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Selenium deficiency may cause cardiomyopathy post-gastric bypass

Case reports highlight importance of vitamin and mineral supplementation after bariatric surgery

Las Vegas, NV - Non-compliance with vitamin and mineral supplementation protocols after bariatric surgery could lead to nutritional deficiencies and related health complications, such as heart damage, according to two separate case reports unveiled today at the American College of Gastroenterology's (ACG) 77th Annual Scientific meeting in Las Vegas.

Case Report 1: "Malnutrition Secondary to Non-Compliance with Vitamin and Mineral Supplements after Gastric Bypass Surgery: Complex Problem, Simple Solution"

Multivitamin supplementation is considered the standard of care for any patient undergoing gastric bypass, according to researchers from the University of Missouri who report a case of a non-compliant patient who failed to maintain regular follow-up after undergoing bariatric surgery leading to severe vitamin and mineral deficiencies managed by a multidisciplinary approach.

In this case, a 38-year old female patient underwent Roux-en-Y (RYGB) gastric bypass surgery but had limited follow-up during the five years since her surgery when she presented with several weeks of fatigue. She lost nearly 104 pounds since her surgery and was poorly compliant with her vitamin and mineral supplements, according to co-investigator Hazem Hammad, M.D.

"When she came in for medical care she was pale and had a slight soft ejection systolic murmur," said Dr. Hammad, who noted that she had hemoglobin of 4.7 g/dL and marked mineral and vitamin deficiencies, including low levels of Vitamin B12, Vitamin D, Zinc, and Iron.

After receiving counseling about the crucial benefits from long term follow-up and compliance with vitamin supplements, the patient was discharged to complete an IV iron supplementation treatment course and to follow up with a bariatric surgery multidisciplinary center, according to the case report.

Two weeks following discharge she received additional counseling from her primary care physician and was given a handout that outlined vitamin supplementation following bariatric surgery along with written information that included how to obtain bariatric vitamins via website, phone and from pharmacies.

Three months following discharge laboratory tests revealed an increase in hemoglobin to 10.8 g/dL and an improvement in her vitamins and mineral deficiency status.

"The pre- and post-operative management of bariatric surgery patients is clearly multidisciplinary. United States guidelines define the primary team as comprising the bariatric surgeon, the obesity specialist and the dietitian," said Dr. Hammad. "Primary care physicians, however, have a significant role in managing and following these patients by providing crucial patient education and support as illustrated in our case."

Selenium Deficiency Causing Cardiomyopathy in a Patient with Gastric Bypass Surgery

In a separate case report, Mustafa Huseini, M.D., Naeem Raza, M.D. and their colleagues from the Geisinger Medical Center in Danville, PA reported that although rare in developed countries, selenium deficiency may occur in individuals with chronic malabsorptive states such as patients with history of gastric bypass, and long term selenium-deficient parenteral nutrition.

"Selenium is an essential trace element that plays an integral role in normal myocardial function so supplementation may be beneficial for individuals who are at risk of low absorption, such as gastric bypass patients," said Dr. Huseini.

He described the case of a 39 year- female who underwent gastric bypass 7 years before presenting to the emergency department for evaluation of change in mental status, generalized weakness and several days of poor oral intake.

On initial evaluation patient was noted to be hypotensive and in mild respiratory distress. After 2 days of hospital admission, she developed respiratory and circulatory collapse requiring endotracheal intubation and mechanical ventilation. A 2D echocardiogram showed a left ventricular ejection fraction of less than 20%. A cardiac catheterization revealed non-obstructive coronary artery disease. Nutritional evaluation revealed decreased levels of selenium (29 mcg/L ; Normal values: 63-160 mcg/L).

"After adequate supplementation with selenium, cardiac function improved and a repeat 2D echocardiogram demonstrated normalized ejection fraction of 55 percent," said Dr. Huseini. "This case emphasizes the role of considering selenium deficiency as a reversible cause of unexplained cardiomyopathy in patients with gastric bypass besides otherwise impaired nutritional status."

http://www.eurekalert.org/pub_releases/2012-10/acoc-ane101612.php

Antibiotics not effective for cough due to 'common cold' in children

New research suggests that antibiotics are not effective in treating cough due to the common cold in children.

The study, presented at CHEST 2012, the annual meeting of the American College of Chest Physicians, found that when children with acute cough were treated with either antitussive medication or antibiotics, antibiotics alone showed a lower percentage of cough resolution.

"In our experience, antibiotics are often prescribed by the general practitioner to treat cough in children, many times to pacify parents," said lead study author Francesco de Blasio, MD, FCCP, Clinic Center Private Hospital, Naples, Italy. "However, antibiotics show very little effectiveness at treating cough due to your average head cold."

To understand how antibiotics were being used in a clinical pediatric setting, Dr. de Blasio and colleagues from the University of Bologna and Dompé SPA in Italy observed the treatment and outcomes of 305 children who required pediatric consultation due to acute cough from the common cold. Of the children, 89 received antibiotics only, while 38 received a combination of antibiotics and antitussives; central (codeine and cloperastine) in 16 cases, and peripheral (levodropropizine) in 22 children. Forty-four and 79 children received only central or peripheral antitussives, respectively, without antibiotics; 55 children did not receive medication. Observational results showed no difference in percentage of cough resolution between children treated with antitussive alone vs children receiving a combination of antibiotics and antitussives. On the contrary, children treated with antibiotics only had a lower percentage of cough resolution than children treated with antitussive only. Furthermore, the use of the peripheral antitussive levodropropizine demonstrated a significant beneficial effect in terms of cough resolution compared with centrally acting antitussive drugs (47% vs28%).

"Few drugs are effective as cough suppressants, and antibiotics are no more effective in relieving cough than the use of no medication," he added. "However, peripheral antitussives, such as levodropropizine, appear to be the best option at relieving cough."

Dr. de Blasio's results support the American College of Chest Physicians evidence-based guidelines for the diagnosis and management of cough, published in the journal CHEST in 2006, which recommend the use of peripheral antitussives for certain types of cough. Although antibiotics may not be an effective therapy for cough, they can be useful in treating underlying infections that may produce cough, adds Dr. de Blasio. But he warns that antibiotics should not be overused. "Using antibiotics as a treatment for cough without suspected infection is unnecessary and can be harmful," explained Dr. de Blasio. "Repeated use of antibiotics, especially when they are ineffective, can lead to adverse allergic reactions or a resistance to the medications."

"As parents, it is difficult to watch our children suffering from a terrible cough, but turning to antibiotics is not always the answer," said ACCP President-Elect Darcy D. Marciniuk, MD, FCCP. "Depending on the underlying cause of the cough, a health-care professional can recommend the best treatment options for a child, which, in some cases, may be no treatment."

http://www.eurekalert.org/pub_releases/2012-10/haog-ico102212.php

Immune cells of the blood might replace dysfunctional brain cells

In certain situations monocytes can enter the brain and contribute to tissue repair or disease progression

The immune system is comprised of multiple cell types each capable of specialized functions to protect the body from invading pathogens and promote tissue repair after injury. One cell type, known as monocytes, circulates throughout the organism in the blood and enters tissues to actively phagocytose (eat!) foreign cells and assist in tissue healing. While monocytes can freely enter most bodily tissues, the healthy, normal brain is different as it is sequestered from circulating blood by a tight network of cells known as the blood brain barrier. Thus, the brain must maintain a highly specialized, resident immune cell, known as microglia, to remove harmful invaders and respond to tissue damage.

In certain situations, such as during disease, monocytes can enter the brain and also contribute to tissue repair or disease progression. However, the potential for monocytes to actively replace old or injured microglia is under considerable debate. To address this, Nicholas Varvel, Stefan Grathwohl and colleagues from the German Center for Neurodegenerative Diseases (DZNE) Tübingen and the Hertie Institute for Clinical Brain Research in Tübingen used a transgenic mouse model in which almost all brain microglia cells (>95%) can be removed within two weeks. This was done by introducing a so-called suicide gene into microglia cells and administering a pharmaceutical agent that leads to acute death of the cells. Surprisingly, after the ablation of the microglia, the brain was rapidly repopulated by blood-circulating monocytes. The monocytes appeared similar, but not identical to resident microglia. The newly populated monocytes, evenly dispersed throughout the brain,

responded to acute neuronal injury and other stimuli - all activities normally assumed by microglia. Most interestingly, the monocytes were still present in the brain six months - nearly a quarter of the life of a laboratory mouse - after initial colonization.

These studies now published in PNAS provide evidence that blood-circulating monocytes can replace brain resident microglia and take over the essential immune surveillance of the brain. Furthermore, the findings highlight a strong homeostatic mechanism to maintain a resident immune cell within the brain. The observation that the monocytes took up long-term residence in the brain raises the possibility that these cells can be utilized to deliver therapeutic agents into the diseased brain or replace microglia when they become dysfunctional. Can monocytes be exploited to combat the consequences of Alzheimer's disease and other neurodegenerative diseases? The scientists and their colleagues in the research groups headed by Mathias Jucker are now following exactly this research avenue.

Original publication: "Microglial repopulation model reveals a robust homeostatic process for replacing CNS myeloid cells", Nicholas H. Varvel, Stefan A. Grathwohl, Frank Baumann, Christian Liebig, Andrea Bosch, Bianca Brawek, Dietmar R. Thal, Israel F. Charo, Frank L. Heppner, Adriano Aguzzi, Olga Garaschuk, Richard M. Ransohoff, and Mathias Jucker, *Proceedings of the National Academy of Sciences (PNAS)*: www.pnas.org/cgi/doi/10.1073/pnas.1210150109

http://www.eurekalert.org/pub_releases/2012-10/uog-ams102212.php

Aspirin may slow the decline in mental capacity among elderly patients
A fourth of an aspirin daily may slow the decline in intellectual capacity among elderly individuals with high cardiovascular risk.

A daily dose of acetylsalicylic acid equivalent to a fourth of an aspirin may slow the decline in intellectual capacity among elderly individuals with high cardiovascular risk. This is shown in a study by Sahlgrenska Academy, University of Gothenburg, Sweden.

Researchers at Sahlgrenska Academy, University of Gothenburg, over a five year period studied how intellectual capacity changes among 681 elderly women (70 to 92 years) with heightened risk of suffering from a heart attack, vascular spasm or stroke. Of the 681 women, 129 received a low daily dose of acetylsalicylic acid, equivalent to a fourth of an aspirin, to prevent heart disease. The Gothenburg study shows that acetylsalicylic acid also slowed decline in brain capacity among the elderly women.

In the study, published in British Medical Journal Open, the women underwent various tests to measure their physical health and intellectual capacity, such as language and memory tests. "At the end of the five year examination period mental capacity had declined among all the women and the portion that suffered from dementia was equally large in the entire group. However, the decline in brain capacity was significantly less and occurred at a slower pace among the women who received acetylsalicylic acid," says Silke Kern, researcher at Sahlgrenska Academy.

The effect remained even when age, genetic factors and use of anti-inflammatory drugs were taken into account. In addition to preventing heart disease, acetylsalicylic acid has been shown to be effective against cancer according to several scientific studies. It is common practice in many countries to treat women at risk for heart disease with a small dose of acetylsalicylic acid – but not in Sweden.

Silke Kern emphasizes that the study is an observational study and that more research is necessary before any definitive conclusions can be made. "Our results indicate that acetylsalicylic acid may protect the brain, at least among women at high risk for a heart attack or stroke. However, we do not know the long term effects of routine treatment. We certainly do not want to encourage the elderly to self-medicate with aspirin to avoid dementia," she states. The research group in Gothenburg has now started a follow-up study that will follow the older women for an additional five years.

The study Does low-dose acetylsalicylic acid prevent cognitive decline in women with high cardiovascular risk? A 5-year follow-up of a non-demented population-based cohort of Swedish elderly women was published in BJM Open on October 3, 2012. Link to the article: <http://bmjopen.bmj.com/content/2/5/e001288.long>

http://www.eurekalert.org/pub_releases/2012-10/uoic-cfm102212.php

Crusty foods may worsen heart problems associated with diabetes
Study suggests avoiding cooking that produces crusty bits, if you have diabetes and know you're at risk for cardiovascular disease

URBANA – A University of Illinois study suggests avoiding cooking methods that produce the kind of crusty bits you'd find on a grilled hamburger, especially if you have diabetes and know you're at increased risk for cardiovascular disease because of your diagnosis.

"We see evidence that cooking methods that create a crust - think the edge of a brownie or the crispy borders of meats prepared at very high temperatures - produce advanced glycation end products (AGEs). And AGEs are associated with plaque formation, the kind we see in cardiovascular disease," said Karen Chapman-Novakofski, a U of I professor of nutrition.

For years nutrition experts have advised people with diabetes to bake, broil, or grill their food instead of frying it, she said. "That's still true, but if you have diabetes, you should know that AGEs - byproducts of food preparation methods that feature very high, intense, dry heat - tend to end up on other tissues in the body, causing long-term damage," she added.

If you're fighting this vascular buildup anyway, Chapman-Novakofski thinks that consuming products containing AGEs could worsen the cardiovascular complications of diabetes.

In the U of I study, the scientists compared the 10-day food intake of 65 study participants in two ethnic groups: Mexicans (who have higher rates of diabetes and a greater risk of complications from the disease) and non-Hispanic whites.

"We found that people with higher rates of cardiovascular complications ate more of these glycated products. For each unit increase in AGEs intake, a study participant was 3.7 times more likely to have moderate to high risk for cardiovascular disease," said Claudia Luevano-Contreras, first author of the study.

The study showed that non-Hispanic whites had a higher intake of AGEs, and they consumed more saturated fats. However, the association between AGEs and cardiovascular disease was stronger than for saturated fats and heart disease, she said.

Eating less saturated fat and more fruits, vegetables, and fiber are important for people with diabetes, but this study shows that food preparation may be important too, she added.

"AGEs are higher in any kind of meat, but especially in ground meat," she said. "If you put hamburgers or brats on the grill, you'll likely have a higher AGEs content than if you chose a whole cut of meat, say round steak or chicken," said Chapman-Novakofski. Boiling or stewing meat would reduce your AGEs intake further. And scrambling an egg with cooking spray instead of frying it leads to a significant reduction in AGEs, she added. The scientists said more research is needed before definite recommendations can be made. They are planning another study in which they'll examine past AGEs intake of diabetes patients.

"These findings are preliminary, but they give us ample reason to further explore the association between AGEs and cardiovascular risk among people with diabetes," Chapman-Novakofski noted.

The study is available online in the International Journal of Food Sciences and Nutrition. Co-authors are Claudia Luevano-Contreras of the University of Illinois and Eugenia Garay-Sevilla and Monica Preciado-Puga of the University of Guanajuato, Mexico. Partial funding was provided by the National Council for Science and Technology of Mexico (CONACYT).

http://www.eurekalert.org/pub_releases/2012-10/ncsu-ara102212.php

Additive restores antibiotic effectiveness against MRSA

Researchers have increased the potency of a compound that reactivates antibiotics against MRSA

Researchers from North Carolina State University have increased the potency of a compound that reactivates antibiotics against methicillin-resistant *Staphylococcus aureus* (MRSA), an antibiotic-resistant form of *Staphylococcus* that is notoriously difficult to treat. Their improved compound removes the bacteria's antibiotic resistance and allows the antibiotic to once again become effective at normal dosage levels.

