrot right in front of the horse,” he said. “The big problem plaguing these vaccines right now is difficulty predicting in humans how well it’s going to work.” Or, he added, “maybe I’m just unlucky.”

The scientific principle behind Dr. Janda’s vaccines is, as he put it, “simplistically stupid.” Much like vaccines against disease, they introduce a small amount of the foreign substance into the blood, causing the immune system to create antibodies that will attack that substance the next time it appears.

The difficulty is that molecules like cocaine, nicotine and methamphetamine are tiny - much smaller than disease molecules - so the immune system tends to ignore them. To overcome that, Dr. Janda attaches a hapten - which is either a bit of the drug itself, or a synthetic version of it - to a larger protein that acts as a platform. The last part of the vaccine is an adjuvant, a chemical cocktail that attracts the immune system’s notice, effectively tricking it into making antibodies against a substance it usually wouldn’t see. “It’s not like some magical premise,” Dr. Janda said. “And the beauty of it is you’re not messing with brain chemistry.”

The contrast, he said, is to anti-opiates like Suboxone or methadone that are currently used to treat heroin addiction. Rather than blocking the drug’s effects, they seek to replace the heroin high.

Dr. Janda says he has tried and failed to make vaccines against alcohol and marijuana abuse. In the case of alcohol, he said, ethanol molecules proved just too small to attach to the protein that would deliver the immunity. And in the case of marijuana, the main ingredient that produces the high - tetrahydrocannabinol, or THC - hides too well inside the body. He has also tried formulating a vaccine against obesity. Rather than block a foreign substance, that vaccine would block the effects of a peptide hormone produced by the stomach called ghrelin that signals hunger in the brain. So far, a version of the vaccine has been shown to lower food intake in animals, though - again - it’s unclear whether it will work in humans.

Even so, addicts and their families are clamoring to get into Dr. Janda’s clinical trials. He says he gets e-mails every week from addicts asking to be included. He has had to turn away parents who showed up at his office with their drug-addicted children after reading about his work.

“What am I supposed to do, go in the lab and pull it out of the refrigerator and inject you?” he said. “I guess it’s been so devastating in their families that they’re looking for anything, and there’s just nothing out there. It’s really sad when you see these types of things.”

Despite the disappointments, some scientists predict that Dr. Janda will succeed. No less an addiction expert than Dr. Nora Volkow, director of the National Institute on Drug Abuse, calls him a “visionary” who saw the opportunity to treat addiction with medicine decades before most. Indeed, one reason that her institute is a chief source of Dr. Janda’s financing is Dr. Volkow’s belief that his work will eventually produce a marketable vaccine.

“Now many people say, ‘Yes, of course’ ” to the idea of treating drugs through vaccines, Dr. Volkow said. “But that took many years, and he traveled the road when there was a lot of skepticism.”

Today, the scientists who are working to create vaccines against narcotics include Thomas Kosten at the Baylor College of Medicine and S. Michael Owens at the University of Arkansas. Dr. Kosten has had limited success with a cocaine vaccine, while Dr. Owens is focused on vaccines for methamphetamines. All three researchers say they are hobbled by a lack of interest - read: financing - from pharmaceutical companies in vaccines for any drug other than nicotine, presumably because there is little money to be made in a shot given once every six months, and because such companies aren't eager to associate their brands with drug addicts.

And yet Dr. Janda's lifelong pursuit of vaccines against narcotics began not with some painful family struggle with addiction, but in a simple request in the 1980s from one of the Scripps Institute's former corporate partners. “They were interested in the whole antibody area,” he said. “They kind of approached me and said, ‘Could you make antibodies to a drug of abuse?’ So we embarked on this.”

Dr. Janda spent many years trying to bring his own vaccines to market. In the '80s and '90s, he helped start some small pharmaceutical companies that patented and tested his work, with varying degrees of success. One burned through \$60 million of venture capital with nothing to show for it; another sold for \$95 million in 1999, but “due to bad management and bad splits, I ended up with about enough money for a case of beer,” he said - even more disappointing, perhaps, for a man with a taste for expensive bourbon.

These days, Dr. Janda prefers to publish his results in scientific journals and let others try to bring the vaccines to market. He is quick to caution that taking away someone's ability to get high off of one drug hardly cures them of their addiction problems. There's nothing to stop a vaccinated cocaine addict, for example, from turning to methamphetamines.

Like any anti-addiction treatment, his vaccines are simply meant as “a crutch for people wanting to go into abstinence,” Dr. Janda said. “The whole thing with addicts is you have to want to get off the drug, or it's not going to happen.” He is also wary of ethical issues posed by his work. Today, a recovering cocaine addict will pass a drug test just days after getting clean. But once vaccinated, that person could be tested for antibodies for up to six months, alerting employers to his struggles with addiction.

“Before a parent takes a kid into college, can she take him in for a round of vaccines against all drugs?” asked Jenny Treweek, a researcher at Janda Laboratories who is working on a vaccine for Rohypnol, otherwise known as the date-rape drug. “Some teenagers might have a real problem with that.”

It's questions like that - and the desire to solve the molecular puzzle he's set up for himself - that motivate Dr. Janda to spend seven days a week in his lab, he said. He spends much of that time tweaking the components of his vaccines - trying different proteins or haptens, adjusting the adjuvants - hoping to hit precisely the right formula. “If I vaccinated three people and they all got the same” immune response, he said, “then you would have a really straightforward shot how to move things forward.”

But with nearly 30 years of tweaking already under his belt, he seems increasingly resigned to the idea that it might not be he who eventually moves it across the finish line. “I figure I have eight or 10 years left,” he said. “If something doesn't go in eight or 10 more years, then it's someone else's turn.”

<http://www.wired.com/wiredscience/2011/10/why-do-some-people-learn-faster-2/>

Why Do Some People Learn Faster?

People learn how to get it right by getting it wrong again and again

By Jonah Lehrer Email Author

The physicist Niels Bohr once defined an expert as “a person who has made all the mistakes that can be made in a very narrow field.” Bohr's quip summarizes one of the essential lessons of learning, which is that people learn how to get it right by getting it wrong again and again. Education isn't magic. Education is the wisdom wrung from failure.

A new study, forthcoming in *Psychological Science*, and led by Jason Moser at Michigan State University, expands on this important concept. The question at the heart of the paper is simple: Why are some people so much more effective at learning from their mistakes? After all, everybody screws up. The important part is what happens next. Do we ignore the mistake, brushing it aside for the sake of our self-confidence? Or do we investigate the error, seeking to learn from the snafu?

The Moser experiment is premised on the fact that there are two distinct reactions to mistakes, both of which can be reliably detected using electroencephalography, or EEG. The first reaction is called error-related negativity (ERN). It appears about 50 milliseconds after a screw-up and is believed to originate in the anterior cingulate cortex, a chunk of tissue that helps monitor behavior, anticipate rewards and regulate attention. This neural reaction is mostly involuntary, the inevitable response to any screw-up.

The second signal, which is known as error positivity (Pe), arrives anywhere between 100-500 milliseconds after the mistake and is associated with awareness. It occurs when we pay attention to the error, dwelling on the disappointing result. In recent years, numerous studies have shown that subjects learn more effectively when their brains demonstrate two properties: 1) a larger ERN signal, suggesting a bigger initial response to the mistake and 2) a more consistent Pe signal, which means that they are probably paying attention to the error, and thus trying to learn from it.

In this new paper, Moser et al. extends this research by looking at how beliefs about learning shape these mostly involuntary error-related signals in the brain, both of which appear in less than half a second. More specifically, the scientists applied a dichotomy first proposed by Carol Dweck, a psychologist at Stanford. In her influential research, Dweck distinguishes between people with a fixed mindset - they tend to agree with statements such as "You have a certain amount of intelligence and cannot do much to change it" - and those with a growth mindset, who believe that we can get better at almost anything, provided we invest the necessary time and energy. While people with a fixed mindset see mistakes as a dismal failure - a sign that we aren't talented enough for the task in question - those with a growth mindset see mistakes as an essential precursor of knowledge, the engine of education.

The experiment began with a flanker task, a tedious assignment in which subjects are supposed to identify the middle letter of a five-letter series, such as "MMMMM" or "NNMNN." Sometimes the middle letter is the same as the other four, and sometimes it's different. This simple change induces frequent mistakes, as the boring task encourages people to zone out. Once they make a mistake, of course, they immediately regret it. There is no excuse for misidentifying a letter.

While performing the flanker task, subjects wore an EEG cap, a monitoring device filled with greased electrodes that records electrical activity in the brain. (Unlike fMRI, EEG gives researchers excellent temporal resolution, allowing them to precisely measure a sequence of neural events. Unfortunately, this comes at the expense of spatial resolution, making it difficult to know where in the brain the signals are coming from.)

It turned out that those subjects with a growth mindset were significantly better at learning from their mistakes. As a result, they showed a spike in accuracy immediately following an error. Most interesting, though, was the EEG data, which demonstrated that those with a growth mindset generated a much larger Pe signal, indicating increased attention to their mistakes. (While those with an extremely fixed mindset generated a Pe amplitude around five, those with a growth mindset were closer to fifteen.) What's more, this increased Pe signal was nicely correlated with improvement after error, implying that the extra awareness was paying dividends in performance. Because the subjects were thinking about what they got wrong, they learned how to get it right.

In her own research, Dweck has shown that these mindsets have important practical implications. Her most famous study, conducted in twelve different New York City schools along with Claudia Mueller, involved giving more than 400 fifth graders a relatively easy test consisting of nonverbal puzzles. After the children finished the test, the researchers told the students their score, and provided them with a single line of praise. Half of the kids were praised for their intelligence. "You must be smart at this," the researcher said. The other students were praised for their effort: "You must have worked really hard."

The students were then allowed to choose between two different subsequent tests. The first choice was described as a more difficult set of puzzles, but the kids were told that they'd learn a lot from attempting it. The other option was an easy test, similar to the test they'd just taken.

When Dweck was designing the experiment, she expected the different forms of praise to have a rather modest effect. After all, it was just one sentence. But it soon became clear that the type of compliment given to the fifth graders dramatically affected their choice of tests. When kids were praised for their effort, nearly 90 percent chose the harder set of puzzles. However, when kids were praised for their intelligence, most of them went for the easier test. What explains this difference? According to Dweck, praising kids for intelligence encourages them to "look" smart, which means that they shouldn't risk making a mistake.

Dweck's next set of experiments showed how this fear of failure can actually inhibit learning. She gave the same fifth graders yet another test. This test was designed to be extremely difficult - it was originally written for eighth graders - but Dweck wanted to see how the kids would respond to the challenge. The students who were initially praised for their effort worked hard at figuring out the puzzles. Kids praised for their smarts, on the other hand, were easily discouraged. Their inevitable mistakes were seen as a sign of failure: Perhaps they really weren't so smart. After taking this difficult test, the two groups of students were then given the option of looking either at the exams of kids who did worse or those who did better. Students praised for their intelligence almost always chose to bolster their self-esteem by comparing themselves with students who had

performed worse on the test. In contrast, kids praised for their hard work were more interested in the higher-scoring exams. They wanted to understand their mistakes, to learn from their errors, to figure out how to do better.