NC State chemist Christian Melander had previously proven the effectiveness of a 2-aminoimidazole compound in reactivating antibiotics against resistant bacterial strains. However, the original compound was not potent enough. In his latest work, described in a paper appearing in *Angewandte Chemie*, Melander, research assistant professor Roberta Worthington and graduate student Tyler Harris have solved the potency issue, bringing them one step closer to in vivo testing.

"You measure antibiotic effectiveness by growing bacteria in the presence of an antibiotic," Melander says.

"The concentration you typically want to observe is about one microgram per milliliter or less of the antibiotic to halt bacterial growth. At that point the bacterial strain is considered susceptible to and treatable by that antibiotic. If a higher concentration of antibiotic is required to halt bacterial growth, the bacterial strain in question is considered untreatable. Some of the MRSA strains we work with require 512 micrograms per milliliter of the antibiotic of choice to control growth – 500 times over the limit. Adding our compound brought the level down to one microgram per milliliter again."

The compound works by short-circuiting the bacteria's ability to mount a defense against the antibiotic. When antibiotics interact with bacteria, receptors on the surface of the bacteria identify the antibiotic as a threat and the bacteria can then choose what to do to survive. MRSA either creates a biofilm or makes genetic changes that prevent the antibiotic from disrupting its cell structure. According to Melander, "We believe that our compound renders the bacteria unable to recognize the antibiotic as a threat, essentially stopping the defensive process before it can begin."

The work was funded by a grant from the U.S. Department of Defense, Defense Medical Research and Development Program.

Note to editors: Abstract of the work follows

"Potent Small-Molecule Suppression of Oxacillin Resistance in Methicillin-Resistant Staphylococcus aureus"

Authors: Tyler L. Harris, Robert J. Worthington and Christian Melander, North Carolina State University

Published: *Angewandte Chemie*

Abstract:

The emergence of resistance to multiple antimicrobial agents in pathogenic bacteria is a significant global public health threat and causes considerable patient mortality and morbidity. In the United States, methicillin-resistant *Staphylococcus aureus* (MRSA) accounts for 80% of all hospital-acquired *S. aureus* infections. In 2005, almost 95 000 people acquired MRSA infections in the United States, of which nearly 19 000 people died - more than die annually from HIV/AIDS, emphysema, Parkinsons disease, and homicide combined. Furthermore, MRSA infections, which are traditionally only observed among hospitalized patients, have now become prevalent outside of the hospital setting, with the emergence of community-associated MRSA (CA-MRSA). In the USA, the USA300 clone is the most prevalent CA-MRSA clone. β -Lactam antibiotics have typically been the most effective drugs for the treatment of infections caused by staphylococci; however, increasing occurrence of resistance means that they are often no longer efficacious.

<http://www.sciencedaily.com/releases/2012/10/121022081141.htm>

Unique Feature of HIV Helps Create Antibodies, Researchers Discover

A unique change in the outer covering of the virus found in two HIV infected South African women enabled them to make potent antibodies which are able to kill up to 88 percent of HIV types from around the world.

ScienceDaily (Oct. 22, 2012) - A new AIDS study, published Oct. 22 in the journal, *Nature Medicine*, describes how a unique change in the outer covering of the virus found in two HIV infected South African women enabled them to make potent antibodies which are able to kill up to 88% of HIV types from around the world. The ground-breaking discovery suggests an important new approach that could be useful in making an AIDS vaccine.

The study, performed by members of the Centre for the Aids Programme of Research in South Africa (CAPRISA) consortium, involves scientists from Wits University, the National Institute for Communicable Diseases (NICD) in Johannesburg, the University of KwaZulu-Natal and the University of Cape Town, who has been studying, over the last five years, how certain HIV-infected people develop very powerful antibody responses.

These antibodies are referred to as broadly neutralising antibodies because they kill a wide range of HIV types from different parts of the world. This CAPRISA team initially discovered that two KwaZulu-Natal women, one of whom participated in the CAPRISA 004 tenofovir gel study, could make these rare antibodies.

Through long-term follow-up laboratory studies on these two women, the team led by Wits researchers and Centre for HIV and STI at the National Institute for Communicable Diseases of the National Health Laboratory Service based scientists Dr Penny Moore and Professor Lynn Morris, discovered that a sugar (known as a glycan) on the surface protein coat of the virus at a specific position (referred to as position 332) forms a site of vulnerability in the virus and enables the body to mount a broadly neutralizing antibody response.

"Understanding this elaborate game of 'cat and mouse' between HIV and the immune response of the infected person has provided valuable insights into how broadly neutralizing antibodies arise," says Moore.

Morris, Head of AIDS Research at the NICD explained: "We were surprised to find that the virus that caused infection in many cases did not have this antibody target on its outer covering. But over time, the virus was pressured by body's immune reaction to cover itself with the sugar that formed a point of vulnerability, and so allowed the development of antibodies that hit that weak spot."

"Broadly neutralising antibodies are considered to be the key to making an AIDS vaccine. This discovery provides new clues on how vaccines could be designed to elicit broadly neutralising antibodies. The world needs an effective AIDS vaccine to overcome the global scourge of AIDS," said Professor Salim Abdool Karim, Director of CAPRISA and President of the Medical Research Council, in his comments on the significance of the finding.

While their existence has been known for a while, highly potent forms of broadly neutralizing antibodies against HIV were only identified about 3 years ago. Until now, it was not known how the human body is able to make broadly neutralizing antibodies.

This study discovered one mechanism by which these antibodies may be made. To make this discovery, the research team studied the target of some of these antibodies, a sugar that coats the surface protein of HIV, forming a site of vulnerability. By tracing back the evolution of the virus that elicited these antibodies, this team showed that this particular weak point was absent from the virus that first infected these women.

However, under constant pressure from other less powerful antibodies that develop in all infected people, their HIV was forced to expose this vulnerability over time. This allowed the broadly neutralizing antibodies to develop.

Analysis of a large number of other viruses from throughout the world, performed in collaboration with scientists from the University of North Carolina and Harvard University, suggest that the vulnerability at position 332 may be present at the time of infection in about two thirds of subtype C viruses (the subtype most common in Africa). Hence, if a vaccine is developed to target this glycan only, it may not be able to uniformly neutralize all subtype C viruses; as a result AIDS vaccines may need to attack multiple targets on the virus.

Penny L Moore, Elin S Gray, C Kurt Wibmer, Jinal N Bhiman, Molati Nonyane, Daniel J Sheward, Tandile Hermanus, Shringkhala Bajimaya, Nancy L Tumba, Melissa-Rose Abrahams, Bronwen E Lambson, Nthabeleng Ranchobe, Lihua Ping, Nobubelo Ngandu, Quarraisha Abdool Karim, Salim S Abdool Karim, Ronald I Swannstrom, Michael S Seaman, Carolyn Williamson, Lynn Morris. Evolution of an HIV glycan-dependent broadly neutralizing antibody epitope through immune escape. Nature Medicine, 2012; DOI: 10.1038/nm.2985

<http://www.sciencedaily.com/releases/2012/10/121022112849.htm>

Water Could Flow On Mars, Model Suggests; Scientists Look at Melting and Evaporation of Frozen Brines

University of Arkansas researchers have created a model that might explain how water could produce the flow patterns seen by a spacecraft orbiting Mars.

ScienceDaily - Research professor Vincent Chevrier and former Doctoral Academy Fellow Edgard Rivera-Valentin, now a postdoctoral associate at Brown University, published their findings in a recent edition of the journal *Geophysical Research Letters*.

The University of Arkansas researchers studied small flow features originally identified by NASA's Mars Reconnaissance Orbiter and detailed in a July 2011 paper published in *Science* magazine. These flow features, which appear and disappear with the seasons and show a strong preference for equator facing slopes, indicate the possible presence of liquid on the Red Planet. Chevrier and Rivera-Valentin have constructed the most comprehensive model to date of the behavior of water-and-salt combinations called brines to show that frozen water could melt, flow and then evaporate, creating these flow features on Mars.

Salts can lower the melting point of water, so the researchers used different forms of salt known to form on Mars to calculate what would melt, how much would become liquid and how long the liquid would last from the time it went from freezing to evaporation. They based their model on soils up to 20 centimeters deep, because beyond that depth the seasonal temperatures would not affect the freezing and melting aspects of the salt-water mixtures.

"We had to find a salt-water mixture that would come and go," in other words, something not completely liquid or solid, said Chevrier, a research assistant professor in the Arkansas Center for Space and Planetary Sciences in the J. William Fulbright College of Arts and Sciences. They found that calcium chloride fits the bill.

"In one day we could form enough liquid to create these flow features on the surface," he said. The researcher's model also explained why the flow features disappeared by incorporating evaporation into the model.

"The easier it becomes to melt, the easier it becomes to evaporate," Chevrier said. At low concentrations of brine, "as soon as it melts, it evaporates and disappears." However, the researchers showed that they could melt enough brine so that it would not completely evaporate, thus creating conditions that might explain the flow features. Their model fits with the seasonal change in flow observations, with the flows occurring on equator facing slopes and with seasonal changes. Also, high surface evaporation rates as demonstrated in their model explain why, if there is water, it would disappear relatively quickly and why imaging spectrometry on Mars has not identified water signatures.

"No other current model really explains all the observations," Chevrier said.

Chevrier, V. F., and E. G. Rivera-Valentin. Formation of recurring slope lineae by liquid brines on present-day Mars. Geophys. Res. Lett., 2012 DOI: 1029/2012GL054119

<http://bit.ly/TKgrKc>

First analysis of beluga whale mimicking human speech

Many of us talk to our pets, but we don't expect them to talk back. A beluga whale has bucked this trend by learning to imitate human speech. (Listen to it here.)

17:00 22 October 2012 by Michael Marshall

Noc was captured in 1977 when he was still a juvenile. By 1984, he was making unusual sounds. One day, a diver in his tank surfaced unexpectedly asking who had called to him to get out. It turned out that the cries of "out, out, out" had come from Noc.

"We were sceptical at first," says Sam Ridgway of the National Marine Mammal Foundation in San Diego, California. So his team analysed Noc's sound waves. "They were definitely unlike usual sounds for a [beluga], and similar to human voices in rhythm and acoustic spectrum," he says. Pressure sensors placed in Noc's nasal cavities revealed he was making the sounds using the same mechanism as his normal calls.

There have been anecdotal reports of belugas imitating human speech, but this is the first time they have been analysed, says Justin Gregg of the Dolphin Communication Project in Mystic, Connecticut.

Talking seal

A few other animals have also mimicked human speech, notably parrots and a harbour seal called Hoover. Famous mimics like lyrebirds do so to defend territories and attract mates, while katydid lures cicadas. SpeakerMovie Camera by mimicking their mating calls. Gregg thinks belugas are more likely to be social mimics, for instance learning a different "dialect" when they join a new group.

Belugas have a range of vocal tricks up their sleeves. A recent study showed that they can also learn to "label" objects with different sounds, and then choose from a selection of objects based on the sound they had heard (*International Journal of Comparative Psychology*, vol 25, p 195).

Journal reference: *Current Biology*, DOI: 10.1016/j.cub.2012.08.044

<http://news.discovery.com/history/oldest-writing-121023.html#mkcpgn=rssnws1>

Oldest Writing Nearly Deciphered

The world's oldest undeciphered writing system is close to being cracked thanks to a new technology and online crowdsourcing,

Analysis by Rossella Lorenzi

Oxford University researchers have announced.

Called proto-Elamite, the writing has its roots in what is now Iran and dates from 3,200 to 3,000 B.C. So far, the 5,000-year-old writing has defied any effort to decode its symbols impressed on clay tablets.

Now a high-tech imaging device developed at the Universities of Oxford and Southampton in England might provide the necessary insight to crack the code once and for all.

Comprising a dome with 76 lights and a camera positioned at the top of the dome, the Reflectance Transformation Imaging (RTI) is able to capture extremely high quality images of ancient documents. As the



object is placed in the center of the dome, 76 photos are taken each with one of the 76 lights individually lit.

The 76 images are then joined in post-processing so that researcher can move the light across the surface of the digital image and use the difference between light and shadow to highlight never before seen details.

"The quality of the images captured is incredible. I have spent the last ten years trying to decipher the proto-Elamite writing system and, with this new technology, I think we are finally on the point of making a breakthrough," Jacob Dahl, from Oxford University's Oriental Studies Faculty, said.

Dahl noted that overlooking differences barely visible to the naked eye may have prevented scholars from deciphering the writing. "Consider for example not being able to distinguish the letter i from the letter t," he said.

The images are now been made available online for free public access on the Cuneiform Digital Library Initiative website. As high definition images of the clay tablets are shared with scholars around the world, it is hoped that the enigmatic right to left writing will be finally deciphered.

Indeed, a few features of the writing system are already known: the scribes had loaned or possibly shared some signs from or with the Mesopotamians, such as the numerical signs and their systems and symbols for objects like sheep, goats, cereals.

In the past 10 years, Dahl himself has deciphered 1,200 separate signs, but he admits this is almost nothing compared to the complexity of the system. About 80-90 percent of the signs are maddening puzzle and even basic words as "cow" or "cattle" remain undeciphered.

"Looking at contemporary and later writing systems, we would expect to see proto-Elamite use only symbols to represent things, but we think they also used a syllabary -- for example 'cat' would not be represented by a symbol depicting the animal, but by symbols for the otherwise unrelated words 'ca' and 'at,'" Dahl said.

According to the researcher, half of the signs used in this way seem to have been completely invented for the sounds they represent.

"If this turns out to be the case, it would transform fundamentally how we understand early writing where phonetecism is believed to have been developed through the so-called rebus principle. A modern example would be for example 'I see you,' written with the three signs 'eye,' the 'sea,' and a 'ewe,'" Dahl said.

Containing depictions of animals and mythical creatures, but no representations of the human form whatsoever, the tablets appear to have been used only in administrative and agricultural records.

No evidence has emerged for learning exercises for scribes to improve and preserve the writing.

"The lack of a scholarly tradition meant that a lot of mistakes were made," Dahl said.

Making the decoding even more difficult, the mistakes basically killed the writing system.

Eventually, the proto Elamite became useless even as an administrative system and after some two hundred years it was abandoned. "This is probably the world's first case of a collapse of knowledge because of the under-funding of education," Dahl said.

<http://www.sciencedaily.com/releases/2012/10/121022162331.htm>

Exercise May Trump Mental Activity in Protecting Against Brain Shrinkage

Regular exercise in old age may protect against brain shrinkage than engaging in mental or social activities

ScienceDaily - Exercising regularly in old age may better protect against brain shrinkage than engaging in mental or social activities, according to a new study published in the October 23, 2012, print issue of *Neurology*®, the medical journal of the American Academy of Neurology. Research suggests that brain shrinkage may lead to problems with memory and thinking.

"People in their seventies who participated in more physical exercise, including walking several times a week, had less brain shrinkage and other signs of aging in the brain than those who were less physically active," said study author Alan J. Gow, PhD, with the University of Edinburgh in Scotland. "On the other hand, our study showed no real benefit to participating in mentally and socially stimulating activities on brain size, as seen on MRI scans, over the three-year time frame." Researchers looked at medical records of 638 people from Scotland born in 1936. The participants were given MRI scans at 73 years old.

The group gave details about their exercise habits, ranging from moving only in connection with necessary household chores to keeping fit with heavy exercise or participating in competitive sports several times per week. They also reported their participation in social and mentally stimulating activities.

The study found that after three years, people who participated in more physical activity experienced less brain shrinkage than those who exercised minimally.

"Our results show that regularly exercising in old age is potentially important to protecting the brain as we age," said Gow.