The final round of tests was the same difficulty level as the initial test. Nevertheless, students who were praised for their effort exhibited significant improvement, raising their average score by 30 percent. Because these kids were willing to challenge themselves, even if it meant failing at first, they ended up performing at a much higher level. This result was even more impressive when compared to students randomly assigned to the smart group, who saw their scores drop by nearly 20 percent. The experience of failure had been so discouraging for the “smart” kids that they actually regressed.

The problem with praising kids for their innate intelligence - the “smart” compliment - is that it misrepresents the psychological reality of education. It encourages kids to avoid the most useful kind of learning activities, which is when we learn from our mistakes. Because unless we experience the unpleasant symptoms of being wrong - that surge of Pe activity a few hundred milliseconds after the error, directing our attention to the very thing we’d like to ignore - the mind will never revise its models. We’ll keep on making the same mistakes, forsaking self-improvement for the sake of self-confidence. Samuel Beckett had the right attitude: “Ever tried. Ever failed. No matter. Try Again. Fail again. Fail better.”

<http://medicalxpress.com/news/2011-10-recognition-anger-disgust-affected-dementia.html>

Recognition of anger, fear, disgust most affected in dementia

A new study on emotion recognition has shown that people with frontotemporal dementia are more likely to lose the ability to recognise negative emotions, such as anger, fear and disgust, than positive emotions such as happiness.

Medical Xpress - "All patients continue to recognise happiness, at least in the initial stages of the disease, even when recognition of other emotions is heavily impaired," says Dr Olivier Piguet, one of the study's authors. "There is something about a happy face that is different from the way other emotions are expressed."

Frontotemporal dementia (FTD) is one of the most common types of dementia in younger adults. The age of onset of FTD is typically in the 50s or 60s but can be as young as 30.

Along with various other symptoms affecting behaviour and language, all people with FTD experience difficulty in recognising emotions (facial expressions). Up until now, however, it was not known whether the three subtypes of FTD (semantic dementia, progressive non-fluent aphasia and behavioural-variant FTD) have the same emotion-recognition deficits, and whether certain techniques could help overcome these deficits.

Dr Piguet's team tested the ability of 41 people with FTD to recognise six basic facial emotions (anger, disgust, fear, happiness, sadness and surprise). The team also performed a second test, using faces with exaggerated emotions, to determine whether more intensely expressed emotions would help with recognition.

Of the three FTD subtypes, Dr Piguet's team found that those people with the semantic dementia subtype were the most impaired when it came to recognising emotions.

"Semantic dementia patients were impaired across the board," says Dr Piguet. "Even when we increased the intensity of the emotions, it didn't make any difference to their ability to recognise them. These patients probably have a disturbance in their core emotion recognition pathways."

Patients with the progressive non-fluent aphasia and behavioural-variant FTD subtypes also had emotion-recognition deficits, particularly for angry and sad faces, but tended to improve if the emotions were made more obvious.

"Problems with emotion recognition had not been observed in patients with progressive non-fluent aphasia before, so this is a new finding," says Dr Piguet. "In both these types of patients, part of the problem is probably due to a deficit in attention, so perhaps they are not paying attention to the right places when looking at faces," he says.

Dr Piguet says these results suggest there may be ways to address the problem of emotion recognition deficits in these patients, at least early on in the disease process. For example, exaggerating facial expressions may aid in communicating certain emotions. A better understanding of emotion recognition deficits in FTD will help with predicting the progression of the disease, says Dr Piguet.

"When patients come to see us, it's important for them to know what's going to happen to them. Unfortunately, we're still not great at predicting disease progression. This research, however, will help us better understand what symptoms patients will develop over time, what they can expect for the future, and hopefully will help with developing some strategies for coping with their disease."

The study was published in the journal Social Neuroscience. Provided by Neuroscience Research Australia

<http://www.scientificamerican.com/article.cfm?id=asteroid-vesta-has-planet-like-features>

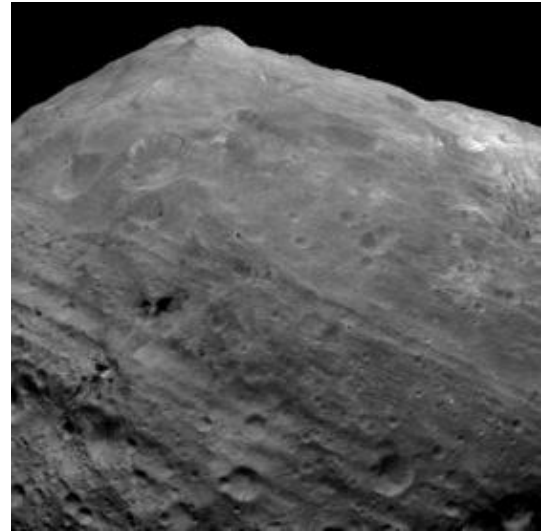
Planetary Pretender: Asteroid Vesta Has Planet-Like Features

NASA's Dawn spacecraft is getting up close and personal with the giant asteroid, revealing rift valleys, mountainous uplifts and a belt of grooves near its equator

By John Matson | Tuesday, October 4, 2011 | 9

NANTES, France - Asteroids are often considered debris, the scraps and odd lumps that went unused in the forming of the planets. But when it comes to Vesta, one of the largest asteroids in our solar system, Chris Russell hardly considers the rock a mere castoff. "I've started calling it the smallest terrestrial planet," said Russell, the principal investigator for NASA's Dawn mission, which sent a spacecraft into orbit at Vesta in July.

Russell and his colleagues gave a sense Monday of why they hold Vesta in such high regard. In a press conference here at a joint meeting of the American Astronomical Society Division for Planetary Sciences and the European Planetary Science Congress, researchers working on the Dawn mission announced some of the findings that the spacecraft has collected since entering orbit - findings that make Vesta look considerably more like a world unto itself than a mere leftover. "We found that Vesta is a really interesting alien, small world," said the mission's deputy principal investigator, Carol Raymond of the NASA Jet Propulsion Laboratory in Pasadena, Calif.



PEAKING INTEREST: A towering mound near Vesta's south pole rivals the largest mountains in the solar system.

Image: NASA/JPL-Caltech/UCLA/MPS/DLR/IDA

Vesta is an irregular ellipsoid just 560 kilometers in diameter - too small and odd-shaped to qualify as a dwarf planet. But it seems to have a large metallic core and a basaltic crust, just like Earth. And it bears scars from past geologic shake-ups, most likely triggered by large impacts, including rift valleys, mountainous uplifts and an intriguing belt of grooves near its equator. "It has tectonic features, like on Earth," Russell said.

The asteroid made a particularly interesting target for Dawn because the space rock carries evidence of the history of much of the solar system as well. Vesta-derived meteorites that landed on Earth allowed planetary scientists to measure the asteroid's age in the laboratory, showing that it is one of the oldest large bodies in the solar system. (Because it is small relative to the terrestrial planets, it would have cooled and solidified much more quickly than those bodies.) As such, Vesta provides a valuable lab for studying the materials and processes that formed the planets during the first millions of years in the early solar system.

It now appears that the past four billion years have been quite an interesting time in Vesta's evolution as well. In fact, the asteroid boasts a mountain that Earth cannot match in terms of altitude. A giant peak at the asteroid's south pole, which is currently unnamed, rises roughly 20 kilometers from its base to its summit, about twice the height of Mauna Kea in Hawaii, the tallest mountain - from its base on the ocean floor to its peak - on Earth.

"The south polar mountain on Vesta is very, very large - almost as large as the largest mountain in the solar system, Olympus Mons," Russell said, referring to the towering, roughly 25-kilometer volcanic peak on Mars. "We have not figured out the tectonic cause of the south polar mountain, so that's work ahead of us."

The mountain rises from the center of a large impact basin, but Raymond cautioned that it was too soon to definitively say that the peak is simply a crater with an impact-uplifted center. A large impact in the south billions of years ago did leave one clearly identifiable mark, blanketing the southern hemisphere in ejecta and filling nearby craters. A preliminary chronology analysis based on crater counts across the asteroid shows that something reset the clock on the southern hemisphere long ago. "Ages from some areas in the south appear to be much younger, as much as a billion years younger, than the north," Raymond said.

<http://www.physorg.com/news/2011-10-atlantic-flotsam-fossil-mysterious-bird.html>

Across the Atlantic on flotsam: New fossil findings shed light on the origins of the mysterious bird Hoatzin

A team has examined fossil relatives of the South American Hoatzin, which point to African origins for the enigmatic bird.

A team comprising German, Brazilian and French scientists, including an ornithologist from the Senckenberg Research Institute Frankfurt, has examined fossil relatives of the South American Hoatzin (*Opisthocomus hoazin*), which point to African origins for the enigmatic bird. The accompanying study is being published by the journal *Naturwissenschaften* today.

The Hoatzin is a funny old bird: a poor flyer, the chicks equipped with claws on their wings, it lives on the banks of the Amazon and Orinoco basins in South America. What is particularly unusual about this bird is its purely vegetarian diet. Digestion does not only take place in the stomach but above all in a greatly enlarged crop, where bacteria help to decompose the food. The digestive system of the Hoatzins is very reminiscent of that of a mammalian ruminant.

But not only is the anatomy of the bird unusual; its relationship is still unclear. Since its scientific description in 1776, the Hoatzin has been bracketed alternatively with game birds, cuckoos or the African turacos. However, no relationship with these groups has been proven convincingly until now. For this reason, the bird is usually allocated its own family and genus. The evolutionary origin of the Hoatzins has been unknown so far, and apart from some very fragmentary remains, there were no fossil remnants.



Hoatzin Chick

Now a team consisting of German, Brazilian and French researchers, including the ornithologist Gerald Mayr from the Senckenberg Research Institute, has not only described the earliest known fossil find of the mysterious bird group, but has also produce the first proof outside of South America.

Upper arm and shoulder girdle bones, around 23 million years old, from a site in southeast Brazil, which are kept in the Museu de História Natural de Taubaté in Brazil, are the first ever fossil finds of a Hoatzin. The large similarity between the fossils and the corresponding bones of the present-day Hoatzins suggest that the bird developed its unusual nutritional biology at a very early stage.

As well as the Brazilian findings the researchers also examined 17 million year old bones from Namibia, which revealed surprising findings on the earlier geographic distribution of the Hoatzins. Until now the African fossil finds, described a few years ago as *Namibiavis senutae*, were allocated to an extinct family of cranes. “However, this allocation can no longer be supported, because the finds demonstrate characteristic bone features of Hoatzins,” explains Gerald Mayr. When two related animal groups are discovered on different continents, this can be explained in principle by two mechanisms: either the continents were once connected by land, or the distribution took place directly across the water.

Africa and South America were once part of a supercontinent called Gondwana, but this had already broken up much longer than 20 million years ago, the continents being separated by the Atlantic. So Hoatzins must have crossed the ocean at some stage in order to get from one continent to the other.

But how does a bird, which is an especially poor long-distance flyer, manage to cross a sea that is over 1,000 kilometres wide? Even if the flying capabilities of the Hoatzin’s ancestors were better, it is highly unlikely that they could have managed this distance in the air.

Gerald Mayr and his colleagues from Brazil and France have an explanation that is somewhat unexpected for birds: “We assume that the bird crossed the Atlantic upon drifting flotsam.” This means of travel using flotsam is already familiar with regard to some primates, rodents and lizards, but it would be the first proof of a similar journey by a bird. Due to the Cenozoic ocean currents and wind directions, a journey across the Atlantic was only probable in a westerly direction. The scientists assume, therefore, that “South America’s most enigmatic bird” has its origins outside of South America and arrived there from Africa.

More information: Gerald Mayr, Herculano Alvarenga and Cécile Mourer-Chauviré, Out of Africa: Fossils shed light on the origin of the Hoatzin, an iconic Neotropical bird, Naturwissenschaften, DOI:10.1007/s00114-011-0849-1 Provided by Senckenberg Research Institute

http://www.eurekalert.org/pub_releases/2011-10/f-sf-swm100511.php

Spanish women marry immigrants with more qualifications

Study results indicate that, unlike Spanish men, Spanish women prefer immigrants with more qualifications

A team at the Complutense University of Madrid (UCM) has studied the marriage strategies of immigrants in order to determine the nature of endogamic (between people of the same nationality) and exogamic partnerships (between people of different nationalities) in Spain. The preliminary results indicate that, unlike Spanish men, Spanish women prefer immigrants with more qualifications.

“It caught our attention that human capital was more important in determining outmarriage amongst Spanish women but this is not the case in Spanish men. In other words, it seems that Spanish women prefer to get

married to an immigrant man who has a higher educational attainment. However, this preference does not exist amongst Spanish men when it comes to getting married to an immigrant woman," explains María Sánchez-Domínguez, investigator at the UCM and co-author of the study that was published in the *International Sociology Journal*.

The researcher and her team gathered data from the National Immigrant Survey of Spain (2007), which was carried out by the UCM's Population and Society Study Group (GEPS) and Spain's National Statistic Institute (INE). The survey acts as a unique source of information and can be used to understand the characteristics of immigrants in Spain since 2007.

Sánchez-Domínguez points out that "although it is from 2007, the survey contains both information on the current situation of those surveyed as well as their migration history. It is the only source of information that we can use to study the marriage strategies of immigrants and link them to integration processes. It is useful not just in understanding immigrant marriages in Spain but also those marriages that took place in the country of origin. From these data, in an initial study, researchers analysed endogamic marriages in Spain and the relationship between marriage and migration strategies. The expert's main conclusion was that Moroccans are more prone towards endogamy, followed by Romanians and Ecuadorians.

64% of Moroccan men are reunited with their wife.

Sánchez-Domínguez states that "Moroccan men show strong endogamic tendencies and use marriage as a way of being reunited later on with their partner within Spain. The most common type of behaviour consists of a Moroccan single man coming to Spain. After a certain amount of time, he returns to Morocco where he gets marriage to a Moroccan woman and then returns to Spain without his spouse. Later on, he is reunited with his wife within Spanish society.

Some 64% of Moroccan immigrant men have employed this strategy. According to experts, religion as well as geographical proximity to Spain are key factors in explaining this phenomenon.

Exogamy is an indication of an immigrant's level of social integration. Those who have higher tendencies towards exogamy are Argentineans and Colombians. According to the researcher, linguistic and cultural proximity means that the number of marriages with the Spanish population is very high "because they see each other as equals." Furthermore, it was observed that Brazilian, Dominican, Cuban and Colombian women display a high percentage of marriage with Spanish men within just a year of arriving in Spain. This is a phenomenon known as "imported brides".

Sánchez-Domínguez highlights that "in general terms, endogamy decreases according to the amount of time that an immigrant spends in a country, which, in turn, is a clear indication of integration. On the other hand, endogamy is higher amongst immigrants with less educational attainment and exogamy is more prevalent amongst immigrants who have a university education."

Endogamy has been on the increase since the year 2000

Whether an immigrant has studied in Spain is also important in determining endogamic and exogamic tendencies. It was found that immigrants who have studied in Spain are less prone to marry a partner of the same nationality because they mix in a social setting with more Spaniards.

Another factor that influences endogamic marriage is whether the immigrant has arrived before or after the year 2000. "In that year, Spain became an immigrant-receiving country," says the researcher. "Endogamy is higher amongst those immigrants who arrived after this year. An explanation for this can be found in the size of the immigrant group: the bigger the amount of immigrants, the higher the chance of endogamy, which is usually the preference, because there are a higher number of potential partners within a given ethnic community."

Those who do not have Spanish nationality at the time of marriage are also more prone to opt for endogamy.

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Last universal common ancestor more complex than previously thought

New evidence suggests that LUCA was a sophisticated organism after all, with a complex structure recognizable as a cell

CHAMPAIGN, Ill. - Scientists call it LUCA, the Last Universal Common Ancestor, but they don't know much about this great-grandparent of all living things. Many believe LUCA was little more than a crude assemblage of molecular parts, a chemical soup out of which evolution gradually constructed more complex forms. Some scientists still debate whether it was even a cell.

New evidence suggests that LUCA was a sophisticated organism after all, with a complex structure recognizable as a cell, researchers report. Their study appears in the journal *Biology Direct*.

The study builds on several years of research into a once-overlooked feature of microbial cells, a region with a high concentration of polyphosphate, a type of energy currency in cells. Researchers report that this polyphosphate storage site actually represents the first known universal organelle, a structure once thought to be absent from bacteria and their distantly related microbial cousins, the archaea. This organelle, the evidence indicates, is present in the three domains of life: bacteria, archaea and eukaryotes (plants, animals, fungi, algae and everything else).

The existence of an organelle in bacteria goes against the traditional definition of these organisms, said University of Illinois crop sciences professor Manfredo Seufferheld, who led the study.

"It was a dogma of microbiology that organelles weren't present in bacteria," he said. But in 2003 in a paper in the *Journal of Biological Chemistry*, Seufferheld and colleagues showed that the polyphosphate storage structure in bacteria (they analyzed an agrobacterium) was physically, chemically and functionally the same as an organelle called an acidocalcisome (uh-SID-oh-KAL-sih-zohm) found in many single-celled eukaryotes.

Their findings, the authors wrote, "suggest that acidocalcisomes arose before the prokaryotic (bacterial) and eukaryotic lineages diverged." The new study suggests that the origins of the organelle are even more ancient.

The study tracks the evolutionary history of a protein enzyme (called a vacuolar proton pyrophosphatase, or V-H+PPase) that is common in the acidocalcisomes of eukaryotic and bacterial cells. (Archaea also contain the enzyme and a structure with the same physical and chemical properties as an acidocalcisome, the researchers report.)

By comparing the sequences of the V-H+PPase genes from hundreds of organisms representing the three domains of life, the team constructed a "family tree" that showed how different versions of the enzyme in different organisms were related. That tree was similar in broad detail to the universal tree of life created from an analysis of hundreds of genes. This indicates, the researchers said, that the V-H+PPase enzyme and the acidocalcisome it serves are very ancient, dating back to the LUCA, before the three main branches of the tree of life appeared.

"There are many possible scenarios that could explain this, but the best, the most parsimonious, the most likely would be that you had already the enzyme even before diversification started on Earth," said study co-author Gustavo Caetano-Anollés, a professor of crop sciences and an affiliate of the Institute for Genomic Biology at Illinois. "The protein was there to begin with and was then inherited into all emerging lineages."

"This is the only organelle to our knowledge now that is common to eukaryotes, that is common to bacteria and that is most likely common to archaea," Seufferheld said. "It is the only one that is universal."

The study lends support to a hypothesis that LUCA may have been more complex even than the simplest organisms alive today, said James Whitfield, a professor of entomology at Illinois and a co-author on the study.

"You can't assume that the whole story of life is just building and assembling things," Whitfield said. "Some have argued that the reason that bacteria are so simple is because they have to live in extreme environments and they have to reproduce extremely quickly. So they may actually be reduced versions of what was there originally. According to this view, they've become streamlined genetically and structurally from what they originally were like. We may have underestimated how complex this common ancestor actually was."

The study team also included Kyung Mo Kim, of the Korea Research Institute of Bioscience and Biotechnology; and Alejandro Valerio, of the Museum of Biological Diversity in Columbus, Ohio.

The National Institute of Allergy and Infectious Diseases and the National Science Foundation provided funding for this study.

http://www.eurekalert.org/pub_releases/2011-10/ps-etr100511.php

Earlier tracheostomies result in better patient outcomes

A tracheostomy performed within the first seven days after a severe head injury results in better overall patient outcome, according to a team of Penn State College of Medicine researchers.

This is especially true for patients who have a greater chance of surviving when admitted to the hospital.

A tracheostomy is an opening created in the front of the neck directly into the trachea to allow unimpeded breathing. (A tracheotomy is the act of making that opening.)

"The CDC estimates that more than 200,000 individuals are hospitalized annually for traumatic brain injury," said Kevin M. Cockroft, M.D., associate professor, neurosurgery. "Severely head-injured patients, particularly those with additional injuries, often require tracheostomy at some point during their hospital stay."

Previous studies have shown mixed results.

"Traditionally, tracheostomy, or 'trach,' has been recommended to prevent airway complications," Cockroft said. "Early trach has been advocated as a means to improve outcome, with various studies suggesting that it may decrease the incidence of pneumonia, reduce intensive care unit days and shorten overall length of stay. Some evidence also exists to suggest that early trach does not improve outcomes. As a result, the timing of

trach in these critically ill patients remains controversial." Early trach patients are defined as those who have a tracheostomy performed during the first seven hospital-stay days. Late trach patients are defined as those who have a tracheostomy performed at greater than seven days after admission.

Researchers used data collected from January 1990 through December 2005 by the Pennsylvania Trauma Society Foundation for its statewide trauma registry. Because of a lack of patients with only head injury, researchers looked at patients with injury to at least one other body system. In total, 3,104 patients were included in the study, with 1,577 in the early trach group and 1,527 in the late trach group. It is the largest study to date to report the effects of tracheostomy timing on outcome after a severe head injury.

In the study population, later trach patients were in the hospital three times longer than early trach patients and also spent an average of four times longer in the ICU. Early trach patients were 1.5 times more likely to be discharged in an independent state. However, later trach patients were twice as likely to live to be discharged from the hospital, potentially because more severe cases would receive an earlier trach.

In addition, later trach patients were about twice as likely to suffer from an adverse pulmonary occurrence such as pneumonia, about 1.5 times as likely to suffer a cardiac event such as a heart attack, and 1.5 times more likely to have an infection. Researchers reported their results in the journal *Neurocritical Care*. The project was funded by the Departments of Neurosurgery and Public Health Sciences, Penn State Milton S. Hershey Medical Center and Penn State College of Medicine.

"These results indicate a complex relationship between tracheostomy timing and outcome, but suggest that a strategy of early tracheostomy, particularly when performed on patients with a reasonable chance of survival, results in a better overall clinical outcome than when the tracheostomy is performed in a delayed manner," Cockroft said.