The study was supported by Research Into Aging, the Age UK-funded Disconnected Mind Project and the United Kingdom's Medical Research Council.

Journal Reference: A. J. Gow, M. E. Bastin, S. Munoz Maniega, M. C. Valdes Hernandez, Z. Morris, C. Murray, N. A. Royle, J. M. Starr, I. J. Deary, J. M. Wardlaw. *Neuroprotective lifestyles and the aging brain: Activity, atrophy, and white matter integrity.* *Neurology*, 2012; 79 (17): 1802 DOI: 10.1212/WNL.0b013e3182703fd2

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Nearly Half of U.S. Adults With High Blood Pressure Have It Under Control

Nearly half of U.S. adults with high blood pressure had their blood pressure under control by the end of 2010 -- a significant increase from the start of the decade, researchers reported in the American Heart Association journal Circulation.

ScienceDaily - Improvements in blood pressure control were most likely due to wider use of multiple drug combinations, researchers said. Researchers at the National Center for Health Statistics (NCHS) interviewed 9,320 hypertensive participants in the National Health and Nutrition Examination Survey (NHANES) 2001-10. By the end of 2010, 47 percent had controlled blood pressure -- up from 29 percent 10 years earlier.

The in-person survey is the first to compare blood pressure control rates before and after the Joint National Committee (JNC7) treatment guidelines were published in 2003. Under JNC7 guidelines, many patients may need combination therapy with two or more drugs to achieve adequate blood pressure control.

In the study, almost two-thirds of those on combination therapy had controlled blood pressure by 2010, and the use of multiple drugs increased from 37 percent in 2001 to 48 percent by 2010. Compared with using one drug, single and multiple-pill combinations were associated with 55 percent and 26 percent increased likelihood of control, respectively.

"Much progress has been made in blood pressure control over the last 10-year period and the use of multiple drug combinations apparently has had an effect," said Qiuping Gu, M.D., Ph.D., an epidemiologist at the NCHS. Lower cost of medications and their availability in generic form as well as increased awareness of the risk of uncontrolled high blood pressure has also had a positive effect.

But some issues continue to be problematic, researchers said.

The national hypertension treatment guidelines recommended thiazide diuretics as initial drug therapy for most patients with uncomplicated hypertension, yet their overall use remains comparatively low. In addition, "nearly half of the hypertensive population is not being treated with combination therapy," said Charles F. Dillon, M.D., Ph.D., co-author of the study. Moreover, rates were lower for older Americans, African-Americans and people with diabetes and chronic kidney disease. Mexican-Americans were least likely to take any kind of blood pressure medication.

"While there are possibly several factors involved, more needs to be learned about why only 34 percent of Mexican-Americans with hypertension have their blood pressure under control," Gu said. Participants were only asked about medications used in the prior month, so those who might have taken medications previously were classified as non-users. Furthermore, NHANES blood pressure measurements were only collected one time, so some people in the study may have been misclassified.

Other co-authors are: Vicki L. Burt, Sc.M., R.N.; Charles F. Dillon, M.D., Ph.D.; and Sarah Yoon, Ph.D. Author disclosures are on the manuscript. NCHS is part of the U.S. Centers for Disease Control and Prevention.

For high blood pressure information visit www.heart.org/hbp.

Q. Gu, V. L. Burt, C. F. Dillon, S. Yoon. Trends in Antihypertensive Medication Use and Blood Pressure Control Among United States Adults With Hypertension: The National Health and Nutrition Examination Survey, 2001 to 2010. Circulation, 2012; 126 (17): 2105 DOI: 10.1161/CIRCULATIONAHA.112.096156

http://www.eurekalert.org/pub_releases/2012-10/rhuo-ngv102312.php

Next-generation vaccines -- eliminating the use of needles

Lead scientist Professor Simon Cutting, from the School of Biological Sciences at Royal Holloway, has developed the jabs through the use of probiotic spores.

He carried out fundamental studies into the biology of the bacterium *Bacillus subtilis* which attracted the attention of microbiologists due to its ability to form spores that can last millions of years before germinating under the appropriate environmental conditions. Professor Cutting says: "The mechanisms by which this process occurs have fascinated microbiologists for decades making it one of the most intensively studied bacteria. Its simple life cycle and ease of use make it an ideal laboratory subject."

Professor Cutting discovered that the *Bacillus* spores act as ideal vehicles to carry antigens and promote an immune response. He explains: "Rather than requiring needle delivery, vaccines based on *Bacillus* spores can be delivered via a nasal spray, or as an oral liquid or capsule. Alternatively they can be administered via a small soluble film placed under the tongue, in a similar way to modern breath fresheners. As spores are exceptionally stable, vaccines based on *Bacillus* do not require cold-chain storage alleviating a further issue with current vaccine approaches."

As well as eliminating the pain associated with needles, oral vaccines provide greater benefits including being safer to administer, especially in developing countries where HIV is rife, being inexpensive to produce and easier to store and reducing concerns of adverse reactions.

Professor Cutting has carried out pre-clinical evaluation of *Bacillus*-based vaccines for a number of diseases including Tuberculosis, influenza and tetanus but most recently he has been investigating the potential for use of the vaccines against a disease of particular relevance to the West - *Clostridium difficile*

"*C. difficile*, is a gastrointestinal infection that is commonly picked up following hospital stays and causes around 50,000 infections and 4,000 deaths per year in the UK, mostly in elderly patients. Currently, there is no vaccine against the disease, and although several approaches are currently undergoing clinical trials, none are expected to provide full protection, and new solutions are urgently needed," says Professor Cutting.

He adds: "*Bacillus* based vaccines offer distinct advantages as unlike other approaches, oral delivery can cause a more specific immune response in the gastrointestinal tract to fully eliminate *C. difficile*."

Professor Cutting has recently received private seed investment to form a company, Holloway Immunology, to develop the *Bacillus* vaccine technology and concentrate on three lead vaccines for Tuberculosis, *C. difficile* infection and influenza (flu). The company is currently looking for investors to help fast track the implementation of these jabs and contribute to the transformation of vaccine delivery around the globe.

http://www.eurekalert.org/pub_releases/2012-10/afot-asa102312.php

Are schizophrenia and autism close relations?

Tel Aviv University researcher discovers that family history of schizophrenia is a risk factor for autism

Autism Spectrum Disorders (ASD), a category that includes autism, Asperger Syndrome, and Pervasive Developmental Disorder, are characterized by difficulty with social interaction and communication, or repetitive behaviors. The U.S. Centers for Disease Control and Management says that one in 88 children in the US is somewhere on the Autism spectrum - an alarming ten-fold increase in the last four decades.

New research by Dr. Mark Weiser of Tel Aviv University's Sackler Faculty of Medicine and the Sheba Medical Center has revealed that ASD appears share a root cause with other mental illnesses, including schizophrenia and bipolar disorder. At first glance, schizophrenia and autism may look like completely different illnesses, he says. But closer inspection reveals many common traits, including social and cognitive dysfunction and a decreased ability to lead normal lives and function in the real world.

Studying extensive databases in Israel and Sweden, the researchers discovered that the two illnesses had a genetic link, representing a heightened risk within families. They found that people who have a schizophrenic sibling are 12 times more likely to have autism than those with no schizophrenia in the family. The presence of bipolar disorder in a sibling showed a similar pattern of association, but to a lesser degree.

A scientific leap forward, this study sheds new light on the genetics of these disorders. The results will help scientists better understand the genetics of mental illness, says Dr. Weiser, and may prove to be a fruitful direction for future research. The findings have been published in the Archives of General Psychiatry.

All in the family

Researchers used three data sets, one in Israel and two in Sweden, to determine the familial connection between schizophrenia and autism. The Israeli database alone, used under the auspices of the ethics committees of both the Sheba Medical Center and the Israeli Defense Forces, included anonymous information about more than a million soldiers, including patients with schizophrenia and ASD.

"We found the same results in all three data sets," he says, noting that the ability to replicate the findings across these extensive databases is what makes this study so significant.

Understanding this genetic connection could be a missing link, Dr. Weiser says, and provides a fresh direction for study. The researchers are now taking this research in a clinical direction. For now, though, the findings shouldn't influence the way that doctors treat patients with either illness, he adds.

This work was done in collaboration with researchers at the University of North Carolina, Karolinska Institute in Sweden, Kings College London, and the Israeli Defense Force Medical Corps.

http://www.eurekalert.org/pub_releases/2012-10/uou-gmh101912.php

Grandmas made humans live longer

Computer model: Chimp lifespan evolves into human longevity

SALT LAKE CITY – Computer simulations provide new mathematical support for the "grandmother hypothesis" – a famous theory that humans evolved longer adult lifespans than apes because grandmothers helped feed their grandchildren.

"Grandmothering was the initial step toward making us who we are," says Kristen Hawkes, a distinguished professor of anthropology at the University of Utah and senior author of the new study published Oct. 24 by the British journal Proceedings of the Royal Society B.

The simulations indicate that with only a little bit of grandmothering – and without any assumptions about human brain size – animals with chimpanzee lifespans evolve in less than 60,000 years so they have a human lifespan. Female chimps rarely live past child-bearing years, usually into their 30s and sometimes their 40s. Human females often live decades past their child-bearing years.

The findings showed that from the time adulthood is reached, the simulated creatures lived another 25 years like chimps, yet after 24,000 to 60,000 years of grandmothers caring for grandchildren, the creatures who reached adulthood lived another 49 years – as do human hunter-gatherers.

The grandmother hypothesis says that when grandmothers help feed their grandchildren after weaning, their daughters can produce more children at shorter intervals; the children become younger at weaning but older when they first can feed themselves and when they reach adulthood; and women end up with postmenopausal lifespans just like ours.

By allowing their daughters to have more children, a few ancestral females who lived long enough to become grandmothers passed their longevity genes to more descendants, who had longer adult lifespans as a result. Hawkes conducted the new study with first author and mathematical biologist Peter Kim, a former University of Utah postdoctoral researcher now on the University of Sydney faculty, and James Coxworth, a University of Utah doctoral student in anthropology. The study was funded by the National Science Foundation and the Australian Research Council.

How Grandmothering Came to Be

Hawkes, University of Utah anthropologist James O'Connell and UCLA anthropologist Nicholas Blurton Jones formally proposed the grandmother hypothesis in 1997, and it has been debated ever since. Once major criticism was that it lacked a mathematical underpinning – something the new study sought to provide.

The hypothesis stemmed from observations by Hawkes and O'Connell in the 1980s when they lived with Tanzania's Hazda hunter-gatherer people and watched older women spend their days collecting tubers and other foods for their grandchildren. Except for humans, all other primates and mammals collect their own food after weaning.

But as human ancestors evolved in Africa during the past 2 million years, the environment changed, growing drier with more open grasslands and fewer forests – forests where newly weaned infants could collect and eat fleshy fruits on their own.

"So moms had two choices," Hawkes says. "They could either follow the retreating forests, where foods were available that weaned infants could collect, or continue to feed the kids after the kids are weaned. That is a problem for mothers because it means you can't have the next kid while you are occupied with this one." That opened a window for the few females whose childbearing years were ending – grandmothers – to step in and help, digging up potato-like tubers and cracking hard-shelled nuts in the increasingly arid environment. Those are tasks newly weaned apes and human ancestors couldn't handle as infants.

The primates who stayed near food sources that newly weaned offspring could collect "are our great ape cousins," says Hawkes. "The ones that began to exploit resources little kids couldn't handle, opened this window for grandmothers and eventually evolved into humans."

Evidence that grandmothers increases grandchildren's survival is seen in 19th and 20th century Europeans and Canadians, and in Hazda and some other African people.

But it is possible that the benefits grandmothers provide to their grandchildren might be the result of long postmenopausal lifespans that evolved for other reasons, so the new study set out to determine if grandmothers alone could result in the evolution of ape-like life histories into long postmenopausal lifespans seen in humans.

Simulating the Evolution of Adult Lifespan

The new study isn't the first to attempt to model or simulate the grandmother effect. A 1998 study by Hawkes and colleagues took a simpler approach, showing that grandmothers accounts for differences between humans and modern apes in life-history events such as age at weaning, age at adulthood and longevity.

A recent simulation by other researchers said there were too few females living past their fertile years for grandmothers to affect lifespan in human ancestors. The new study grew from Hawkes' skepticism about that finding.

Unlike Hawkes' 1998 study, the new study simulated evolution over time, asking, "If you start with a life history like the one we see in great apes – and then you add grandmothers, what happens?" Hawkes says. The simulations measured the change in adult longevity – the average lifespan from the time adulthood begins. Chimps that reach adulthood (age 13) live an average of another 15 or 16 years. People in developed nations who reach adulthood (at about age 19) live an average of another 60 years or so – to the late 70s or low 80s. The extension of adult lifespan in the new study involves evolution in prehistoric time; increasing lifespans in recent centuries have been attributed largely to clean water, sewer systems and other public health measures. The researchers were conservative, making the grandmother effect "weak" by assuming that a woman couldn't be a grandmother until age 45 or after age 75, that she couldn't care for a child until age 2, and that she could care only for one child and that it could be any child, not just her daughter's child.

Based on earlier research, the simulation assumed that any newborn had a 5 percent chance of a gene mutation that could lead to either a shorter or a longer lifespan.

The simulation begins with only 1 percent of women living to grandmother age and able to care for grandchildren, but by the end of the 24,000 to 60,000 simulated years, the results are similar to those seen in human hunter-gatherer populations: about 43 percent of adult women are grandmothers.

The new study found that from adulthood, additional years of life doubled from 25 years to 49 years over the simulated 24,000 to 60,000 years.

The difference in how fast the doubling occurred depends on different assumptions about how much a longer lifespan costs males: Living longer means males must put more energy and metabolism into maintaining their bodies longer, so they put less vigor into competing with other males over females during young adulthood. The simulation tested three different degrees to which males are competitive in reproducing.

What Came First: Bigger Brains or Grandmothering?

The competing "hunting hypothesis" holds that as resources dried up for human ancestors in Africa, hunting became better than foraging for finding food, and that led to natural selection for bigger brains capable of learning better hunting methods and clever use of hunting weapons. Women formed "pair bonds" with men who brought home meat.

Many anthropologists argue that increasing brain size in our ape-like ancestors was the major factor in humans developing lifespans different from apes. But the new computer simulation ignored brain size, hunting and pair bonding, and showed that even a weak grandmother effect can make the simulated creatures evolve from chimp-like longevity to human longevity.

So Hawkes believes the shift to longer adult lifespan caused by grandmothering "is what underlies subsequent important changes in human evolution, including increasing brain size."

"If you are a chimpanzee, gorilla or orangutan baby, your mom is thinking about nothing but you," she says. "But if you are a human baby, your mom has other kids she is worrying about, and that means now there is

selection on you – which was not on any other apes – to much more actively engage her: 'Mom! Pay attention to me!'"

"Grandmothering gave us the kind of upbringing that made us more dependent on each other socially and prone to engage each other's attention," she adds.

That, says Hawkes, gave rise to "a whole array of social capacities that are then the foundation for the evolution of other distinctly human traits, including pair bonding, bigger brains, learning new skills and our tendency for cooperation."

http://www.eurekalert.org/pub_releases/2012-10/plos-lcb101812.php

Lives could be saved by removing age restrictions on rotavirus vaccination

The additional children's lives saved by removing the age restrictions for rotavirus vaccination in low- and middle-income countries would be much greater than any extra deaths from vaccine-associated complications

A study published in this week's PLOS Medicine, which suggests that the additional children's lives saved by removing the age restrictions for rotavirus vaccination in low- and middle-income countries would be much greater than any extra deaths from vaccine-associated complications (namely, intussusception—a form of bowel obstruction), has informed policy regarding the age restrictions for this vaccine.