Other researchers are Elias B. Rizk and Akshal S. Patel, Department of Neurosurgery; Christina M. Stetter and Vernon M. Chinchilli, Department of Public Health Sciences.

http://www.eurekalert.org/pub_releases/2011-10/sumc-un092811.php

US not taking basic step to prevent toxoplasmosis in newborns, Stanford researcher contends

North American babies who acquire toxoplasmosis infections in the womb show much higher rates of brain and eye damage than European infants with the same infection, according to new research from the Stanford University School of Medicine.

STANFORD, Calif. -- Eighty-four percent of the North American infants studied had serious complications of the parasitic infection, including calcium deposits in the brain, water on the brain and eye disease that caused visual impairment or blindness. By contrast, few European infants had these problems -- for instance, about 17 percent of French infants with the infection develop complications.

"It was a shock," said Jose Montoya, MD, the study's senior author and an associate professor of infectious diseases at Stanford. "We were dismayed to see so many little ones with severe eye disease, hydrocephalus and brain calcifications."

The study, which will be published online Oct. 5 in the *Pediatric Infectious Disease Journal*, examined 155 U.S. and nine Canadian infants whose congenital toxoplasmosis infections were confirmed by screening tests at the Palo Alto Medical Foundation Toxoplasmosis Serology Laboratory, the nation's toxoplasmosis reference laboratory, between 1991 and 2005. Montoya is the director of the lab. The study is the most comprehensive to date on congenital toxoplasmosis in the United States, where it is estimated to affect 500 to 5,000 pregnancies per year. (Other studies with more Canadian subjects have explored toxoplasmosis infections there in more detail.)

The infection, which is caused by the parasite *Toxoplasma gondii*, can be acquired several ways, such as by eating raw or undercooked meat or shellfish, contact with cat feces, or being exposed to soil while gardening. Infants whose mothers first acquire the parasite during pregnancy are vulnerable to the congenital infection. Medication can potentially prevent mother-to-child transmission, but none of the mothers in the new study received treatment for toxoplasmosis during pregnancy.

Clinical information was available for 138 infants in the study. Of those who showed toxoplasmosis complications, 92 percent had eye disease, nearly 80 percent had brain calcifications and 68 percent had hydrocephalus. About 61 percent of the infants with complications had all three complications together. The complications were severe enough to cause permanent visual or mental impairments for many of the infants, Montoya said, though the study did not track the children beyond infancy.

In contrast, the rate of complications among Western European infants with congenital toxoplasmosis is much lower. Recent findings from another research team showed that 15 percent of European infants had eye

disease and 6 percent had cranial calcifications, for example. The European literature has rarely reported cases of hydrocephalus in recent decades.

The difference between continents has several possible explanations, Montoya said. One possibility is referral bias -- the U.S. lab that provided data for the new study tends to see only the country's most severe cases, whereas European labs have comprehensive data on all pregnancies affected by toxoplasmosis. Another possibility is that the two continents harbor different strains of toxoplasma parasite, though John Boothroyd, a Stanford professor of microbiology and immunology who studies toxoplasma but was not involved in this research, said the same strains appear to explain most human infections on both continents.

A third explanation, and the possibility that worries Montoya, is that the difference is due to shortfalls in U.S. prenatal care. Pregnant women in Europe are screened regularly for new toxoplasma infections and treated to prevent transmission of the parasite to the fetus. But prenatal screening and treatment is rarely offered in the United States. Screening is needed because toxoplasmosis can occur even in pregnant women who carefully avoid known transmission methods. What's more, the infection can occur without any symptoms in the mother.

"There is a tragedy out there that can be prevented through thoughtful, low-cost serological screening of one of our most vulnerable populations -- the mother-baby pair," Montoya said. "The sad part is that in the U.S., although we have the tools at both the medical and the lab level to detect and treat prenatal toxoplasma infections, we don't apply them."

Testing pregnant women for toxoplasmosis infection would not be complicated, Montoya said. The existing tests require a blood sample and can be conducted at any commercial laboratory. Although research is still needed to verify the cost-effectiveness of such testing, the tests could be made quite inexpensive -- in the range of \$5 to \$10 each, he said. The testing could be performed on blood that is already drawn for other tests during pregnancy. "We are strong believers that pregnant women have the right to know whether the baby is at risk, or whether the baby has been infected, in the same way that parents have a right to know if their baby has a metabolic defect or a hearing problem," Montoya said.

Montoya's collaborators included researchers at the University of Chicago School of Medicine and Stanford scientists Tudor Olariu, MD, Ph.D, a visiting professor from Victor Babes University of Medicine and Pharmacy in Romania, and Jack Remington, MD, emeritus professor of medicine at Stanford. The research was funded by grants from the National Institutes of Health and the Cornwell and Mann Family Foundation. Information about the Department of Pediatrics, which also supported the research, is available at <http://pediatrics.stanford.edu/>.

<http://www.nytimes.com/2011/10/04/science/04evolve.html?partner=rss&emc=rss>

Natural Selection Leaves Fresh Footprints on a Canadian Island

From parish records in a French-Canadian island, researchers have uncovered what may be the most recent known instance of human evolution in response to natural selection.

By NICHOLAS WADE

The island, Île aux Coudres, lies in the St. Lawrence River 50 miles northeast of Quebec. Its church registries hold an unusually complete record of births, marriages and deaths. From this data, a team of researchers led by Emmanuel Milot and Denis Réale of the University of Quebec at Montreal have extracted the histories of women born on the island between 1799 and 1940.

Over this 140-year period, the age at which a woman had her first child - a trait that is highly heritable - fell to 22 years, from 26. Because of this change, women on average had four more children during their reproductive lifetime, the researchers report. The finding "supports the idea that humans are still evolving," the researchers write in Monday's issue of *The Proceedings of the National Academy of Sciences*.

Dr. Milot said statistical tests allowed the researchers to distinguish between the effects of natural selection and those of cultural practices affecting the age of marriage. "The common view is that evolution is a slow process," he said. "But evolutionary biologists have known for several decades that evolution can occur fast."

It was long assumed that people protected themselves from the forces of natural selection when they learned to put a roof over their heads and grow their own food. Data from the human genome in the last decade has shown this assumption is untrue: The fingerprints of natural selection are visible across at least 10 percent of the genome.

And this is selection that occurred in just the last 25,000 to 5,000 years, because the signal from older episodes of selection is muffled by constant mutation in the DNA sequence.

Geneticists examining that sequence cannot spot episodes of natural selection more recent than 5,000 years or so, unless the signal is particularly strong, because it takes many generations for a new and improved version



of a gene to sweep through a population. But evolutionary biologists believe they can detect natural selection at work in the very recent past by looking at so-called phenotypic, or bodily, data.

These data are found in large medical studies, like the Framingham heart study, in which many traits of a population are monitored over many years. Using sophisticated statistical techniques, biologists say they can distinguish traits that are changing under pressure of natural selection from both those caused by environmental effects and those due to genetic drift — the random genetic change that takes place between generations.

Summarizing the results of 14 such studies in an article last year in *Nature Reviews Genetics*, a group led by Stephen C. Stearns of Yale wrote that “the emerging picture is that selection is acting in postindustrial societies to reduce age at first reproduction in both sexes, to increase age at menopause in females and to improve traits such as total blood cholesterol that are associated with the risk of disease and mortality.”

The study by the University of Quebec biologists is a good analysis of an “extraordinary data set,” Dr. Stearns said, and is “the most recent known example of a genetic response to selection in a human population.”

“Our culture is changing and our biology is trying to keep up,” he said. “But culture changes faster — genes can’t change fast enough to keep up with iPads.”

Dr. Milot said the genetic changes in his study showed up so clearly because other factors that might cloud them had been held to a minimum by the particular social conditions on Île aux Coudres. The island was granted by royal decree to the priests who managed the Quebec seminary and was settled by 30 families who arrived between 1720 and 1773. The families took up farming, then other professions, like fishing. Throughout the period, considerable equality was maintained, and the population lacked the gradations of wealth that can influence who has how many children.

Also, because most people married locally, the island’s population became considerably inbred, despite a ban on marrying first or second cousins. These two factors, and the homogeneity of the population, left the field open for genetic effects to become prominent, Dr. Milot said.

Studies like those of Île aux Coudres can detect the hand of natural selection only in the data that happen to be recorded in church registries. But many human traits besides those of life history are probably being shaped by natural selection. Many aspects of personality are heritable, Dr. Milot said, and “it would be extremely interesting to see whether our changing societies cause modifications in the selection pressures on such traits in humans.”

Jonathan Pritchard, a population geneticist at the University of Chicago, said that “rapid adaptation of this sort is plausible in principle.” In traits that are influenced by many genes, natural selection can act quickly because it does not have to wait for a favorable new mutation to come along. All it needs to do is increase the abundance of some of the genes affecting the trait in question, a process known as a “soft sweep.” If the age of first reproduction is influenced by many different genes, “it is conceivable that selection might be extremely strong,” he said.

http://www.eurekalert.org/pub_releases/2011-10/uom-fcf100411.php

First comet found with ocean-like water

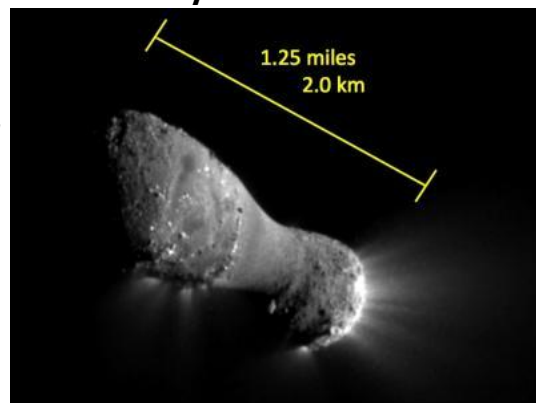
New evidence supports the theory that comets delivered a significant portion of Earth's oceans, which scientists believe formed about 8 million years after the planet itself.

ANN ARBOR, Mich. -- The findings, which involve a University of Michigan astronomer, are published Oct. 5 online in *Nature*.

"Life would not exist on Earth without liquid water, and so the questions of how and when the oceans got here is a fundamental one," said U-M astronomy professor Ted Bergin, "It's a big puzzle and these new findings are an important piece."

Bergin is a co-investigator on HiFi, the Heterodyne Instrument for the Infrared on the Hershel Space Observatory. With measurements from HiFi, the researchers found that the ice on a comet called Hartley 2 has the same chemical composition as our oceans. Both have similar D/H ratios. The D/H ratio is the proportion of deuterium, or heavy hydrogen, in the water. A deuterium atom is a hydrogen with an extra neutron in its nucleus.

This is the comet Hartley, as imaged by NASA's EPOXI spacecraft. Image courtesy of NASA



This was the first time ocean-like water was detected in a comet. "We were all surprised," Bergin said.

Six other comets HiFi measured in recent years had a much different D/H ratio than our oceans, meaning similar comets could not have been responsible for more than 10 percent of Earth's water.

The astronomers hypothesize that Hartley 2 was born in a different part of the solar system than the other six. Hartley most likely formed in the Kuiper belt, which starts near Pluto at about 30 times farther from the sun than the Earth is. The other six hail from the Oort Cloud more than 5,000 times farther out.

The source of earth's oceans has been a subject for debate among astronomers for decades. Until now, asteroids were thought to have provided most of the water. Now, however, Herschel has shown that at least one comet does have ocean-like water. "The results show that the amount of material out there that could have contributed to Earth's oceans is perhaps larger than we thought," Bergin said.

Herschel, a European Space Agency mission with NASA participation, is an orbiting telescope that allows astronomers to observe at the far-infrared wavelengths where organic molecules and water emit their chemical signatures.

The paper is called "Ocean-like water in the Jupiter-family comet 103P/Hartley 2."

<http://www.bbc.co.uk/news/magazine-15125287>

Six ways to never get lost in a city again

Many people now rely on their smartphones, sat-navs or other GPS devices to find their way around. But when these fail us, and there's no-one to ask for directions, there's a more natural way to navigate, says Tristan Gooley.

It's not every week that a massive solar flare knocks out the GPS network, but all it takes is a flat battery or a mechanical fault to hobble your automated orientation aids.

And if there's no-one around to ask and no paper map on hand, you could be in trouble.

Natural navigation may be just what you need. This involves working out which way to go without using maps, compasses or any other instruments. It relies on awareness and deduction, so does depend on retaining some awareness of direction throughout each journey.

1. TV satellite dishes

These really are the "get out of jail free" cards in an urban area. This is because the dishes point at a geostationary satellite, one that stays over the same point on the Earth's surface. In the UK there is a dominant satellite broadcaster, hence nearly all the dishes tend to point in the same direction - close to southeast. The same applies in rural areas - especially those blessed with pubs screening sport.

2. Religious buildings

From earliest times, religious buildings and sacred sites have been laid out to give clues as to direction.

Christian churches are normally aligned west-east, with the main altar at the eastern end to face the sunrise. Gravestones, too, are aligned west-east.

To find direction from a mosque, you need to go inside and look for the niche in one wall, which indicates the direction for prayer. This niche, known as al-Qibla, will be the direction of Mecca, wherever you are in the world.

And synagogues normally place the Torah Ark at the eastern end, positioned so worshippers face towards Jerusalem. (Synagogues in countries east of Israel will face west.)

3. Weathering

The prevailing winds carry rain and pollution. These then hit the buildings, leaving patterns.

The wind comes from the southwest in the UK more often than from any other direction. This results in asymmetrical weathering patterns on buildings - similar to the erosion seen in nature.

Look up, above the cleaned glass and metals of the lower floors, to the natural stone or weathered bricks higher up. Notice how the building's corners all show subtly different weathering patterns.

The contrast between southwest and northeast corners is the greatest. But the shifts in colours, where the rain and pollutants have left their mark, can be read on all sides with a little practice.

Trees, too, indicate direction, with the very tops combed over by the prevailing wind.

4. Flow of people

Pacific navigators learned to follow the birds in their search of land. They quickly realised that while an individual bird can behave eccentrically, a pair - or even better a flock - will follow a pattern.

The same is true of human beings. There is no point following an individual, you could end up anywhere. But following a crowd in the late afternoon will take you towards a station or other transport hub. In the mornings, walk against the flow to find these stations.

At lunchtime in sunny weather, crowds move from office blocks towards the open spaces of parks and rivers.

5. Road alignment

Roads do not spring up randomly, they grow to carry traffic - and the bulk of traffic is either heading into or out of a town. So the biggest roads tend to be aligned in a certain way, depending on whether you are in the centre or on the outskirts.

In the north or south of town, the major roads will tend to be aligned north/south. In the northwest or southeast, they will have a bias towards northwest/southeast. This is why road maps of big towns show a radial pattern. It is common sense, but very few people realise this when they feel lost in a big city.

6. Clouds

One of the best ways not to lose your sense of direction is to hold onto it. My favourite way of doing this in a city is to orientate myself - using some of the clues above - and then note the direction the clouds are moving.

The wind pushing the clouds will remain fairly constant, providing there's no dramatic change in the weather.

This technique really earns its keep on underground journeys, especially to a new part of town. Simply look up before you head underground, and remember the direction of the clouds. When you emerge in a strange part of the city, look up again and you'll be able to work out which way is which from the clouds overhead.

<http://www.newscientist.com/article/dn21015-zoologger-the-first-reptile-with-a-true-placenta.html>

Zoologger: The first reptile with a true placenta

This arrangement was thought to have only evolved once. It now appears that it evolved at least twice: once in mammals, and once in an African lizard

12:00 06 October 2011 by Michael Marshall

In evolution, as in life, some things are easier than others. It seems to be pretty straightforward to evolve complex eyes, which have turned up dozens of times.

Similarly, for some groups of animals it's easy to stop laying eggs and start giving birth to live young. Backboned animals have evolved live birth no fewer than 132 times, and nowadays a fifth of lizards and snakes give birth. Human mothers may disagree, but live birth is clearly not that difficult.

What is difficult, however, is nourishing unborn young the way mammals do. A female mammal allows each embryo to burrow deep into the wall of her womb, where it takes nutrients straight from her blood. This intimate arrangement was long thought to have only evolved once, in mammals.

Not so. It now appears that it evolved at least twice: once in mammals, and once in an obscure African lizard called *Trachylepis ivensii*.

Mother lizard

These lizards don't look like rule-breakers. *T. ivensii* are fairly typical skinks, one of around 1200 species. Adult females grow to 9 to 14 centimetres long, plus tail. They are rarely seen: only a few specimens have been collected. "We don't know much about them," says Daniel Blackburn of Trinity College in Hartford, Connecticut.

Blackburn began studying *T. ivensii* in earnest after his colleague Alexander Flemming of Stellenbosch University, South Africa, found nine females preserved in a museum. Blackburn and Flemming worked together to dissect them and find out how their young developed. They focused on the oviducts – tubes that run from the ovaries to the outside. Live-bearing reptiles release eggs into the oviducts, where they develop into babies before being born. The question is, how were the developing embryos fed while in the oviduct?

All live-bearing reptiles have a basic placenta, but unlike its mammalian counterpart the embryo doesn't get much food that way. It can't: although it nestles up against the oviduct wall, the embryo remains inside a remnant of eggshell that acts as a barrier. Instead, it is nourished by a large yolk.

A very few reptiles, including *T. ivensii*, break this rule. Their eggs are small, with little yolk, so they must get lots of food from their mothers via the placenta. But only *T. ivensii* allows the embryo to implant itself in the oviduct wall. "It's unprecedented," Blackburn says.

Feed me!

Blackburn and Flemming found 42 embryos preserved in the females. More advanced embryos had shed their shells and attached themselves to the oviduct wall.

It works like this. Cells on the outside of the embryo send out extensions that burrow between the cells of the oviduct wall and then swell into knobs. These knobs then produce more embryonic cells, which spread beneath the outer layer of the wall. Eventually, the original wall cells are sloughed off, and the oviduct is lined with cells from the embryo.

Lizards are moms too



Species: Trachylepis ivensii

Habitat: Angola, Zambia and the Democratic Republic of the Congo, being very hard to find

Image: Philipp Wagner

This arrangement means that embryonic cells are pressed right up against the mother's blood vessels, where they can take in lots of nutrients. That's why the eggs don't need much yolk.

But the arrangement has its problems, Blackburn says. An embryo in close contact with its mother's blood risks being attacked by her immune system. Male embryos could also be "feminised" by her sex hormones. That might explain why full-scale placental feeding has evolved so rarely.

The only reptiles that come close to *T. ivensii* belong to a South American skink called Mabuya. Their placentas are complex and transfer plenty of nutrients, and there is some evidence of embryonic cells being able to invade the oviduct wall in a limited way. Another African species, *Eumecia anchietae*, also feeds its young entirely through its placenta.

Neither shows as much intimacy as *T. ivensii*, however, and Blackburn also says their placentas are "fundamentally different". That may mean placental feeding has evolved in skinks not once, but three times. Clearly, in evolutionary terms these reptiles have the knack.

Journal reference: Journal of Morphology, DOI: 10.1002/jmor.11011

http://www.eurekalert.org/pub_releases/2011-10/uocp-aaw100611.php

Archaeologist argues world's oldest temples were not temples at all
Ancient structures uncovered in Turkey and thought to be the world's oldest temples may not have been strictly religious buildings after all, according to an article in the October issue of Current Anthropology.

Archaeologist Ted Banning of the University of Toronto argues that the buildings found at Göbekli Tepe may have been houses for people, not the gods.

The buildings at Göbekli, a hilltop just outside of the Turkish city of Urfa, were found in 1995 by Klaus Schmidt of the German Archaeological Institute and colleagues from the Şanlıurfa Museum in Turkey. The oldest of the structures at the site are immense buildings with large stone pillars, many of which feature carvings of snakes, scorpions, foxes, and other animals.

The presence of art in the buildings, the substantial effort that must have been involved in making and erecting them, and a lack of evidence for any permanent settlement in the area, led Schmidt and others to conclude that Göbekli must have been a sacred place where pilgrims traveled to worship, much like the Greek ruins of Delphi or Olympia. If that interpretation is true it would make the buildings, which date back more than 10,000 years to the early Neolithic, the oldest temples ever found.

However, Banning offers an alternative interpretation that challenges some of Schmidt's claims.

He outlines growing archaeological evidence for daily activities at the site, such as flintknapping and food preparation. "The presence of this evidence suggests that the site was not, after all, devoid of residential occupation, but likely had quite a large population," Banning said. Banning goes on to argue that the population may have been housed in the purported temples themselves. He disagrees with the idea that the presence of decorative pillars or massive construction efforts means the buildings could not have been residential space.

"The presupposition that 'art,' or even 'monumental' art, should be exclusively associated with specialized shrines or other non-domestic spaces also fails to withstand scrutiny," Banning writes. "There is abundant ethnographic evidence for considerable investment in the decoration of domestic structures and spaces, whether to commemorate the feats of ancestors, advertise a lineage's history or a chief's generosity; or record initiations and other house-based rituals."

Archaeological evidence for domestic art from the Neolithic period exists as well, Banning says, such as the wall paintings at Çatalhöyük, another archaeological site in Turkey. Banning suggests that the purported temples may instead have been large communal houses, "similar in some ways to the large plank houses of the Northwest Coast of North America with their impressive house posts and totem poles."

"If so, they would likely have housed quite large households that might provide an extremely early example of what the French anthropologist, Claude Lévi-Strauss, called 'house societies,'" Banning said. "Such societies often use house structures for competitive display, locations for rituals, and explicit symbols of social units."

Banning hopes that more excavation at the site will ultimately shed more light on how these buildings were used. In the meantime, he hopes that researchers will not automatically assume that the presence of art or decoration in structures at Göbekli and elsewhere denotes an exclusively religious building.

"It is ... likely that some of these buildings were the locus for a variety of rituals, probably including feasts, mortuary rites, magic, and initiations," he writes. "Yet there is generally no reason to presume a priori, even when these are as impressive as the buildings at Göbekli Tepe, that they were not also people's houses."