Hundreds of thousands of infants world-wide have been vaccinated against rotavirus (which causes vomiting and diarrhea and can kill young children) but this vaccine can slightly increase the risk of intussusception, with some countries reporting a risk of 1-4 additional cases per 100,000 vaccinated infants. As older infants have a higher risk of naturally occurring intussusception, the World Health Organization previously decided that the course of rotavirus vaccination should be initiated before the age of 15 weeks and completed before the age of 32 weeks. In poorer countries, where access to health facilities is more difficult, this age restriction could exclude many eligible infants from being vaccinated against rotavirus because of delays in the vaccination program.

In a modelling study, the authors from the Centers for Disease Control and Prevention and the London School of Hygiene and Tropical Medicine analysed the benefits and risks of rotavirus vaccination if the age restrictions were removed, and the rotavirus vaccine given to children alongside other routine childhood immunizations. Using their model, the authors found that that in low- and low-middle income countries, keeping the age restrictions would prevent 155,800 rotavirus deaths, while potentially causing 253 deaths from intussusception. However, lifting the age restrictions would prevent 203,000 rotavirus deaths while potentially causing 547 intussusception deaths. Overall, the authors found that lifting the age restriction would result in an additional 47,200 deaths from rotavirus prevented versus 294 intussusception deaths caused, translating to 154 deaths prevented for every death caused by complications of the vaccine.

Experts from the World Health Organization reviewed the results from this study and while still encouraging timely vaccination, the World Health Organization no longer universally recommends age restrictions and supports removing age restrictions in settings where the benefits outweigh the risks.

The authors say: "Our analysis suggests that in low- and middle-income countries the additional lives saved by removing age restrictions for rotavirus vaccination would far outnumber the potential excess vaccine-associated intussusception deaths."

The authors continue: "Age restriction policies will ultimately be decided at country level, but this analysis has shown a clear case for a change in policy that will be particularly instrumental for saving lives in settings where mortality from rotavirus is high and delays in timing of vaccination are common."

Funding: CS has received salary support from WHO's Initiative for Vaccine Research for collecting some of the data (vaccine timeliness and age distribution of rotavirus deaths) used in the model. AC was funded by PanAmerican Health Organization's ProVac Initiative. MMP, UDP, and JT were personally salaried by their institutions during the period of writing (though no specific salary was set aside or given for the writing of this paper). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the US Centers for Disease Control and Prevention (CDC).

Competing Interests: The authors have declared that no competing interests exist.

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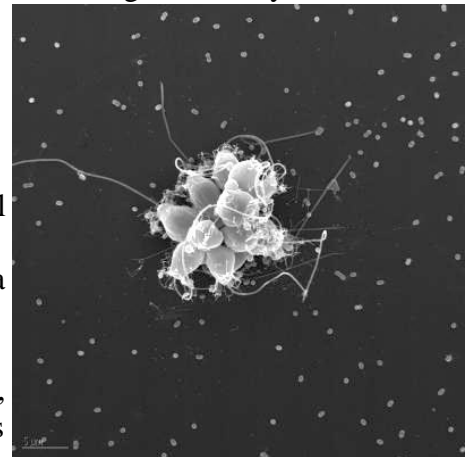
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Did bacteria spark evolution of multicellular life?

New study finds bacteria cue single-celled choanoflagellates to form colonies

Bacteria have a bad rap as agents of disease, but scientists are increasingly discovering their many benefits, such as maintaining a healthy gut. A new study now suggests that bacteria may also have helped kick off one of the key events in evolution: the leap from one-celled organisms to many-celled organisms, a development that eventually led to all animals, including humans.

Published this month in the inaugural edition of the new online journal eLife, the study by University of California, Berkeley, and Harvard Medical School scientists involves choanoflagellates (aka "choanos"), the closest living relatives of animals. These microscopic, one-celled organisms sport a long tail or flagellum, tentacles for grabbing food and are members of the ocean's plankton community. As our closest living relative, choanos offer critical insights into the biology of their last common ancestor with animals, a unicellular or colonial organism that lived and died over 650 million years ago.



Triggered by the presence of bacteria, the single-celled choanoflagellate Salpingoeca rosetta divides and aggregates with its sisters into a colony. One reason may be that the colony is a more efficient way of capturing food, like a "Death Star" sitting amidst the bacteria and chowing down. Scanning electron microscope image courtesy of Nicole King.

"Choanoflagellates evolved not long before the origin of animals and may help reveal how animals first evolved," said senior author Nicole King, UC Berkeley associate professor of molecular and cell biology. Since first starting to study choanoflagellates as a post-doc, King has been trying to figure out why some choanoflagellates live their lives as single cells, while others form colonies. After years of dead ends, King and undergraduate researcher Richard Zuzow discovered accidentally that a previously unknown species of bacteria stimulates one choanoflagellate, Salpingoeca rosetta, to form colonies. Because bacteria were abundant in the oceans when animals first evolved, the finding that bacteria influence choano colony formation means it is plausible that bacteria also helped to stimulate multicellularity in the ancestors of animals.

"I would be surprised if bacteria did not influence animal origins, since most animals rely on signals from bacteria for some part of their biology," King said. "The interaction between bacteria and choanos that we discovered is interesting for evolutionary reasons, for understanding how bacteria interact with other organisms in the oceans, and potentially for discovering mechanisms by which our commensal bacteria are signaling to us."

No one is sure why choanoflagellates form colonies, said one of the study's lead authors, UC Berkeley post-doctoral fellow Rosanna Alegado. It may be an effective way of exploiting an abundant food source: instead of individual choanoflagellates rocketing around in search of bacteria to eat, they can form an efficient bacteria-eating "Death Star" that sits in the middle of its food source and chows down.

Whatever the reasons, colonies of unicellular organisms may have led the way to more permanent multicellular conglomerations, and eventually organisms comprised of different cell types specialized for specific functions. Sequencing the choanoflagellate genome

King's 12-year search for the trigger of choanoflagellate colony development was reignited in 2005 when she started to prime cultures of the choanoflagellate *S. rosetta* for a genome sequencing project. The sequencing of another choanoflagellate, the one-celled *Monosiga brevicollis*, gave some clues into animal origins, but she needed to compare its genome to that of a colony-forming choanoflagellate.

Surprisingly, when Zuzow tried to isolate the colony-forming choanoflagellate by adding antibiotics to the culture dish to kill off residual bacteria, strange things happened, said King.

"When he treated the culture with one cocktail of antibiotics, he saw a bloom of rosette colony formation," she said, referring to the rose petal-shaped colonies that were floating in the culture media. "When he treated with a different cocktail of antibiotics, that got rid of colony formation altogether."

That "rather mundane but serendipitous observation" led Zuzow and Alegado to investigate further and discover that only one specific bacterial species in the culture was stimulating colony formation. When other bacteria outnumbered it, or when antibiotics wiped it out, colony formation stopped. Alegado identified the colony-inducing bacteria as the new species, *Algoriphagus machipongonensis*. While she found that other bacteria in the *Algoriphagus* genus can also stimulate colony formation, other bacteria like *E. coli*, common in the human gut, cannot.

Working with Jon Clardy of Harvard Medical School, a natural products chemist, the two labs identified a molecule – a fatty acid combined with a lipid that they called RIF-1 – that sits on the surface of bacteria and is the colony development cue produced by the bacteria. "This molecule may be betraying the presence of bacteria," Alegado said. "Bacteria just sit around blebbing off little membrane bubbles, and if one of them has this molecule, the choanoflagellates all of a sudden say, 'Aha, there are some bacteria around here.'"

The signal sets off a predetermined program in the choanoflagellate that leads to cell division and the development of rosettes, she said. The molecule RIF-1 is remarkably potent; choanos detect and respond to it at densities that are about one billionth that of the lowest concentration of sugar that humans can taste in water.

"We are investigating this molecule from many sides. How and why do bacteria make it? How do choanoflagellates respond to it, and why?" King said. She and her team also are analyzing the genome of the colony-forming choanoflagellate and the colony-inducing bacteria for clues to their interaction.

King hopes that this unexpected signaling between choanoflagellates and bacteria can yield insights into other ways in which bacteria influence biology, particularly the biology of the gut.

Coauthors with King, Alegado and Clardy are Zuzow, now a graduate student at Stanford University; Laura Brown, now a faculty member at Indiana University; Shugeng Cao and Renee Dermenjian of Harvard Medical School; and Stephen Fairclough of UC Berkeley. Dermenjian is now at Merck.

The research is funded by the National Institutes of Health and the Gordon and Betty Moore Foundation Marine Microbiology Initiative.

http://www.eurekalert.org/pub_releases/2012-10/uoc--oua102312.php

Oxygen's ups and downs in the early atmosphere and ocean

UC Riverside-led research team finds evidence for a dramatic rise in early oxygen about 2.3 billion years ago followed, more surprisingly, by an equally impressive fall

RIVERSIDE, Calif. - Most researchers imagine the initial oxygenation of the ocean and atmosphere to have been something like a staircase, but with steps only going up. The first step, so the story goes, occurred around 2.4 billion years ago, and this, the so-called Great Oxidation Event, has obvious implications for the origins and evolution of the first forms of eukaryotic life. The second big step in this assumed irreversible rise occurred almost two billion years later, coinciding with the first appearances and earliest diversification of animals. Now a team led by geochemists at the University of California, Riverside challenges the simple notion of an up-only trend for early oxygen and provides the first compelling direct evidence for a major drop in oxygen after the first rise.

"Our group is among a subset of scientists who imagine that oxygen, once it began to accumulate in the ocean-atmosphere system, may have ultimately risen to very high levels about 2.3-2.2 billion years ago, perhaps even to concentrations close to what we see today," said Timothy Lyons, a professor of biogeochemistry and the principal investigator of the project. "But unlike the posited irreversible rise favored by many, our new data point convincingly to an equally impressive, and still not well understood, fall in oxygen about 200 million years later."

According to Lyons, this drop in oxygen may have ushered in more than a billion years that were marked by a return to low-oxygen concentrations at Earth's surface, including the likelihood of an oxygen-free deep ocean. "It is this condition that may have set the environmental stage and ultimately the clock for the advance of eukaryotic organisms and eventually animals," he said.

Study results appear online this week in the Proceedings of the National Academy of Sciences.

"The time window between 2.3 and 2.1 billion years ago is famous for the largest and longest-lived positive carbon isotope excursion in Earth history," said Noah Planavsky, a recent Ph.D. graduate from UC Riverside, current postdoctoral fellow at Caltech, and first author of the research paper.

He explained that carbon isotopes are fractionated during photosynthesis. When organic matter is buried, oxygen is released and rises in the biosphere. The burial of organic matter is tracked by the positive or heavy isotopic composition of carbon in the ocean.

"Some workers have attributed the carbon isotope excursion to something other than organic burial and associated release of oxygen," Planavsky said. "We studied the sulfur isotope composition of the same rocks used for the carbon isotope analyses - from Canada, South Africa, the U.S., and Zimbabwe - and demonstrated convincingly that the organic burial model is the best answer."

The researchers' sulfur data point to high sulfate concentrations in the ocean, which, like today, is a classic fingerprint of high oxygen levels in the ocean and atmosphere. Sulfate, the second most abundant negatively charged ion in the ocean today, remains high when the mineral pyrite oxidizes easily on the continents and is buried in relatively small amounts in the oxygen-rich ocean.

"What is equally impressive is that the rise in oxygen was followed by a dramatic fall in sulfate and therefore oxygen," Lyons said. "Why the rise and fall occurred and how that impacted the billion years or more of ocean chemistry that followed and the life within that ocean are hot topics of research."

The research team is thrilled to have found strong chemical evidence for oxygen variability on the early Earth. "The idea that oxygen levels at Earth's surface went up and down must be vital in any effort to understand the links between environmental and biological evolution on broad, geologic time scales," Planavsky said.

He and Lyons were joined in the study by Andrey Bekker at the University of Manitoba, Axel Hofmann at the University of Johannesburg and Jeremy Owens at UCR.

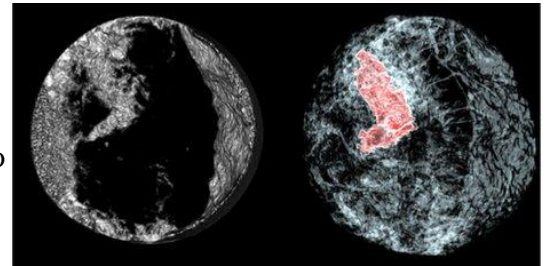
The NASA Exobiology Program supported this research. A National Science Foundation (NSF) Graduate Research Fellowship and a postdoctoral fellowship from the NSF Division of Earth Sciences covered Planavsky's salary.

<http://www.bbc.co.uk/news/science-environment-20026939>

X-ray imaging tricks increase resolution and cut dose

An international research team has proposed a way to make high-resolution, 3D images of breast tissue while reducing the delivered X-ray dose.

Breast tissue is particularly susceptible to X-ray radiation so 3D scanning is generally not employed. Now a team reporting in Proceedings of the National Academy of Sciences suggests a different form of X-rays and a new image analysis approach. However, new compact X-ray sources are needed to bring the idea to the clinic. Taken together, the two improvements lead to high-resolution 3D images while reducing the delivered dose to just 4% that of standard "computed tomography" (CT) scans.



The image compares a conventional CT scan (l) and a scan with the new approach and 1/25th the dose

A cancer charity called the work "a promising step" toward earlier, more accurate breast cancer diagnosis. A phenomenally successful technique in X-ray scanning over the past half-century, CT scans are made with a number of X-ray images taken from various angles that are analysed to yield a 3D view. The approach is reserved for the imaging of parts of the body for which these multiple X-ray exposures is deemed safe, generally excluding "radiosensitive" breast tissue. Instead, what is known as dual-view mammography is employed, producing two conventional X-ray images of the breast - a methodology that is known to miss 10-20% of tumours.

One to watch

Recent years have seen growth in the use of what is called phase contrast imaging, which measures not only how much X-ray light gets through tissue, but also in a sense how long it takes to get there. This yields a far clearer picture of subtle changes in density that can show tumours.

Now researchers from the US and Germany working at the European Synchrotron Radiation Facility in France have refined the phase contrast approach using what they call equally sloped tomography.

The improvement is in the mathematics used to analyse X-ray images - instead of taking a number of images at evenly spaced angles around a sample, EST takes images at irregular angle intervals and uses improved equations to reconstruct the 3D representation.

Co-author of the study Paola Coan of Ludwig Maximilians University explained that an analogy of the process is a watch. "Instead of having a hand that measures every second, we have a hand that follows a certain scheme, the first hand movement is 1.2 seconds, then 0.7 then maybe 0.9, but at the end, thanks to EST, we still measure perfectly the minute," she explained to BBC News. "With this mathematical trick we avoid interpolation and the image looks better - we even need to take fewer radiographs to reconstruct the computed tomography full image."

Testing the approach at the ESRF with a whole mastectomized breast, the team showed that they could acquire images as sharp as those of conventional CT scans using just a quarter of the delivered X-ray dose.

But they carried the work further by using the ESRF's capabilities to run the same test with higher-energy X-rays. Soft tissue is more transparent to these "harder" X-rays and therefore less radiation is absorbed.

As members of the team showed in an article in *Physics in Medicine and Biology* in April, images of a quality comparable to standard CT can be acquired with harder X-rays corresponding to just a sixth the radiation dose. In combination, the techniques result in the resolution of a full CT scan while delivering a dose just 4% as large.

"We've demonstrated that by combining X-rays at high energy plus this sophisticated CT reconstruction, we're able to perform a complete CT with high resolution, but with a dose that is much lower than than in conventional CT and potentially... lower than dual-view mammography," Prof Coan said. "This is an extraordinary result." However, she added that compact, high-quality X-ray sources capable of the higher-

energy regime are still necessary to get the technique established in the clinical setting, a research effort that is underway for a number of industries.

Emma Smith, Cancer Research UK's senior science information officer, said: "The results of this study show that powerful new technology could give doctors a more detailed image of the breast without increasing the dose of radiation." "This research is still at an early stage and the technique has not yet been tested to see if it's safe and effective in women, but it is a promising step towards doctors being able to spot breast cancer earlier."

<http://phys.org/news/2012-10-oldest-primate-trees-extinction-dinosaurs.html>

Oldest primate lived in trees after the extinction of dinosaurs

For many mammals, including our own ancestors, the late Cretaceous marked a beginning rather than the end

Phys.org - The Cretaceous-age Hell Creek Formation of Montana is best known for the discovery over a century ago of Tyrannosaurus rex. It also has produced some of the best fossils from the end of the Age of the Dinosaurs about 65 million years ago. At that time, the planet experienced a mass extinction that wiped out many species including non-avian dinosaurs. However, for many mammals, including our own ancestors, this marked a beginning rather than the end.

Teeth of the oldest primate (called Purgatorius) have been known from rocks that are slightly younger than the Hell Creek Formation for decades (from a period of time known as the Paleocene), but the rest of the skeleton of this animal has remained elusive. A new study presented at the 72nd Annual Meeting of the Society of Vertebrate Paleontology in Raleigh, North Carolina, describes the first ankle bones of Purgatorius from northeastern Montana. This new discovery provides important new information about the ecology of the first primate.

Analysis of these new fossils has led paleontologists Stephen Chester of Yale University, Jonathan Bloch of the Florida Museum of Natural History, and William Clemens of the University of California Museum of Paleontology to conclude that Purgatorius had an ankle joint with a fairly wide range of motion. This type of ankle is characteristic of tree-living animals that can adjust their feet to uneven branches and trunks when climbing.

"The way in which the earliest primates lived has been a subject of great debate for many years, but these fossils are the first direct evidence that show that these primates spent most of their time in the trees following their divergence from other mammals in the earliest Paleocene," said Chester.

The authors of this study believe that the specialized ankle bones of Purgatorius likely played a key role in the evolutionary success of early primates. "These new fossils support the idea that the first 10 million years of primate evolution happened in the context of an intense period of similar diversification in flowering plants, including the ability to climb in branches and collect fruits and other products of the trees at the very beginning," said Bloch. Many other mammals living during the earliest Paleocene were land-dwelling, and by living in the trees, Purgatorius was able to exploit new resources in its environment.

Ongoing expeditions to northeastern Montana led by Clemens, Greg Wilson from the University of Washington, and colleagues from other institutions continue to yield important fossils and geological information documenting the pattern of change of the fauna and flora some 65 million years ago. "The new ankle bones are an extraordinary discovery. We plan to continue research in Montana in order to address other critical questions about causes of the mass extinction as well as the origin of primates and other animals that characterize the beginning of the age of mammals," said Clemens. *Provided by Society of Vertebrate Paleontology*

<http://bit.ly/UTYCOR>

Italian earthquake case is no anti-science witch-hunt

Manslaughter verdicts for six seismologists highlight the need for scientists to speak for themselves

It is easy to feel outrage at the jail terms handed down to six Italian seismologists and a civil servant this week. How could anyone hope to have predicted the earthquake that devastated L'Aquila in 2009?

That is the rallying cry, but failure to predict the quake is not, in fact, what the seven men have been convicted of (see "Seismologists found guilty of manslaughter"). The prosecution made it crystal clear all along that their case was about poor risk communication; it was built on an accusation of giving out "inexact, incomplete and contradictory information".

On this charge, there was clearly a case to answer. Employed by Italy's Major Hazards Committee to assess earthquake risks and communicate them to the government and the public, the seismologists got the science right, but left the job of public communication to a civil protection official with no specialist knowledge of seismology. His statement to the press was, to put it mildly, a grossly inaccurate reflection of the situation: "The scientific community tells us there is no danger, because there is an ongoing discharge of energy. The situation

looks favourable." At this point, the seismologists should have stepped in. But they did not, and the message stuck.

Of course, it is debatable whether this neglect merits a manslaughter conviction and six-year jail term. That is a matter for the Italian justice system. The appeals have already started. But there are broader issues to consider. Many commentators argue that the L'Aquila verdict will have a chilling effect on the provision of scientific advice in Italy and beyond. That is clearly a concern worth taking seriously.

However, it should also encourage scientists who take on those roles to think long and hard about the responsibilities that come with them. It is tempting for scientists to defer communication with the public to others who are supposedly "experts" in doing so. But this approach often leads to confusion, as evidenced by a litany of failures in the past: BSE, vaccines, genetically modified crops and many more.

This cannot continue. Scientists valued for their expertise should speak for themselves rather than letting others speak for them. Lives are at stake.

<http://www.sciencedaily.com/releases/2012/10/121023133759.htm>

Promising New Biomarker for Aggressiveness of Prostate Cancer

For the first time data produced showing that levels of serum glutamate are increased in patients with primary and metastatic prostate cancer

ScienceDaily - Research out of Roswell Park Cancer Institute (RPCI) supports the adoption of a new biomarker to measure the aggressiveness of primary prostate tumors. A team of investigators from three institutions, led by Shahriar Koochekpour, MD, PhD, Associate Professor of Cancer Genetics, Urology and Oncology in RPCI's Department of Cancer Genetics, has for the first time produced data showing that levels of serum glutamate, a naturally occurring nonessential amino acid that plays a key role in cancer metabolism, are increased in patients with primary and metastatic prostate cancer.

Collaborators included James L. Mohler, MD, Gissou Azabdaftari, MD, and Kristopher Attwood, PhD, from RPCI; Robert L. Vessella, PhD, from the University of Washington School of Medicine; and Oliver Sartor, MD, from Tulane Cancer Center and the Tulane University School of Medicine. In a study involving 366 men, the team measured serum glutamate levels in 60 healthy adult males, 197 with primary prostate cancer and 109 with metastatic castration-resistant prostate cancer -- cancer that progresses following androgen depletion therapy.

"Comparing normal, primary and metastatic prostate cancer tissues, we discovered that glutamate receptor is expressed at very high levels in primary and metastatic tumors, but at very weak or undetectable levels in benign prostate tissues," notes Dr. Koochekpour. "And serum glutamate was detected at increased levels proportional to Gleason score, the standard index for rating prostate cancer aggressiveness and prognosis in patients with primary tumors."

The researchers also demonstrated, for the first time, that glutamate deprivation significantly decreases the growth, migration and invasiveness of prostate cancer cell lines, suggesting potential clinical applications. They also report that the glutamate antagonist riluzole (Rilutek), a well-tolerated oral medicine used for mood and anxiety disorders, depression and amyotrophic lateral sclerosis (ALS), induces cell death while inhibiting the progression and motility of human prostate cancer cells.

"We detected one major difference between African-Americans and Caucasians in the study," Dr. Koochekpour notes. "In African-Americans, serum glutamate levels were higher among those men with metastatic disease than in those with primary prostate cancer, and we didn't see that trend in Caucasian men. This finding may implicate a role for glutamate metabolism in inter-racial disparities of prostate cancer."

Shahriar Koochekpour, Sunipa Majumdar, Gissou Azabdaftari, Kristopher Attwood, Ray Scioneaux, Dhatchayini Subramani, Charles Manhardt, Giovanni D. Lorusso, Stacey S. Willard, Hillary Thompson, Mojgan Shourideh, Katayoon Rezaei, Oliver Sartor, James L. Mohler, And Robert L. Vessella. Serum Glutamate Levels Correlate with Gleason Score and Glutamate Blockade Decreases Proliferation, Migration, and Invasion and Induces Apoptosis in Prostate Cancer Cells. Clinical Cancer Research, 2012 DOI: 10/1078-0432.CCR-12-1308

http://www.sciencenews.org/view/generic/id/345987/title/Human_blood_types_have_deep_evolutionary_roots

Human blood types have deep evolutionary roots

ABO system may date back 20 million years or more

By Rachel Ehrenberg

Chimps, gibbons and other primates are not just humans' evolutionary cousins; a new analysis suggests they are also our blood brothers. The A, B and O blood types in people evolved at least 20 million years ago in a common ancestor of humans and other primates, new research suggests.

The analysis deepens a mystery surrounding the evolutionary history of the ABO blood system, and should prompt further research into why the different blood groups have persisted over time, Laure Ségurel of the

University of Chicago and colleagues report online October 22 in the Proceedings of the National Academy of Sciences.

“Their evidence is rather convincing that this is a shared, very old capability that has remained throughout the divergence of the species,” says doctor and transfusion specialist Martin Olsson of Lund University in Sweden. Different forms of a single blood type gene determine what types of molecules sit on your red blood cells: type A molecules, type B molecules, A and B together, or no intact surface molecules in the case of type O (O was originally called type C, then was changed to O for the German “ohne,” meaning “without”).

The A, B and O versions of the gene differ only slightly, and scientists have debated two scenarios to explain their evolution. One posits that the A version of the gene existed long ago, and the B and/or O versions later cropped up independently in several species (including humans, gorillas, baboons and chimps). Alternatively, all of those species may have inherited the A and B types from a single ancestor.

To get some bloody perspective on the matter, researchers led by Ségurel looked at a particular stretch of DNA in the blood type gene in humans, bonobos, chimpanzees, gorillas, orangutans and several species of monkey. Then the scientists compared that stretch of DNA across species on the larger primate family tree. The pattern they saw suggests that the A and B blood groups were around at least 20 million years ago, well before the chimp-human split, and probably as far back as the common ancestor of humans and old-world monkeys. Sections of DNA in the human A version, for example, more closely matched the A version that gibbons have than the human B version of the gene.

Exactly why evolution would favor a mix of blood types in so many species is a mystery. Depending on blood type, people are more or less susceptible to particular pathogens. Type O people, for example, are more susceptible to cholera and plague, while people with type A are more susceptible to smallpox. Blood group diversity may have been maintained for so long because each version was immunologically advantageous in certain times and places.

“That diversity may have led to protection against whatever might come your way,” says glycoimmunologist Brian Cobb of Case Western Reserve University in Cleveland.

People with type A are also more prone to dangerous blood clots, Olsson says. That’s a disadvantage in the modern world, but in the days when humans and their ancestors were having babies in caves and fighting predators without the option of an emergency room, such clotting may have been beneficial.

“When we couldn’t do transfusions or patch people together it may have been good to coagulate better,” he says. “If that mammoth or Siberian tiger got you, you wouldn’t want to bleed to death.”

L. Ségurel et al. The ABO blood group is a trans-species polymorphism in primates. Proceedings of the National Academy of Sciences. doi:10.1073/pnas.1210603109

http://www.eurekalert.org/pub_releases/2012-10/nu-abc102412.php

Parkinson's breakthrough could slow disease progression

Scientists, including Lyrica inventor, create new class of potential therapeutics

CHICAGO --- In an early-stage breakthrough, a team of Northwestern University scientists has developed a new family of compounds that could slow the progression of Parkinson's disease. Parkinson's, the second most common neurodegenerative disease, is caused by the death of dopamine neurons, resulting in tremors, rigidity and difficulty moving. Current treatments target the symptoms but do not slow the progression of the disease. The new compounds were developed by Richard B. Silverman, the John Evans Professor of Chemistry at the Weinberg College of Arts and Sciences and inventor of the molecule that became the well-known drug Lyrica, and D. James Surmeier, chair of physiology at Northwestern University Feinberg School of Medicine. Their research was published Oct. 23 in the journal Nature Communications.

The compounds work by slamming the door on an unwelcome and destructive guest -- calcium. The compounds target and shut a relatively rare membrane protein that allows calcium to flood into dopamine neurons. Surmeier's previously published research showed that calcium entry through this protein stresses dopamine neurons, potentially leading to premature aging and death. He also identified the precise protein involved -- the Cav1.3 channel.

"These are the first compounds to selectively target this channel," Surmeier said. "By shutting down the channel, we should be able to slow the progression of the disease or significantly reduce the risk that anyone would get Parkinson's disease if they take this drug early enough."

"We've developed a molecule that could be an entirely new mechanism for arresting Parkinson's disease, rather than just treating the symptoms," Silverman said.

The compounds work in a similar way to the drug isradipine, for which a Phase 2 national clinical trial with Parkinson's patients — led by Northwestern Medicine neurologist Tanya Simuni, M.D. -- was recently completed. But because isradipine interacts with other channels found in the walls of blood vessels, it can't be

used in a high enough concentration to be highly effective for Parkinson's disease. (Simuni is the Arthur C. Nielsen Professor of Neurology at the Feinberg School and a physician at Northwestern Memorial Hospital.) The challenge for Silverman was to design new compounds that specifically target this rare Cav1.3 channel, not those that are abundant in blood vessels. He and colleagues first used high-throughput screening to test 60,000 existing compounds, but none did the trick.

"We didn't want to give up," Silverman said. He then tested some compounds he had developed in his lab for other neurodegenerative diseases. After Silverman identified one that had promise, Soosung Kang, a postdoctoral associate in Silverman's lab, spent nine months refining the molecules until they were effective at shutting only the Cav1.3 channel.

In Surmeier's lab, the drug developed by Silverman and Kang was tested by graduate student Gary Cooper in regions of a mouse brain that contained dopamine neurons. The drug did precisely what it was designed to do, without any obvious side effects.

"The drug relieved the stress on the cells," Surmeier said. For the next step, the Northwestern team has to improve the pharmacology of the compounds to make them suitable for human use, test them on animals and move to a Phase 1 clinical trial. "We have a long way to go before we are ready to give this drug, or a reasonable facsimile, to humans, but we are very encouraged," Surmeier said.

The research was supported by the Michael J. Fox Foundation and the RJG Foundation.

http://www.eurekalert.org/pub_releases/2012-10/hms-cpd102412.php

Challenging Parkinson's dogma

Scientists may have discovered why the standard treatment for Parkinson's disease is often effective for only a limited period of time.

Their research could lead to a better understanding of many brain disorders, from drug addiction to depression, that share certain signaling molecules involved in modulating brain activity.

A team led by Bernardo Sabatini, Takeda Professor of Neurobiology at Harvard Medical School, used mouse models to study dopamine neurons in the striatum, a region of the brain involved in both movement and learning.

In people, these neurons release dopamine, a neurotransmitter that allows us to walk, speak and even type on a keyboard. When those cells die, as they do in Parkinson's patients, so does the ability to easily initiate movement. Current Parkinson's drugs are precursors of dopamine that are then converted into dopamine by cells in the brain.

The flip side of dopamine dearth is dopamine hyperactivity. Heroin, cocaine and amphetamines rev up or mimic dopamine neurons, ultimately reinforcing the learned reward of drug-taking. Other conditions such as obsessive-compulsive disorder, Tourette syndrome and even schizophrenia may also be related to the misregulation of dopamine.

In the October 11 issue of *Nature*, Sabatini and co-authors Nicolas Tritsch and Jun Ding reported that midbrain dopamine neurons release not only dopamine but also another neurotransmitter called GABA, which lowers neuronal activity.