E. B. Banning, "So Fair a House: Göbekli Tepe and the Identification of Temples in the Pre-Pottery Neolithic of the Near East." Current Anthropology 52:5 (October 2011)

Marijuana component could ease pain from chemotherapy drugs

A chemical component of the marijuana plant could prevent the onset of pain associated with drugs used in chemo therapy, particularly in breast cancer patients, according to researchers at Temple University's School of Pharmacy.

The researchers published their findings, "Cannabidiol Prevents the Development of Cold and Mechanical Allodynia in Paclitaxel-Treated Female C57Bl6 Mice," in the journal *Anesthesia and Analgesia*.

The researchers developed animal models and tested the ability of the compound cannabidiol, which is the second most abundant chemical found in the marijuana plant, to relieve chemo-induced neuropathic pain, said Sara Jane Ward, research assistant professor of pharmaceutical sciences in Temple's School of Pharmacy and the study's lead author.

"We found that cannabidiol completely prevented the onset of the neuropathic, or nerve pain caused by the chemo drug Paclitaxel, which is used to treat breast cancer," said Ward, who is also a research associate professor in Temple's Center for Substance Abuse Research.

Ward said that one of cannabidiol's major benefits is that, unlike other chemicals found in marijuana such as THC, it does not produce psycho-active effects such as euphoria, increased appetite or cognitive deficits. "Cannabidiol has the therapeutic qualities of marijuana but not the side effects," she said.

Ward's research has long focused on systems in the brain that are impacted by marijuana and whether those systems could be targeted in the treatment of various disorders. "Marijuana binds to the cannabinoid receptors in the body and researchers have long been interested in whether there is therapeutic potential for targeting this receptor system," she said.

Ward became interested in this current study after attending a conference in which she learned about a pain state that is induced by chemo-therapeutic agents, especially those used to treat breast cancer, which can produce really debilitating neuropathic pain.

Cannabidiol has also demonstrated the ability to decrease tumor activity in animal models, said Ward, which could make it an effective therapeutic for breast cancer, especially if you "combined it with a chemo agent like Paclitaxel, which we already know works well."

According to Ward, there are currently about 10 clinical trials underway in the United States for cannabidiol on a range of different disorders, including cannabis dependence, eating disorders and schizophrenia. Because of this, she believes it will be easier to establish a clinical trial for cannabidiol as a therapeutic against neuropathic pain associated with chemo drugs.

In addition to Ward, Temple researchers involved in the study included Michael David Ramirez, Harshini Neelakantan and Ellen Ann Walker. The study was supported by grants from the National Institutes of Health and the Peter F. McManus Charitable Trust.

<http://www.newscientist.com/article/dn21019-diabetic-rats-cured-with-their-own-stem-cells.html>

Diabetic rats cured with their own stem cells

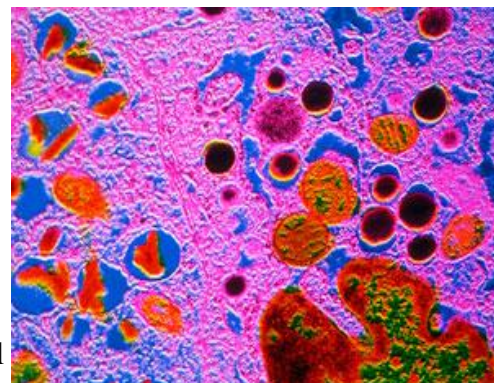
00:01 07 October 2011 by Andy Coghlan

A cure for diabetes could be sitting in our brains. Neural stem cells, extracted from rats via the nose, have been turned into pancreatic cells that can manufacture insulin to treat diabetes.

Beta cells in the pancreas produce insulin, which regulates glucose levels. People with diabetes either have type 1, in which native beta cells are destroyed by the immune system, or type 2, in which beta cells cannot produce enough insulin. To replace lost or malfunctioning beta cells, Tomoko Kuwabara of the National Institute of Advanced Industrial Science and Technology in Tsukuba Science City, Japan, and colleagues turned to neural stem cells in the brain.

Nasal extraction

First, they extracted a tiny amount of tissue from the rats' olfactory bulb, the part of the brain which deals with smell, or from the hippocampus, involved in memory. Each area is accessible through the nose, both in rats and humans. Next, the team extracted neural stem cells from the tissue and exposed them to Wnt3a – a human protein that switches on insulin production – and to an antibody that blocks a natural inhibitor of insulin production.



False-colour image of cells comprising an islet of Langerhans, the endocrine component of the human pancreas. Beta cells secreting insulin are shown in green and orange Image: CNRI/SPL

After multiplying the stem cells for two weeks, they placed them on thin sheets of collagen which act as a removable scaffold. This allowed the team to lay the sheets incorporating the cells on top of the rats' pancreas without harming the organ itself. Within a week, concentrations of insulin in the blood of both type 1 and type 2 rats that had received treatment matched those in non-diabetic rats. Elevated blood glucose concentrations also returned to normal. The cells successfully tackled diabetes for 19 weeks until researchers halted the treatment by removing the sheets of cells, after which the rats' diabetes returned.

Natural change

Crucially, the cells did not have to be genetically manipulated outside of the body.

Many other labs around the world have tried altering stem cells from other parts of the body, including the gut, the liver and blood, to change them into beta cells. But these all require alterations or genetic manipulations which could pose safety concerns when transferring the treatment to humans. Because the cells in the current study come from the same animal in which they are transplanted, they also overcome hurdles of rejection or the need for immunosuppressive drugs, such is the case when people receive donor pancreatic cells.

No manipulation

The researchers believe that it would be safe to access neural stem cells in humans. "It would be possible to extract adult neural stem cells from the olfactory bulb surgically using an endoscope," they say, adding that other groups have already done such extractions, proving that they are practical.

"The most important improvement offered by this study is the derivation of insulin-expressing cells from diabetes patients without the need for genetic manipulation," say Onur Basak and Hans Clevers of the Hubrecht Institute for Development Biology and Stem Cell Research in Utrecht, the Netherlands, in a commentary published alongside the work (EMBO Molecular Medicine, DOI: 10.1002/emmm.201100178).

"It will be essential to validate these results in available human neuronal stem cell lines as well as patient-derived olfactory bulb neural stem cells," they add.

Journal reference: EMBO Molecular Medicine, DOI: 10.1002/emmm.201100177

<http://medicalxpress.com/news/2011-10-scientists-liver-cells-neurons-technique.html>

Scientists turns liver cells directly into neurons with new technique

Fully mature liver cells from laboratory mice have been transformed directly into functional neurons by researchers at the Stanford University School of Medicine.

Medical Xpress - The switch was accomplished with the introduction of just three genes and did not require the cells to first enter a pluripotent state. It is the first time that cells have been shown to leapfrog from one fundamentally different tissue type to another. The accomplishment extends previous research by the same group, which showed in 2009 that it is possible to directly transform mouse fibroblasts, or skin cells, into neurons.

"These liver cells unambiguously cross tissue-type boundaries to become fully functional neural cells," said Marius Wernig, MD, PhD assistant professor of pathology and a member of Stanford's Institute for Stem Cell Biology and Regenerative Medicine. "Even more surprising, these cells also simultaneously silence their liver-gene expression profile. They are not hybrids; they are completely switching their identities."

The cells make the change without first becoming a pluripotent type of stem cell - a step long thought to be required for cells to acquire new identities. Wernig is the senior author of the research, published online Sept. 29 in *Cell Stem Cell*. Postdoctoral scholar Samuele Marro, PhD, is the first author of the study.

The researchers used a technique developed by Stanford bioengineer Stephen Quake, PhD, to analyze the gene expression profiles of individual hepatocytes (liver cells) and fibroblasts to show that both types of transformed cells not only begin looking and acting like true neurons, they also decisively shut down nearly all gene expression associated with their former, very different identities.

"This is fascinating," said Wernig. "We can imagine ways that the three introduced factors could stimulate neural gene expression, but how do they also down-regulate two completely unrelated donor networks — those of skin and liver cells?"

Understanding how this down-regulation works will help scientists and clinicians determine whether these so-called transdifferentiated cells can be used to learn more about diseases or even be safely used in human therapy. It would not be good, for example, if newly derived neurons began to again express skin or liver proteins. It also may help researchers understand the process of development, during which cells commit to certain fates while also turning off other potential pathways.

Wernig and Marro began investigating whether hepatocytes could transform into neurons because the fibroblasts they first transformed into neurons in 2010 are a notoriously messy groups of cells. Fibroblasts can be found in almost any organ in the body and contain mixtures of cell types. This made it extremely difficult to

identify a cell-of-origin for the resulting neurons and to figure out exactly how big of a developmental leap the cells were making.

In contrast, hepatocytes are fairly homogenous and well-defined. Developmentally speaking, they are also worlds away from neurons: Hepatocytes arise from one of three classes of embryonic tissue called the endoderm; neurons from the ectoderm. The remaining tissue, the mesoderm, is, for the most part, sandwiched between the two. To put it simply: Your innards mostly arise from endoderm, your nervous system and the outer layer of your skin from ectoderm, and your connective tissue and muscles from mesoderm. Transforming endodermal cells into ectodermal cells is a testament to the power of the transdifferentiation technique.

To accomplish the transformation of the hepatocytes, the researchers used a virus to introduce the same three genes that they used for the fibroblasts: Brn2, Asc11 and Myt11. As with the fibroblasts, the hepatocytes began to exhibit neuronal characteristics within two weeks, and express neuronal genes within three weeks. Simultaneously, the cells began to suppress the expression of liver-specific genes.

Marro and Wernig used a sophisticated cell-labeling technique to confirm that the new neurons had indeed arisen from the former liver cells, and Fluidigm dynamic polymerase chain reaction assays to analyze gene expression patterns of individual neuronal cells. They found that even “true” neurons express low levels of liver genes in the form of transcriptional noise. However, the newly differentiated neurons did express marginally higher levels of the same genes.

“Although the donor gene program is dramatically shut down, there are some remnants of their former life, like a kind of a memory,” said Wernig. “But the vast majority of expressed genes demonstrate a clear dominance of the neuronal transcription program.” Furthermore, the fact that the newly derived neurons generate electrical signals and form junctions with other neurons, and that they exhibit no residual liver function, indicates that this memory has no functional relevance, according to Wernig. *Provided by Stanford University Medical Center*

<http://www.scientificamerican.com/article.cfm?id=uranus-axial-tilt-obliquity>

Double Impact: Did 2 Giant Collisions Turn Uranus on Its Side?

A pair of giant impacts early in solar system history could reconcile the dramatic tilt of Uranus with the equatorial orbit of its satellites

By John Matson | October 7, 2011 | 10

NANTES, France - Knock, knock. That's not the start of a joke but the hard-luck history of Uranus. New research suggests that the giant planet may have suffered two massive impacts early in its history, which would account for its extreme, mysterious axial tilt.

Uranus orbits nearly on its side; its axis of rotation is skewed by 98 degrees relative to an ordinary upright orientation, perpendicular to the orbital plane. Many planetary scientists have sought to explain the odd tilt by invoking a giant impact into Uranus billions of years ago. But the giant planet has a system of moons circling its equator that would have been disrupted by such an impact.