The previously unsuspected presence of GABA could explain why restoring only dopamine could cause initial improvements in Parkinson's patients to eventually wane. And if GABA is made by the same cells that produce other neurotransmitters, such as depression-linked serotonin, similar single-focus treatments could be less successful for the same reason.

"If what we found in the mouse applies to the human, then dopamine's only half the story," said Sabatini. The surprising GABA story began in the Sabatini lab with a series of experiments designed to see what happens when cells release dopamine. The scientists used optogenetics, a powerful technique that relies on genetic manipulation to selectively sensitize cells to light.

In laboratory dishes, researchers tested brain tissue from mice engineered to show activity in dopamine neurons. Typically in such experiments, other neurotransmitters would be blocked in order to highlight dopamine, but Tritsch, a postdoctoral fellow in the Sabatini lab, decided instead to keep the cell in as natural a state as possible. When Tritsch activated the dopamine neurons and examined their effects on striatal neurons, he naturally expected to observe the effects of dopamine release. Instead, he saw rapid inhibition of the striatal neurons, making it clear that another neurotransmitter – which turned out to be the quick-acting GABA – was at work. This was so unusual that the team launched a series of experiments to confirm that GABA was being released directly by these dopamine neurons.

A standard way to detect GABA is to look for vesicular GABA transporter, or VGAT, a protein that packages and carries GABA into neurotransmitter vesicles. The scientists silenced the gene that makes VGAT in mice and found that the dopamine neurons released GABA even in the absence of VGAT.

The researchers then tested other transporters, zeroing in on one that ferries dopamine and a variety of other neurotransmitters. For reasons they don't yet understand, this protein – the vesicular monoamine transporter – also shuttles GABA.

"What makes this important now is that every manipulation that has targeted dopamine by targeting the vesicular monoamine transporter has altered GABA as well. And nobody's paid any attention to it," said Sabatini. "Every Parkinsonian model that we have in which we've lost dopamine has actually lost GABA, too. So we really have to go back now and think: Which of these effects are due to loss of GABA and which are due to loss of dopamine?"

Anatol Kreitzer, an assistant investigator at the Gladstone Institute of Neurological Disease in San Francisco, who was not involved in the research, called the findings remarkable.

"It was totally unexpected," said Kreitzer, who is also an assistant professor of physiology and neurology at the University of California, San Francisco. "At the molecular level, nobody really expected dopamine neurons to be releasing significant amounts of GABA. At the functional level, it's surprising that this major modulator of plasticity in the brain, which is so critical for Parkinson's, for learning and rewards, and for other psychiatric illnesses, can also release GABA. That raises a question as to what role GABA has."

GABA can very quickly change the electrical state of cells, inhibiting their activity by making them less excitable. Sabatini wonders if the loss of GABA in dopamine neurons could explain why hyperactivity is sometimes seen after chronic loss of these neurons.

The next challenge will be to explore whether other neurons that express the vesicular monoamine transporter also release GABA in addition to neurotransmitters such as serotonin and noradrenaline. "These findings highlight how little we actually know about the most basic features of cell identity in the brain," said Sabatini. Tritsch said what started out as a straightforward project to understand dopamine quickly changed direction, with lots of starts and stops on the way to some exciting new findings. "It can be nice to come up with a hypothesis, test it, verify it, and have everything fall into place," he said. "But biology rarely works that way."

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http://www.eurekalert.org/pub_releases/2012-10/aaon-tie101712.php

Timing is everything: Hormone use may reduce or increase Alzheimer's disease risk in women

A new study suggests that women who begin taking hormone therapy within five years of menopause may reduce their risk of developing Alzheimer's disease.

MINNEAPOLIS – The research is published in the October 24, 2012, online issue of *Neurology*®, the medical journal of the American Academy of Neurology.

"This has been an area of debate because observational studies have shown a reduced risk of Alzheimer's disease with hormone therapy use, while a randomized controlled trial showed an increased risk. Our results suggest that there may be a critical window near menopause where hormone therapy may possibly be beneficial," said study author Peter P. Zandi, PhD, with Johns Hopkins University in Baltimore.

"On the other hand, if started later in life, hormone therapy could be associated with an increased risk of developing Alzheimer's disease."

For the study, researchers followed 1,768 women ages 65 and older for 11 years. The women provided a history of their hormone therapy use and the date at which menopause began. A total of 1,105 women had used hormone therapy, consisting of estrogen alone or in combination with a progestin. During the study, 176 women developed Alzheimer's disease dementia, including 87 of the 1,105 women who had taken hormone therapy compared to 89 of the 663 others.

The study found that women who began hormone therapy within five years of menopause had a 30-percent lower risk of Alzheimer's dementia than those who had not used hormone therapy. The risk was unchanged among other hormone users who had begun treatment more than five years after menopause, but a higher risk of dementia was observed among women who had started a combined therapy of estrogen and progestin when they were at least 65 years old.

"While this well-designed study supports the possibility that short-term hormone use may reduce the risk of Alzheimer's disease, more research is needed before we can make new clinical recommendations for women and their use of hormone therapy," said Victor Henderson, MD, MS, with Stanford University in Stanford, Calif., and a Fellow of the American Academy of Neurology, who wrote an accompanying editorial.

The study was supported by the National Institute on Aging.

http://www.eurekalert.org/pub_releases/2012-10/w-had102412.php

Herbal and dietary supplements can adversely affect prescribed drugs says extensive review

Findings could be just the tip of the iceberg says accompanying editorial

A number of herbs and dietary supplements (HDS) can cause potentially harmful drug interactions, particularly among people receiving medication for problems with their central nervous or cardiovascular systems.

Those are the key findings of an extensive research review published in the November issue of IJCP, the International Journal of Clinical Practice. Researchers examined 54 review articles and 31 original studies.

They found that the greatest problems were caused by interactions between prescribed drugs and HDS that included ingredients such as St John's Wort, magnesium, calcium, iron or ginkgo.

"Consumer use of HDS has risen dramatically over the past two decades" says co-author Dr Hsiang-Wen Lin from the College of Pharmacy, China Medical School, Taiwan. "In the USA, for example, it is estimated that more than 50 per cent of patients with chronic diseases or cancer use them and that many patients take them at the same time as prescribed medication. "Despite their widespread use, the potential risks associated with combining HDS with other medications, which include mild-to-severe heart problems, chest pain, abdominal pain and headache, are poorly understood."

Key findings of the review included:

The literature covered 213 HDS entities and 509 prescribed medications, with 882 HDS-drug interactions described in terms of their mechanisms and severity.

Warfarin, insulin, aspirin digoxin and ticlopidine had the greatest number of reported interactions with HDS.

More than 42 per cent of the drug interactions were caused by the HDS altering the pharmacokinetics of the prescribed drugs - the process by which a drug is absorbed, distributed, metabolised and eliminated by the body.

Just over 26 per cent of the total were described as major interactions.

Among the 152 identified contraindications, the most frequent involved the gastrointestinal system (16.4%), neurological system (14.5%) and andrenal/ genitourinary diseases (12.5%).

Flaxseed, echinacea and yohimbe had the largest number of documented contraindications.

"Our extensive review clearly shows that some HDS ingredients have potentially harmful drug interactions that are predominately moderate in their severity" says Dr Lin. "It also showed that herbal and botanical remedies were more likely to have documented drug interactions and contraindications than the other dietary supplements, such as vitamins, minerals and amino acids."

In an editorial on the review, Professor Edzard Ernst, Emeritus Professor, University of Exeter says that the authors provide an impressively complete overview of a fascinating and potentially important subject.

"Survey after survey shows that large proportions of the population are trying 'natural' remedies for illness-prevention, all sorts of ailments, diseases or for states of reduced well-being" he says. "Most experts therefore agree that the potential for such interactions is substantial. "Despite this consensus and despite the considerable amount of documented harm generated by such interactions, our current knowledge is still woefully incomplete."

Professor Ernst believes that the number of interactions between HDS and prescribed drugs could be under-reported and just the tip of the iceberg. He feels that the situation calls for rigorous research, increased awareness of possible HDS prescription interactions by physicians and patients and greater government control of this public health issue.

"Patients deserve reliable information, and it is our duty to provide it" he says. "We have to become vigilant and finally agree to monitor this sector adequately. Each individual doctor can contribute to this process by routinely including questions about alternative medicine use in their medical history taking."

http://www.eurekalert.org/pub_releases/2012-10/ru-mdd102412.php

Moderate drinking decreases number of new brain cells

Rutgers researchers say daily drinking is risky

Drinking a couple of glasses of wine each day has generally been considered a good way to promote cardiovascular and brain health. But a new Rutgers University study indicates that there is a fine line between moderate and binge drinking – a risky behavior that can decrease the making of adult brain cells by as much as 40 percent.

In a study posted online in the journal Neuroscience, scheduled to be published on November 8, lead author Megan Anderson, a graduate student working with Dr. Tracey J. Shors, Professor II in Behavioral and Systems Neuroscience in the Department of Psychology at Rutgers, reported that moderate to binge drinking – drinking less during the week and more on the weekends – significantly reduces the structural integrity of the adult brain.

"Moderate drinking can become binge drinking without the person realizing it," said Anderson. "In the short term there may not be any noticeable motor skills or overall functioning problems, but in the long term this type of behavior could have an adverse effect on learning and memory."

Shors and Anderson worked with postdoctoral fellow Miriam Nokia from the University of Jyväskylä in Finland to model moderate to heavy drinking in humans – the rodents voluntarily reaching a blood alcohol level of 0.08 percent, the legal driving limit in the United States and many other countries – brain cell production was affected negatively.

The researchers discovered that at this level of intoxication in rats – comparable to about 3-4 drinks for women and five drinks for men – the number of nerve cells in the hippocampus of the brain were reduced by nearly 40 percent compared to those in the abstinent group of rodents. The hippocampus is a part of the brain where the new neurons are made and is also known to be necessary for some types of new learning.

This level of alcohol intake was not enough to impair the motor skills of either male or female rats or prevent them from associative learning in the short-term. Still, Anderson said, this substantial decrease in brain cell numbers over time could have profound effects on the structural plasticity of the adult brain because these new cells communicate with other neurons to regulate brain health.

"If this area of your brain was affected every day over many months and years, eventually you might not be able to learn how to get somewhere new or to learn something new about your life," said Anderson, a graduate fellow in the Department of Neuroscience and Cell Biology at Rutgers. "It's something that you might not even be aware is occurring."

According to the National Institute of Alcohol Abuse and Alcoholism, men who drink 14 drinks a week and women who drink seven are considered at-risk drinkers. Although college students commonly binge drink, according to the institute, 70 percent of binge drinking episodes involved adults age 26 and older.

"This research indicates that social or daily drinking may be more harmful to brain health than what is now believed by the general public," she said.

<http://nyti.ms/VTPfjB>

U.S. Concern Over Compounders Predates Outbreak of Meningitis

A year before people began dying of meningitis caused by a tainted drug, the FDA worried that compounders across the country might be selling another substandard drug

By WALT BOGDANICH and SABRINA TAVERNISE

A year before people began dying of meningitis caused by a tainted drug from a compounding pharmacy in Massachusetts, the Food and Drug Administration worried that compounders across the country might be selling another substandard drug, one possibly made with unapproved Chinese ingredients.

But when the F.D.A. began seeking samples to test, the trade group representing compounding pharmacists went on the offensive. Instead of encouraging members to help the agency determine if the injectable drug, used to reduce the risk of premature birth, was substandard, the group tutored pharmacists on how to sidestep requests.

In an e-mail to members, the International Academy of Compounding Pharmacists suggested that they respond to any request for samples by saying, "We do not compound or distribute 'samples' of any of our prescription medications to anyone." And if a compounded drug was on the premises, the trade group added, a pharmacist should say it was awaiting pickup by a patient.

A spokesman for the trade group said the instructions were intended to guard against unauthorized release of samples to corporate competitors and not to hinder the F.D.A. investigation. But the memo is emblematic of the industry's frequent and often successful attempts to fend off regulators at a time when concerns are growing about the quality of compounded drugs and the uncertain provenance of their ingredients, some of which originate in China and flow through various repackagers and middlemen with little scrutiny, according to interviews with health experts and government records.

Drugs made by compounders - who mix or alter ingredients to create customized medicine for a specific patient - are rarely tested, unless someone is harmed or a complaint is filed. But in the only two states that randomly test compounded drugs, Texas and Missouri, significant problems have surfaced.

In Texas, a hub of compounding pharmacies, random tests by the state's pharmacy board over the last several years found that as many as one in four compounded drugs was either too weak or too strong. The testing results are just slightly better in Missouri. Potency varied by as much as 300 percent in the Missouri tests. And records of F.D.A. drug seizures at United States borders, as well as several criminal cases, point to a link between drug compounders and Chinese manufacturers, some not registered with the F.D.A. Records analyzed by The New York Times show that in 62 cases over the last decade, the F.D.A. blocked the importation of

drugs for use in compounding; nearly half were from China, one of the largest producers of raw pharmaceutical ingredients, where many manufacturers operate outside the regulatory net.

The F.D.A. said on Friday that investigators did not believe that original ingredients used by the Massachusetts pharmacy, the New England Compounding Center in Framingham, were the source of the crisis unfolding in 16 states, where at least 297 people have contracted meningitis and 23 have died.

Beyond the Massachusetts case, though, United States authorities have expressed concern that compounders, far less stringently regulated than commercial drug makers, have been using ingredients manufactured overseas in factories not approved by the F.D.A.

Last year, the F.D.A. issued an import warning after noticing that “a large increase” in unapproved human growth hormone, manufactured overseas, was being offered to compounding pharmacies.

In March, an upstate New York company, Medisca, which sells ingredients to compounders, forfeited \$1.7 million from the unlawful sale of human growth hormone supplied by an unapproved Chinese drug maker. Two other compounding pharmacies were also found in recent years to have illegally sold anabolic steroids and human growth hormone made in China.

As companies increasingly buy raw materials from foreign sources - about 80 percent of active pharmaceutical ingredients in products sold in the United States are from overseas - regulators are struggling to keep up. Modern supply chains are a maze of importers, repackagers and dealers. But while large drug companies, bound by F.D.A. rules, must keep meticulous track of who has handled their raw materials, compounding pharmacies are not bound by those guidelines, even though some have grown so large that they resemble commercial manufacturers.

Michael Chappell, a former high-ranking F.D.A. official who helped to oversee the agency’s regulatory policies, said federal officials have had difficulty at times getting answers to questions about where compounders bought their ingredients. “Is it being repackaged in the back of a ’57 Buick in a parking lot somewhere?” Mr. Chappell asked. “The answer was always, ‘We get them from our suppliers.’ But what do you know about that supplier? Who makes the original chemical?”

Some compounding pharmacies have taken advantage of the legal no-man’s land in regulation. The F.D.A. can inspect them and issue warnings, but the agency says states have ultimate jurisdiction.

“You can ask a question, but does a company have to answer you?” said Robert Coleman, who was an F.D.A. investigator for three decades and is now a consultant based in Atlanta. “That’s up for debate. It always made me wonder as an investigator, ‘Why don’t you want to tell me that? Is there some problem?’ ”

The F.D.A. has authority if it decides that a compounding pharmacy is manufacturing, and not simply mixing drugs for individual patients. But to make that determination, the agency has to look at a pharmacy’s records to see its volume, and pharmacies argue that the law does not require them to produce those records.