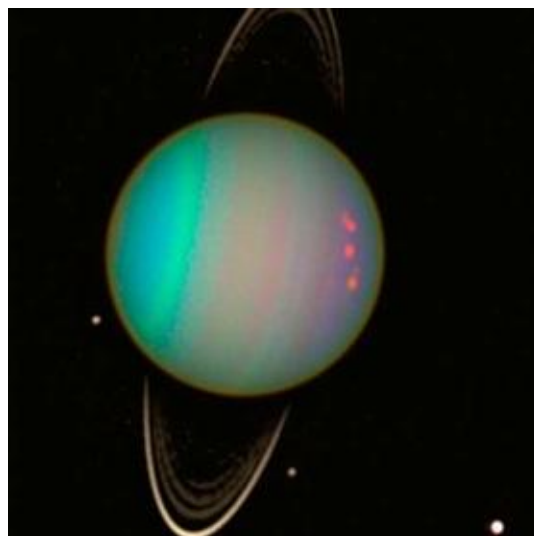
"If Uranus is suddenly tilted, the satellites keep moving like that from north pole to south pole, and [wouldn't be] equatorial at all," Alessandro Morbidelli of the Observatory of Côte d'Azur in Nice, France, reported here Thursday at a joint meeting of the American Astronomical Society Division for Planetary Sciences and the European Planetary Science Congress. [Read more planetary news from the meeting here.]

TWICE TILTED? New simulations indicate that Uranus experienced at least two large impacts, leaving the planet with its modern-day, near-sideways tilt. Image: NASA and Erich Karkoschka, University of Arizona

But what if the tilting was a more gradual process, caused not by one mammoth impact but by two somewhat smaller nudges? Simulations show that the two-strike mechanism appears to solve the problem, knocking Uranus sideways and allowing it to develop equatorially orbiting moons, Morbidelli said.

The key is that the impacts must have come very early, before Uranus's moons had coalesced from a disk of gas and dust surrounding the planet. That disk, supplemented by debris stirred up by the collisions, would have migrated around the planet to form a thin equatorial disk that gave rise to Uranus's five large moons.

In the simulations, the same sort of equatorial migration also worked for the single-impact tilt scenario, but that scenario came with one important and disqualifying caveat: the moons orbited in the wrong direction,



counter to Uranus's rotation. "If you tilt Uranus all in one shot, you produce regular satellites on the equator, but they will all be retrograde, and the satellites are actually prograde," Morbidelli said.

The only way for Uranus to have kept its moons in the right place, moving in the right direction, was to have suffered multiple giant impacts. "If we are right, Uranus was hit at least twice by big objects, about the mass of the Earth," Morbidelli said. He noted that Neptune's tilt, although only about one third that of Uranus, is also best explained by a giant impact.

"He solved the problem with the giant-impact hypothesis," said Hal Levison of the Southwest Research Institute in Boulder, Colo. "I've always been worried about this problem." But, Levison noted, "that doesn't mean that the giant-impact hypothesis is right." There are several other ways to change a planet's tilt, or obliquity, including tidal forces and resonances between a planet's spin and its orbit.

But if Uranus did suffer two large collisions, and Neptune absorbed one as well, that would indicate that massive impacts played a significant role in shaping the giant planets. That would be a surprise, given the traditional view that the gas giants grew by sweeping up smaller planetesimals. "This is quite an unconventional scenario for the formation of the giant planets, but I think that the obliquities of Uranus and Neptune point in this direction," Morbidelli said.

<http://medicalxpress.com/news/2011-10-extra-calcium-pregnancy-benefits-hypertension.html>

Extra calcium during pregnancy has no benefits, except to prevent hypertension
Most physicians instruct pregnant women to increase their calcium intake, but a new evidence review of potential benefits of calcium supplementation for mom and baby found none, except for the prevention of pregnancy-related hypertension.

Experts agree that during pregnancy, a mother's diet and nutritional status contribute significantly to the health and wellbeing of her offspring. Yet, the effects of supplementation with calcium, or the amounts to supplement, have remained unclear.

A review led by researcher Pranom Buppasiri, MD, of the department of obstetrics and gynecology at Khon Kaen University in Thailand, shows that calcium supplementation has no effect on preventing preterm birth or low infant birth weight and no effect on bone density in pregnant women. Buppasiri notes, however, that previous reviews have shown that calcium supplementation does help in the prevention of preeclampsia.

Preeclampsia is a dangerous condition marked by hypertension and protein in the urine that can develop into serious complications for the mother and baby. The definitive treatment for pre-eclampsia is delivery of the baby, often resulting in preterm and/or low birth weight babies.

More than 16,000 women participated in the 21 studies included in the review. The review did find a small difference in average infant birth weight, but the authors were unable to ascertain the clinical significance in the diverse population examined.

Buppasiri and colleagues' review appears in the latest issue of The Cochrane Library, a publication of the Cochrane Collaboration, an international organization that evaluates medical research. Systematic reviews draw evidence-based conclusions about medical practice after considering both the content and quality of existing medical trials on a topic.

Stephen Contag, MD, a perinatologist at Sinai Hospital of Baltimore's Institute of Maternal Fetal Medicine called the review confusing and said, "There is an inherent confounding effect between the two interventions in that whenever maternal hypertensive disease is prevented, preterm labor is less likely to occur." In other words, calcium supplementation might prevent preterm labor indirectly by preventing high blood pressure. He added that, "the definitive treatment for pregnancy related hypertensive disease is delivery, which often occurs preterm depending on the severity and timing of onset." Contag stated that according to current Institute of Medicine recommendations, "calcium supplementation is recommended in addition to dietary calcium intake, in order to achieve recommended daily allowance of 1,000 mg/day."

However, John McDougall, MD, an internist, nutrition expert and medical director of the McDougall Program in Santa Rosa, California, cited a July 2010 study in the British Medical Journal to support the fact that he does not prescribe calcium supplements, because they increase the risk of heart attacks and strokes.

"Certainly, taking isolated concentrated minerals, such as calcium, creates physiological imbalances in the body," McDougall said in a commentary regarding the July study. "Immediately after consuming calcium supplements, the calcium in the blood increases. Thereafter, the body must adjust to this large burden of minerals. One of the adverse effects appears to be artery damage."

Buppasiri said there were still not enough studies to draw a meaningful conclusion about supplementation. "We need more high quality studies to address this review question, especially in low calcium intake populations," he said.

More information: Buppasiri P, et al. Calcium Supplementation (other than for preventing or treating hypertension) for improving pregnancy and infant outcomes. Cochrane Database of Systematic Reviews 2011, Issue 10. Provided by Health Behavior News Service

<http://news.discovery.com/animals/paleolithic-dogs-111007.html>

Prehistoric Dog Found with Mammoth Bone in Mouth

The dogs' brains may have been used for ritualistic purposes by humans.

By Jennifer Viegas | Fri Oct 7, 2011 01:12 PM ET

The remains of three Paleolithic dogs, including one with a mammoth bone in its mouth, have been unearthed at Předmostí in the Czech Republic, according to a new Journal of Archaeological Science paper.

The remains indicate what life was like for these prehistoric dogs in this region, and how humans viewed canines. The dogs appear to have often sunk their teeth into meaty mammoth bones. These weren't just mammoth in terms of size, but came from actual mammoths. In the case of the dog found with the bone in its mouth, the researchers believe a human inserted it there after death.



The fossilized dog skull with the mammoth bone sticking out the front. Mietje Germonpré

"The thickness of the cortical bone shows that it is from a large mammal, like a rhinoceros, steppe bison or mammoth," lead author Mietje Germonpré told Discovery News. "At Předmostí, mammoth is the best represented animal, with remains from more than 1,000 individuals, so it is probable that the bone fragment is from a mammoth."

Germonpré, a paleontologist at the Royal Belgian Institute of Natural Sciences, and colleagues Martina Laznickova-Galetova and Mikhail Sablin, first studied the remains, focusing on the skulls, to see what animals they represented. In the fossil record, there is sometimes controversy over what is a wolf, dog or other canid.

"These skulls show clear signs of domestication," Germonpré said, explaining they are significantly shorter than those of fossil or modern wolves, have shorter snouts, and noticeably wider braincases and palates than wolves possess. She described them as large, with an estimated body weight of just over 77 pounds. The shoulder height was at least 24 inches. "The shape of their skull resembles that of a Siberian husky, but they were larger and heavier than the modern Husky," she said.

The dogs died when they were between 4 and 8 years old, suffering from numerous broken teeth during their lifetimes. Based on what is known of the human culture at the site, the researchers believe these dogs "were useful as beasts of burden for the hauling of meat, bones and tusks from mammoth kill sites and of firewood, and to help with the transport of equipment, limiting the carrying costs of the Předmostí people."

Since mammoth meat was likely the food staple, the scientists further believe that the surplus meat "would have been available to feed the dogs." The dog skulls show evidence that humans perforated them in order to remove the brain. Given that better meat was available, the researchers think it's unlikely the brains served as food. Instead, based on these archaeological finds and the ethnographic record, it's possible that the body manipulation after death held ritual importance.

"Among many northern indigenous peoples, it was believed that the head contains the spirit or soul," Germonpré explained. "Some of these peoples made a hole in the braincase of the killed animal so that the spirit might be released." The mammoth bone in the dog's mouth could signify "that the dog was 'fed' to accompany the soul of the dead person on its journey."

Rob Losey, an associate professor of anthropology at the University of Alberta, told Discovery News that the new study is "very convincing," and shows "quite clearly that the dog domestication process was underway thousands of years earlier than previously thought." He added, "The distinctive treatment given some of the remains also is compelling, and this indicates to me that a special connection had developed between people and some canids quite early on -- long prior to any good evidence for dogs being buried."

http://www.eurekalert.org/pub_releases/2011-10/wt-bir100611.php

Brain imaging reveals why we remain optimistic in the face of reality

For some people, the glass is always half full.

Even when a football fan's team has lost ten matches in a row, he might still be convinced his team can reverse its run of bad luck. So why, in the face of clear evidence to suggest to the contrary, do some people remain so optimistic about the future?

In a study published today in Nature Neuroscience, researchers at the Wellcome Trust Centre for Neuroimaging at UCL (University College London) show that people who are very optimistic about the

outcome of events tend to learn only from information that reinforces their rose-tinted view of the world. This is related to 'faulty' function of their frontal lobes.

People's predictions of the future are often unrealistically optimistic. A problem that has puzzled scientists for decades is why human optimism is so pervasive, when reality continuously confronts us with information that challenges these biased beliefs. "Seeing the glass as half full rather than half empty can be a positive thing – it can lower stress and anxiety and be good for our health and well-being," explains Dr Tali Sharot. "But it can also mean that we are less likely to take precautionary action, such as practising safe sex or saving for retirement. So why don't we learn from cautionary information?"

In this new study, Dr Sharot and Professor Ray Dolan from the Wellcome Trust Centre for Neuroimaging, together with Christoph Korn from the Berlin School of Mind and Brain have shown that our failure to alter optimistic predictions when presented with conflicting information is due to errors in how we process the information in our brains.