“There is some legal dispute about our ability to look at records and pharmacies and it is the records that help us determine whether a pharmacy is acting as a pharmacy or as a manufacturer,” Deborah M. Autor, the F.D.A.’s deputy commissioner for global regulatory operations and policy, said in a phone call with journalists. Some consumer advocates say that the F.D.A. has the authority to investigate compounding pharmacies but often chooses not to.

Unlike commercial drug manufacturers, compounding pharmacies are not bound by the agency’s so-called good manufacturing practices, which require companies to report instances when their medicine might have harmed patients. Usually the F.D.A. learns about such cases only through the news media or voluntary reporting.

There have been virtually no federal efforts to quantify the problem of large-scale compounding pharmacies or their rapid growth, but the F.D.A. has occasionally taken a limited look at the quality of their drugs. In 2001, the agency looked at samples of compounded products from 12 different pharmacies and found that a third of the products failed one or more standard quality tests, mostly having to do with potency. A similar F.D.A. survey in 2006 found the failure rate about the same.

After a pharmacist in Kansas City, Mo., pleaded guilty to watering down chemotherapy drugs, the Missouri Board of Pharmacy began in 2006 randomly sampling compounded drugs. In 2008, one in four samples failed a potency test. The failure rate dropped to 15 percent in 2010, the most recent year available.

The Texas State Board of Pharmacy started its own random testing program after seeing what Missouri had done. That state’s failure rate has generally hovered between 20 percent and 25 percent. “If you take a drug, you should expect to get the amount of drug listed on the bottle,” said Gay Dodson, the board’s executive director.

In April, a compounding pharmacy in Dallas, ApotheCure Inc., and its owner, pleaded guilty in federal court to two misdemeanors for shipping a misbranded drug that led to the deaths of three people in the Pacific

Northwest. Subsequent testing by the F.D.A. found that some vials were superpotent, containing 640 percent of the drug listed on the label, while others were subpotent.

K V Pharmaceuticals, a drug company in St. Louis, did not rely on the government to assess the quality of compounded drugs that competed with its F.D.A.-approved product, Makena, used to reduce the risk of premature birth. K V hired a corporate intelligence firm to obtain and test samples of the compounded version, 17P, for potency and purity.

In January, the company's researchers published their findings, alleging that 80 percent of the drug did not meet purity specifications. Michael J. Jozwiakowski, a co-author of the study, said the only companies they could find that manufactured the active pharmaceutical ingredient, available to compounders, were Chinese companies not registered with the F.D.A. One sample contained nothing but glucose.

When the F.D.A. was given the data last fall, the agency decided to take its own samples of the compounded version, prompting the International Academy of Compounding Pharmacists, the trade organization, to offer its members advice on how to respond to F.D.A. requests, in an e-mailed member alert titled, "F.D.A. Calling Compounders about 17-P."

The trade group spokesman, David Miller, said the alert, despite its title, was intended to defend against data collectors from K V Pharmaceuticals, who member pharmacies said had been calling them asking for samples. "There was no evidence that any of the calls pharmacies received were coming from a genuine governmental official," Mr. Miller said. "Regulators do not 'call around' asking for information. They come to a pharmacy with an official inspection form."

He denied that the alert contained language instructing members not to cooperate with federal regulators.

"There is not one word in that document that says do not comply with a regulator," he said.

Dr. Michael Carome, deputy director of Public Citizen's Health Research Group, a nonprofit consumer organization, said the group's advice to members should have been to cooperate fully and answer all their questions. Instead, Dr. Carome said, the group suggested answers "for which the implicit, if not explicit message was to stonewall and obstruct" the F.D.A.'s attempt to assess the quality of the compounded drug. The F.D.A. said in June that after obtaining and testing 13 samples of the compounded drug, it had found no significant quality problems. K V Pharmaceuticals filed for bankruptcy this year, and is suing the F.D.A.

Sarah Cohen contributed reporting.

<http://www.sciencedaily.com/releases/2012/10/121024175240.htm>

Area of the Brain That Processes Empathy Identified

An international team has shown that the anterior insular cortex is the activity center of human empathy, whereas other areas of the brain are not

ScienceDaily - An international team led by researchers at Mount Sinai School of Medicine in New York has for the first time shown that one area of the brain, called the anterior insular cortex, is the activity center of human empathy, whereas other areas of the brain are not. The study is published in the September 2012 issue of the journal *Brain*.

Empathy, the ability to perceive and share another person's emotional state, has been described by philosophers and psychologists for centuries. In the past decade, however, scientists have used powerful functional MRI imaging to identify several regions in the brain that are associated with empathy for pain. This most recent study, however, firmly establishes that the anterior insular cortex is where the feeling of empathy originates. "Now that we know the specific brain mechanisms associated with empathy, we can translate these findings into disease categories and learn why these empathic responses are deficient in neuropsychiatric illnesses, such as autism," said Patrick R. Hof, MD, Regenstreif Professor and Vice-Chair, Department of Neuroscience at Mount Sinai, a co-author of the study. "This will help direct neuropathologic investigations aiming to define the specific abnormalities in identifiable neuronal circuits in these conditions, bringing us one step closer to developing better models and eventually preventive or protective strategies."

Xiaosi Gu, PhD, who conducted the research in the Department of Psychiatry at Mount Sinai, worked with researchers from the United States and China, to evaluate Chinese patients, at Beijing Tiantan Hospital, who were shown color photographs of people in pain. Three patients had lesions caused by removing brain tumors in the anterior insular cortex; nine patients had lesions in other parts of the brain and 14 patients (the controls) had neurologically intact brains. The research team found that patients with damage restricted to the anterior insular cortex had deficits in explicit and implicit empathetic pain processing.

"In other words, patients with anterior insular lesions had a hard time evaluating the emotional state of people in pain and feeling empathy for them, compared to the controls and the patients with anterior cingulate cortex lesions," said Dr. Jin Fan, corresponding author of this study and an assistant professor at the Department of Psychiatry at Mount Sinai.

According to Dr. Gu, this study provides the first evidence suggesting that the empathy deficits in patients with brain damage to the anterior insular cortex are surprisingly similar to the empathy deficits found in several psychiatric diseases, including autism spectrum disorders, borderline personality disorder, schizophrenia, and conduct disorders, suggesting potentially common neural deficits in those psychiatric populations.

"Our findings provide strong evidence that empathy is mediated in a specific area of the brain," said Dr. Gu, who now works at University College London. "The findings have implications for a wide range of neuropsychiatric illnesses, such as autism and some forms of dementia, which are characterized by prominent deficits in higher-level social functioning."

This study suggests that behavioral and cognitive therapies can be developed to compensate for deficits in the anterior insular cortex and its related functions such as empathy in patients. These findings can also inform future research evaluating the cellular and molecular mechanisms underlying complex social functions in the anterior insular cortex and develop possible pharmacological treatments for patients.

The study was funded by the National Institute of Health, the James S. McDonnell Foundation and a Brain and Behavior Research Foundation NARSAD young investigator award.

X. Gu, Z. Gao, X. Wang, X. Liu, R. T. Knight, P. R. Hof, J. Fan. Anterior insular cortex is necessary for empathetic pain perception. Brain, 2012; 135 (9): 2726 DOI: 10.1093/brain/aws199

<http://bit.ly/Pdo8vJ>

Easter Island Statues Might Have Been "Walked" Out of Quarry ***A contentious theory was recently put to the test with an almost life-size replica*** **By Ewen Callaway | Wednesday, October 24, 2012 | 6**

Easter Island's gargantuan stone statues walked. That is the controversial claim from archaeologists who have demonstrated the feat with a 4.4-tonne model of one of the baffling busts. They describe their work in the *Journal of Archaeological Science*.

Nearly 1,000 statues litter Easter Island's 163 square kilometers, with the largest weighing 74 tons and standing 10 meters tall. Much about the megaliths is mystery, but few of the enigmas are more perplexing than how the statues were shuttled kilometers from the rock quarries where they were carved.

Archaeologists have proposed that the Polynesians who settled Easter Island 800 years ago or more laid the statues (called moai) prone and rolled them along on logs. That idea supports the theory that the settlers, known as Rapa Nui, became so obsessed with statue-building that they denuded the island of its forests. In his book *Collapse* (Viking, 2005), Jared Diamond, a geographer at the University of California, Los Angeles, touted Easter Island as the poster child for a civilization that blew through its natural resources and folded.

"It's a great story but the archaeological evidence doesn't really support it," says Carl Lipo, an archaeologist at California State University, Long Beach, whose team instead proposes that the Rapa Nui 'walked' the moai by rocking them from side to side, as one might move a refrigerator.



Researchers have used a replica moai to show how the giant statues may have been "walked" to where they are displayed. Image: Courtesy of Carl Lipo

Made to walk

Some statues are found on stone pedestals; others are in incomplete forms along roads or in a quarry. The incomplete statues - which Lipo says would have been modified once they reached their pedestals - lean noticeably forward, in a posture that doesn't lend itself to horizontal transport, says Lipo. Broken moai along roads, which were presumably abandoned, also point to vertical transport. On roads that slope upwards away from the quarry, the statues lie on their backs, whereas downwards-sloping roads tend to be littered with face-planted moai, Lipo notes.

Lipo and Terry Hunt, an archaeologist at the University of Hawaii in Honolulu, noted these points in their contentious book *The Statues That Walked* (Free Press, 2011; see 'Anthropology: Head to head'). A US television program later asked the pair to test their hypothesis with a life-size model. With the help of a ship-building company, they constructed a 3-metre-tall concrete model of one of the statues.

The researchers had no clue how to get the model walking. "An aeronautical engineer can explain why a plane flies, but you don't want one flying a plane," says Lipo. "Here we have this giant 5-ton thing, now figure out how it actually moves. It was quite frustrating."

The statue could not stand on its own and had to be rested on supports. But after several trying days, a team of 18 people chanting "heave-ho" managed to get the thing walking with three hemp ropes - one tied to it from behind to keep the statue from falling on its face and two on either side (see video). "It really hauls," says Lipo: the team got the statue to travel 100 meters in under an hour. Lipo suggests that a small number of people working part time could efficiently transport moai, questioning a scenario in which Easter Island's population ballooned and later crashed, as Diamond and others have proposed.

Off the mark

But not everyone is convinced by Lipo and Hunt's work. "What they did was a stunt and not an experiment," says Jo Anne Van Tilburg, director of the Easter Island Statue Project at the University of California, Los Angeles.

The shape of the team's model statue is not an accurate facsimile of the moai, she says, so any conclusions drawn from it are irrelevant. "What this work has done is disengaged the statues from the archaeological context, and I think any time you do that, you enter, however gingerly, into fantasy and speculation on a level that isn't scientific," says Van Tilburg, whose own team has demonstrated that moai can be moved horizontally along logs (see video).

Yet aspects of the statues' design seem intended for walking, contends Lipo. Their centre of mass is centered vertically and horizontally, but sits slightly forward of centre on the front-to-back axis, making it easy to rock the statues back and forth. Furthermore, the statues' relatively broad bodies and elongated heads make them stable when walking. "What's cool is that their shape really reflects the engineering of the Rapa Nui people. They built these things to do this," says Lipo.

http://www.eurekalert.org/pub_releases/2012-10/mc-gtu102512.php

Gene that's usually bad news loses its punch if you live to your 90s, Mayo study finds ***A gene linked to the risk of developing Alzheimer's, heart disease and diabetes becomes less important to quality of life once people hit their 90s, a Mayo Clinic study shows.***

ROCHESTER, Minn. - At that point, good friends and a positive attitude have a bigger impact, the researchers say. The findings are published this month in the Journal of American Medical Directors Association.

Researchers used the National Institutes of Health-supported Rochester Epidemiology Project, a database of patient records in Olmsted County, Minn., to find people ages 90 to 99 living on their own or in long-term care. The 121 participants completed an interview, a physical exam and a quality-of-life questionnaire. Participants were divided into groups based on their cognitive function, to sort out the effects of age and disease on well-being, and blood samples were taken for genotyping.

Researchers discovered that those who carried the gene in question, known as ApoE4, were no worse off than others in the study. "We found if people had good physical, intellectual, and emotional well-being, more social connectedness, and if they perceived themselves to have better coping skills, they felt they had better quality of life," says co-author Maria Lapid, M.D., a Mayo Clinic psychiatrist.

"The study shows that the ApoE4 genotype doesn't determine what your quality of life will be, and that, regardless of your gender, environmental factors play a significant role in your physical, emotional, spiritual, and social well-being," she says. "You can have good quality of life regardless of this gene."

The median age of those studied was 93; 87 percent were women. Those reporting poorer quality of life tended to be men, for reasons that are unclear, and people who experienced pain.

The Alzheimer's Association, National Institute on Aging, and Robert H. and Clarice Smith and Abigail Van Buren Alzheimer's Disease Research Program of the Mayo Foundation funded the study.

http://www.eurekalert.org/pub_releases/2012-10/uoia-ato102412.php

Antibiotics that only partly block protein machinery allow germs to poison themselves ***Powerful antibiotics that scientists and physicians thought stop the growth of harmful bacteria by completely blocking their ability to make proteins actually allow the germs to continue producing certain proteins - which may help do them in.***

The finding, by a team at the University of Illinois at Chicago College of Pharmacy, clarifies how antibiotics work and may aid in the discovery of new drugs or improve clinical therapy with existing ones. The study is published in the Oct. 26 issue of the journal Cell. Among the most complex molecular machines in the cell are the ribosomes, responsible for churning out all the proteins a cell needs for survival. In bacteria, ribosomes are the target of many important antibiotics, says Alexander Mankin, professor and director of the UIC Center for Pharmaceutical Biotechnology, who led the study.

Mankin and his colleagues picked apart the process of protein synthesis inside the ribosome, comparing the action of the classic antibiotics erythromycin and azithromycin and newer drugs called ketolides, which are

used to treat serious infections. Surprisingly, the more powerful drugs were the more "leaky" in blocking the production of proteins.

"We were shocked to discover that ketolides, which are known to be better antibiotics, allow for many more proteins to be made compared to the older, less efficient drugs," Mankin said. "We now believe that allowing cells to make some proteins could be much more damaging for a microbe than not letting it make any proteins at all."

The findings may point the way to better and more potent antibiotics, Mankin said. But he and colleagues are "thinking beyond just antibiotics." "If a chemical can be designed that binds to the human ribosome and allows it to make good proteins but not bad ones, such as mutant enzymes or proteins that promote cancer, then such new drugs can treat many human maladies," he said.

Co-authors on the Cell paper are graduate student Krishna Kannan and research associate professor Nora Vazquez-Laslop. The study was funded by the National Science Foundation.

http://www.eurekalert.org/pub_releases/2012-10/bmj-st1102412.php

Smoking takes 10 years off life expectancy in Japan, not 4 as previously thought, experts warn

But much of the risk can be avoided if smoking is stopped, preferably well before age 35

Smoking reduces life expectancy by ten years in Japan, but much of the risk can be avoided by giving up smoking, a paper published on bmj.com today shows.

Previous studies in Japan suggested smoking reduced life expectancy by only a few years compared with about ten years in Britain and the USA. This new report, from researchers in Oxford and Japan, investigates the impact of smoking on mortality in a large group of Japanese people who were living in Hiroshima or Nagasaki in 1950. The findings are, however, nothing to do with radiation exposure from the bombs.

The Life Span Study (LSS) was initiated in 1950 to investigate the effects of radiation, tracking over 100,000 people. However, most received minimal radiation exposure, and can therefore provide useful information about other risk factors. Surveys carried out later obtained smoking information for 68,000 men and women, who have now been followed for an average of 23 years to relate smoking habits to survival.