Nineteen volunteers were presented with a series of negative life events, such as car theft or Parkinson's disease, whilst lying in a functional magnetic resonance imaging (fMRI) scanner, which measures activity in the brain. They were asked to estimate the probability that this event would happen to them in the future. After a short pause, the volunteers were told the average probability of this event to occur. In total, the participants saw eighty such events.

After the scanning sessions, the participants were asked once again to estimate the probability of each event occurring to them. They were also asked to fill in a questionnaire measuring their level of optimism.

The researchers found that people did, in fact, update their estimates based on the information given, but only if the information was better than expected. For example if they had predicted that their likelihood of suffering from cancer was 40%, but the average likelihood was 30%, they might adjust their estimate to 32%. If the information was worse than expected – for example, if they had estimated 10% – then they tended to adjust their estimate much less, as if ignoring the data.

The results of the brain scans suggested why this might be the case. All participants showed increased activity in the frontal lobes of the brain when the information given was better than expected, this activity actively processed the information to recalculate an estimate. However, when the information was worse than estimated, the more optimistic a participant was (according to the personality questionnaire), the less efficiently activity in these frontal regions coded for it, suggesting they were disregarding the evidence presented to them.

Dr Sharot adds: "Our study suggests that we pick and choose the information that we listen to. The more optimistic we are, the less likely we are to be influenced by negative information about the future. This can have benefits for our mental health, but there are obvious downsides. Many experts believe the financial crisis in 2008 was precipitated by analysts overestimating the performance of their assets even in the face of clear evidence to the contrary."

'Understanding the brain' is one of the Wellcome Trust's key strategic challenges. At the Wellcome Trust Centre for Neuroimaging, clinicians and scientists study higher cognitive function to understand how thought and perception arise from brain activity, and how such processes break down in neurological and psychiatric disease.

Commenting on the study, Dr John Williams, Head of Neuroscience and Mental Health at the Wellcome Trust, said: "Being optimistic must clearly have some benefits, but is it always helpful and why do some people have a less rosy outlook on life? Understanding how some people always manage to remain optimistic could provide useful insights into happens when our brains do not function properly."

The research was funded by the Wellcome Trust, the British Academy and the German Academic Exchange Service.

<http://medicalxpress.com/news/2011-10-antiretroviral-therapy-tripled-proportion-adults.html>

Antiretroviral therapy has tripled the proportion of adults achieving undetectable levels of HIV

Almost one in five patients achieved undetectable levels of HIV in 2000 and this increased substantially to nearly three in five patients in 2009

Over the past decade in western Europe there has been a dramatic improvement in the ability of antiretroviral therapy to keep HIV under control in adults with virological failure to drugs from all three of the original antiretroviral classes, and an accompanying decrease in the rates of AIDS, according to a study published Online First in *The Lancet Infectious Diseases*. The authors claim that this effect is probably the result of several new drugs being introduced over the same period that are more tolerable, easier to use, and active against virus resistant to typical first-line and second-line drugs.

Since 1998, all patients have been recommended to start antiretroviral therapy (ART) with three or more drugs from two or more different classes in order to significantly reduce viral load (the amount of virus in the

blood) and to suppress HIV replication and the development of drug resistance. However, until recently, limited treatment options were available for individuals who developed resistance to drugs from each of the three original classes, known as triple-class virological failure (TCVF).

To assess whether there has been an improvement in outcomes for people with TCVF over the past decade, the Pursuing Later Treatment Option II (PLATO II) project investigators analysed data from the COHERE database (a collaboration of 33 observational studies of HIV in Europe). The analysis included 91 764 adults, of whom 2476 experienced TCVF.

Modelling was used to assess trends in virological suppression (a viral load under 500 copies per mL) after controlling for factors that could affect the likelihood of virological response including sex, mode of transmission, age, presence of AIDS, and CD4 count. The incidence of AIDS or death after TCVF was also calculated.

Almost one in five patients achieved undetectable levels of HIV (a viral load under 50 copies per mL) after TCVF in 2000 and this increased substantially to nearly three in five patients in 2009. The authors note that the trend for improved virological outcome was strongest in 2008 and 2009, soon after four new drugs were approved in Europe. The incidence of any AIDS event declined from 7.7 per 100 person-years between 2000 and 2002 to 2.3 in 2008 and 1.2 in 2009.

The authors say: "Whether the improving trend, or even the current rate of viral suppression in 2009, can be sustained in the future is unclear. Continued improvement will likely need continued development of new drugs, which are active against virus with resistance to existing drugs."

In a Comment, Jens Lundgren from Copenhagen University Hospital and Jeff Lazarus from Copenhagen University, Copenhagen, Denmark caution: "The results presented by the PLATO II collaboration should not lead to complacency. The number of people with resistant HIV infection will increase as the number of people receiving ART increases...Of particular worry is that the pace of clinical programmes of HIV-drug development has slowed down in the past couple of years."

They also stress the need for access to alternative, less toxic, and more affordable drugs in sub-Saharan Africa and Eastern Europe: "As access to ART is scaled up, a sizeable proportion of people living with HIV in these regions will live for extended periods on virologically failing ART. This scenario allows for renewed progression of their HIV condition and the transmission of resistant HIV to others. Recognition of the problem and innovation to addressing it are vital to the response."

More information: Paper online: [http://www.thelancet ... 1473-3099\(11\)70248-1/abstract](http://www.thelancet.com/doi/full/10.1016/S0140-6736(11)70248-1) Provided by Lancet

http://www.eurekalert.org/pub_releases/2011-10/gsoa-gkl100611.php

Giant kraken lair discovered

Long before whales, the oceans of Earth were roamed by a very different kind of air-breathing leviathan.

Boulder, CO, USA - Snaggle-toothed ichthyosaurs larger than school buses swam at the top of the Triassic Period ocean food chain, or so it seemed before Mount Holyoke College paleontologist Mark McMenemy took a look at some of their remains in Nevada. Now he thinks there was an even larger and more cunning sea monster that preyed on ichthyosaurs: a kraken of such mythological proportions it would have sent Captain Nemo running for dry land. McMenemy will be presenting the results of his work on Monday, 10 October at the Annual Meeting of The Geological Society of America in Minneapolis.



"Specimen U" illustrates a fossil bed showing shonisaur vertebral disks arranged in curious linear patterns with almost geometric regularity. The arranged vertebrae resemble the pattern of sucker discs on a cephalopod tentacle, with each vertebra strongly resembling a coleoid sucker. Credit: Used with permission of Mark McMenemy.

The evidence is at Berlin-Ichthyosaur State Park in Nevada, where McMenemy and his daughter spent a few days this summer. It's a site where the remains of nine 45-foot (14-meter) ichthyosaurs, of the species *Shonisaurus popularis* can be found. These were the Triassic's counterpart to today's predatory giant squid-eating sperm whales. But the fossils at the Nevada site have a long history of perplexing researchers, including the world's expert on the site: the late Charles Lewis Camp of U.C. Berkeley.

"Charles Camp puzzled over these fossils in the 1950s," said McMenemy. "In his papers he keeps referring to how peculiar this site is. We agree, it is peculiar." Camp's interpretation was that the fossils probably represented death by an accidental stranding or from a toxic plankton bloom. But no one had ever been able to

prove that the beasts died in shallow water. In fact more recent work on the rocks around the fossils suggest it was a deep water environment, which makes neatly arranged carcasses even more mysterious.

This question - shallow or deep ocean death - is what attracted McMenamini to the site.

"I was aware that anytime there is controversy about depth, there is probably something interesting going on," McMenamini said. And when they arrived at the remote state park and started looking at the fossils, McMenamini was struck by their strangeness. "It became very clear that something very odd was going on there," said McMenamini. "It was a very odd configuration of bones."

First of all, the different degrees of etching on the bones suggested that the shonisaur were not all killed and buried at the same time. It also looked like the bones had been purposefully rearranged. That it got him thinking about a particular modern predator that is known for just this sort of intelligent manipulation of bones.

"Modern octopus will do this," McMenamini said. What if there was an ancient, very large sort of octopus, like the kraken of mythology. "I think that these things were captured by the kraken and taken to the midden and the cephalopod would take them apart."

In the fossil bed, some of the shonisaur vertebral disks are arranged in curious linear patterns with almost geometric regularity, McMenamini explained. The proposed Triassic kraken, which could have been the most intelligent invertebrate ever, arranged the vertebral discs in double line patterns, with individual pieces nesting in a fitted fashion as if they were part of a puzzle. Even more creepy: The arranged vertebrae resemble the pattern of sucker discs on a cephalopod tentacle, with each vertebra strongly resembling a coleoid sucker. In other words, the vertebral disc "pavement" seen at the state park may represent the earliest known self portrait.

But could an octopus really have taken out such huge swimming predatory reptiles? No one would have believed such a tale until the staff of the Seattle Aquarium set up a video camera at night a few years ago to find out what was killing the sharks in one of their large tanks. What they were shocked to discover was that a large octopus they had in the same tank was the culprit. The video of one of these attacks is available on the web to anyone who uses the search terms "shark vs octopus."

"We think that this cephalopod in the Triassic was doing the same thing," said McMenamini. Among the evidences of the kraken attacks are many more ribs broken in the shonisaur fossils than would seem accidental and the twisted necks of the ichthyosaurs. "It was either drowning them or breaking their necks."

Of course, it's the perfect Triassic crime because octopuses are mostly soft-bodied and don't fossilize well. Only their beaks, or mouth parts, are hard and the chances of those being preserved nearby are very low. That means the evidence for the murderous Kraken is circumstantial, which may leave some scientists rather skeptical. But McMenamini is not worried. "We're ready for this," he said. "We have a very good case."

<http://www.physorg.com/news/2011-10-siberian-region-yeti.html>

Siberian region 'confirms Yeti exists'

A Russian region in Siberia on Monday confidently proclaimed that its mountains are home to yetis after finding "indisputable proof" of the existence of the hairy beasts in an expedition.

The local administration of the Kemerovo region in the south of Siberia said in a statement on its website that footprints and possibly even hair samples belonging to the yeti were found on the research trip to its remote mountains.

"During the expedition to the Azasskaya cave, conference participants gathered indisputable proof that the Shoria mountains are inhabited by the 'Snow Man'," the Kemerovo region administration said in a press-release.

The expedition was organised after Kemerovo's governor invited researchers from the United States, Canada, and several other countries to share their research and stories of encounters with the creature at a conference.

"They found his footprints, his supposed bed, and various markers with which the yeti marks his territory," the statement said. The collected "artifacts" will be analysed in a special laboratory, it said.

Yetis, or Abominable Snowmen, are hairy ape-like creatures of popular myth, that are generally held to inhabit the Himalayas. But some believe Russia also holds a population of yetis, which it calls Snow Men, in remote areas of Siberia.

Kemerovo region's Shoria is a sparsely populated territory in Western Siberia that has historically been a territory of coal and metal mining. The region, the administrative center of Kuznetsk coal basin, has pursued the elusive Yeti for several years as it tries to develop tourism into its mostly industrial economy.

Considering the latest findings, the region may "create a special research center to study the Yeti" in the regional university and "create a journal" dedicated to the science of the Yeti, the administration's statement said. (c) 2011 AFP