The younger a person was when they started smoking the higher the risk in later life. Older generations did not usually start to smoke until well into adult life, and usually smoked only a few cigarettes per day. In contrast, Japanese born more recently (1920-45) usually started to smoke in early adult life, much as smokers in Britain and the USA.

These differences in smoking habits are reflected in the mortality patterns. Smokers born before 1920 lost just a few years. In contrast, men born later (1920-45) who started to smoke before age 20 lost nearly a decade of life expectancy, and had more than double the death rate of lifelong non-smokers, suggesting that more than half of these smokers will eventually die from their habit. Results on the few women who had smoked since before age 20 were similar.

Previous studies of the effects of smoking in Japan had been mainly of individuals born in the first few decades of the twentieth century who probably didn't start to smoke until well into adult life and smoked only a few cigarettes per day. This explains why the risks of smoking seemed low. Nowadays, however, young Japanese smokers tend to smoke more cigarettes per day and to start at a younger age, so their risks will be higher.

In addition to studying the risk of smoking, the researchers were able to examine the benefits of stopping. As elsewhere, those who stopped smoking before age 35 avoided almost all the excess risk among continuing smokers, and even those who stopped around age 40 avoided most of it.

The researchers conclude that the future health risks to young smokers are likely to be just as big in Japan as in other countries although much of the risk can be avoided by stopping.

http://www.eurekalert.org/pub_releases/2012-10/wuso-rfs102412.php

Resveratrol falls short in health benefits

Studying healthy, middle-aged women, researchers found that supplementation with resveratrol, an ingredient in red wine, does not offer the medical benefits previously thought.

Resveratrol, an ingredient in red wine thought to improve insulin sensitivity, reduce risk of heart disease and increase longevity, does not appear to offer these benefits in healthy women, new research at Washington University School of Medicine in St. Louis indicates. The study, reported online Oct. 25 in *Cell Metabolism*, involved 29 post-menopausal women who did not have type 2 diabetes and who were reasonably healthy. For 12 weeks, half took an over-the-counter resveratrol supplement, and the rest got a placebo, or sugar pill.

"Resveratrol supplements have become popular because studies in cell systems and rodents show that resveratrol can improve metabolic function and prevent or reverse certain health problems like diabetes, heart disease and even cancer," says senior investigator Samuel Klein, MD, director of Washington University's

Center for Human Nutrition. "But our data demonstrate that resveratrol supplementation does not have metabolic benefits in relatively healthy, middle-aged women."

The results were somewhat surprising because earlier studies suggested that drinking red wine lowers the risk of health problems.

"Few studies have evaluated the effects of resveratrol in people," Klein explains. "Those studies were conducted in people with diabetes, older adults with impaired glucose tolerance or obese people who had more metabolic problems than the women we studied. So it is possible that resveratrol could have beneficial effects in people who are more metabolically abnormal than the subjects who participated in the study."

Klein, the Danforth Professor of Medicine and Nutritional Science, directs the Division of Geriatrics and Nutritional Science and the Center for Applied Research Sciences. He says many people who have heard about red wine's health benefits want to take resveratrol supplements to get the benefits of red wine without consuming large amounts of alcohol. In recent years, annual U.S. sales of resveratrol supplements have risen to \$30 million.

As part of the study, Klein and his colleagues gave 15 post-menopausal women 75 milligrams of resveratrol daily, the same amount they'd get from drinking 8 liters of red wine, and compared their insulin sensitivity to 14 others who took a placebo.

The team measured the women's sensitivity to insulin and the rate of glucose uptake in their muscles, infusing insulin into their bodies and measuring their metabolic response to different doses.

"It's the most sensitive approach we have for evaluating insulin action in people," he says. "And we were unable to detect any effect of resveratrol. In addition, we took small samples of muscle and fat tissue from these women to look for possible effects of resveratrol in the body's cells, and again, we could not find any changes in the signaling pathways involved in metabolism."

But if resveratrol doesn't have a health benefit, then why are red wine drinkers less likely to develop heart disease and diabetes? Klein says there may be something else in red wine that provides the benefit.

"The purpose of our study was not to identify the active ingredient in red wine that improves health but to determine whether supplementation with resveratrol has independent, metabolic effects in relatively healthy people," he says. "We were unable to detect a metabolic benefit of resveratrol supplementation in our study population, but this does not preclude the possibility that resveratrol could have a synergistic effect when combined with other compounds in red wine."

Yoshino J, Conte C, Fontana L, Mittendorfer B, Imai S, Schechtman KB, Gu C, Kunz I, Fanelli FR, Patterson BW, Klein S. Resveratrol supplementation does not improve metabolic function in non-obese women with normal glucose tolerance. Cell Metabolism vol 16, published on line Oct. 25, 2012

Funding for this research comes from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH), and grants from DSM Nutritional Products, the Longer Life Foundation, the Japanese Research Foundation for Clinical Pharmacology, the Manpei Suzuki Diabetes Foundation and the Kanae Foundation for the Promotion of Medical Science. NIH grant numbers UL1 RR024992, DK 56341 and DK 37948.

http://www.eurekalert.org/pub_releases/2012-10/cp-adr102212.php

Anesthesia drugs really do put us to sleep

When patients are put under anesthesia, they are often told they will be "put to sleep," and now it appears that in some ways that's exactly what the drugs do to the brain.

New evidence in mice reported online on October 25 in *Current Biology*, a Cell Press publication, shows that the drugs don't just turn wakefulness "off," they also force important sleep circuits in the brain "on."

"Despite more than 160 years of continuous use in humans, we still do not understand how anesthetic drugs work to produce the state of general anesthesia," said Max Kelz of the University of Pennsylvania.

"We show that a commonly used inhaled anesthetic drug directly causes sleep-promoting neurons to fire. We believe that this result is not simply a coincidence. Rather, our view is that many general anesthetics work to cause unconsciousness in part by recruiting the brain's natural sleep circuitry, which initiates our nightly journey into unconsciousness."

Kelz is himself an anesthesiologist, and he had long wondered just how accurate this notion of putting his patients to sleep really was. After all, there are important differences between natural sleep and the unconsciousness that comes with anesthesia. Even the soundest sleeper can be roused, while anesthetized patients maintain their slumber through the incredible insults that surgeries unavoidably bring.

In the new study, Kelz's team focused on a particular part of the brain, deep within the hypothalamus, which is known to increase in activity as one drifts off to sleep.

Through a combination of direct electrical recording and other methods, they found that the anesthetic drug known as isoflurane boosts activity in this sleep-promoting brain area in mice. As further evidence of a connection, animals lacking the function of those neurons became more resistant to entering states of anesthesia.

The findings not only provide important clinical insights, but they might also go a long way toward reawakening our curiosity about anesthesia - to say nothing of the very mysterious nature of human consciousness itself.

"The development of anesthetic drugs has been hailed as one of humankind's greatest discoveries in the last thousand years," Kelz said. "Anesthetics are annually given to over 230 million patients worldwide. Yet as a society, and even within the anesthesia community, we seem to have lost our curiosity for how and why they work."

Moore et al.: "Direct Activation of Sleep-Promoting VLPO Neurons by Volatile Anesthetics Contributes to Anesthetic Hypnosis."

<http://nyti.ms/TnXj8A>

If Smart Is the Norm, Stupidity Gets More Interesting

Instead of thinking about the genetics of intelligence, we should be trying to parse "the genetics of stupidity"

By DAVID DOBBS

Few of us are as smart as we'd like to be. You're sharper than Jim (maybe) but dull next to Jane. Human intelligence varies. And this matters, because smarter people generally earn more money, enjoy better health, raise smarter children, feel happier and, just to rub it in, live longer as well.

But where does intelligence come from? How is it built? Researchers have tried hard to find the answer in our genes. With the rise of inexpensive genome sequencing, they've analyzed the genomes of thousands of people, looking for gene variants that clearly affect intelligence, and have found a grand total of two.

One determines the risk of Alzheimer's and affects I.Q. only late in life; the other seems to build a bigger brain, but on average it raises I.Q. by all of 1.29 points.

Other genetic factors may be at work: A report last year concluded that several hundred gene variants taken together seemed to account for 40 to 50 percent of the differences in intelligence among the 3,500 subjects in the study. But the authors couldn't tell which of these genes created any significant effect. And when they tried to use the genes to predict differences in intelligence, they could account for only 1 percent of the differences in I.Q.

"If it's this hard to find an effect of just 1 percent," Robert Plomin, a professor of behavioral genetics at King's College London, told *New Scientist*, "what you're really showing is that the cup is 99 percent empty."

But is the genetic cup really empty, or are we just looking for the wrong stuff? Kevin Mitchell, a developmental neurogeneticist at Trinity College Dublin, thinks the latter. In an essay he published in July on his blog, *Wiring the Brain*, Dr. Mitchell proposed that instead of thinking about the genetics of intelligence, we should be trying to parse "the genetics of stupidity," as his title put it. We should look not for genetic dynamics that build intelligence but for those that erode it.

The premise for this argument is that once natural selection generated the set of genes that build our big, smart human brains, those genes became "fixed" in the human population; virtually everyone receives the same set, and precious few variants affect intelligence. This could account for the researchers' failure to find many variants of measurable effect.

But in some other genetic realms we do differ widely, for example, mutational load - the number of mutations we carry. This tends to run in families, which means some of us generate and retain more mutations than others do. Among our 23,000 genes, you may carry 500 mutations while I carry 1,000.

Most mutations have no effect. But those that do are more likely to bring harm than good, Dr. Mitchell said in an interview, because "there are simply many more ways of screwing something up than of improving it."

Open the hood of a smooth-running car and randomly turn a few screws, and you'll almost certainly make the engine run worse than before. Likewise, mutations that change the brain's normal development or operation will probably slow it down. Smart Jane may be less a custom-built, high-performance model than a standard version pulling a smaller mutational load.

We also inherit - through genes yet to be identified, of course - a trait known as developmental stability. This is essentially the accuracy with which the genetic blueprint is built. Developmental stability keeps the project on track. It reveals itself most obviously in physical symmetry. The two sides of our bodies and brains are constructed separately but from the same 23,000-gene blueprint. If you have high developmental stability, you'll turn out highly symmetrical. Your feet will be the same shoe size, and the two sides of your face will be identical.

If you're less developmentally stable, you'll have feet up to a half-size different and a face that's like two faces fused together. Doubt me? Take a digital image of your face and split it down the middle. Then make a mirror-

image copy of each half and attach it to its original. In the two faces you've just made - one your mirrored left side, the other your right - you'll behold your own developmental stability, or lack thereof.

Both those faces might be better-looking than you are, for we generally find symmetrical faces more attractive. It also happens that symmetry and intelligence tend to run together, because both run with developmental stability. We may find symmetrical faces attractive because they imply the steadiness of genetic development, which creates valuable assets for choosing a mate, like better general fitness and, of course, intelligence - or as Dr. Mitchell might put it, a relative lack of stupidity.

These ideas don't strike geneticists as radical or contrary. Leonid Kruglyak, a Princeton geneticist who studies yeast and roundworms, noted in an e-mail that geneticists had long recognized that mutations could "throw sand in the gears of the brain" and that complex traits arose in complicated ways. "Talking about 'a gene for a trait' is a shorthand at best," he wrote, "and a well-known fallacy at worst."

Dr. Mitchell agreed. "This isn't a brand-new idea," he said. "But it's not one that has been generally adhered to in intelligence studies."

Not brand-new, perhaps. But it's this kind of "inversion of thought" (as Janet Kwasniak, a retired biologist, put it on her neuroscience blog, Thoughts on Thoughts) that can often spark new approaches to intractable problems.

Dr. Jay Giedd, who studies brain development at the National Institutes of Health, has done research suggesting that the brain blooms through many small arcs of development that make it responsive to experience - and vulnerable to error. At first, he said in an e-mail, he was skeptical of Dr. Mitchell's idea. Then he discussed it with colleagues at a neuroscience meeting.

"My initial thought was that it would be easy to sink the argument," Dr. Giedd said. But the more they discussed it, the more sense it made. "Everybody I ran it by seemed to feel the logic is sound."

David Dobbs is the author of the coming book "Orchids and Dandelions," which will explore the genetic and cultural roots of temperament.

*This article has been revised to reflect the following correction: **Correction: October 25, 2012***

An article on Tuesday about efforts to understand the genetic factors that build or erode intelligence misidentified one of the research subjects of the Princeton geneticist Leonid Kruglyak. Dr. Kruglyak studies yeast and roundworms, not flatworms.

<http://phys.org/news/2012-10-cool-planet-biofuel-production-gallon.html>

'Cool Planet' projects biofuel-production cost of \$1.50 per gallon

Cost of biofuel made from corn cobs and stover just \$1.50 per gallon without government subsidies

Phys.org - Cool Planet Energy Systems has announced a projected production cost for its biofuel, made from corn cobs and stover (dried stalks and leaves of cereal crops), of just \$1.50 per gallon sans the benefit of government subsidies. Company representatives also said they have completed a successful test trial of a newly developed process for converting feed stock to fuel, and that Google has been field testing the results with fleet vehicles.

The company has a test facility in Camarillo, CA that creates fuel by pressing feedstock between plates under high pressure, and then placing the plates in a device called a fractionator. This process results in a release of a gas which is then captured and then converted, using catalysts, to a liquid. The resultant fuel is mixed with gasoline. In tests thus far, the company has used a mixture composed of 5 percent biofuel and 95 percent gasoline. Google fleet vehicles - part of its GRide on-demand campus vehicle program - have traveled 2,400 miles on this mixture to-date.

In separate testing, Cool Planet fueled one car with the biofuel mixture and a control car with 100 percent gasoline and found that the test-fueled car met the Low Carbon Fuel Standard California has set for 2020. They also ran both cars through five smog tests and found no measurable differences between them.

The company claims the new biofuel is actually carbon negative because a byproduct of the production process is activated carbon, which can be used as a soil enhancer. They also note that their process doesn't require the use of any food crops.

Cool Planet says the new biofuel can be made in a manufacturing facility just one-hundredth the size of traditional gasoline refineries. These micro-refineries - which can reportedly produce 10 million gallons of fuel per year - are potentially transportable. This capability would allow for on-site production, thereby removing the environmental impact of shipping from a central production facility.

Because of the fuel's early success so far, Cool Planet has attracted investors such as BP, Google Ventures, General Electric, the Constellation Energy division of Exelon, NRG and ConocoPhillips.

<http://phys.org/news/2012-10-racial-hierarchy-bias-decision-armed.html>

Racial 'hierarchy of bias' drives decision to shoot armed, unarmed suspects, study finds
Some people exhibit a "hierarchy of bias" in split-second decisions whether to shoot suspects who appear to be carrying a gun or a benign object like a cell phone

Police officers and students exhibit an apparent "hierarchy of bias" in making a split-second decision whether to shoot suspects who appear to be wielding a gun or, alternatively, a benign object like a cell phone, research conducted by the University of Colorado Boulder and San Diego State University has found.

Both the police and student subjects were most likely to shoot at blacks, then Hispanics, then whites and finally, in a case of what might be called a positive bias, Asians, researchers found.

In the first study of its kind, Joshua Correll, Bernadette Park and Charles M. Judd of CU-Boulder's Department of Psychology and Neuroscience and Melody Sadler of San Diego State University examined how police and a group of undergraduate subjects decide whether to shoot or not to shoot "suspects" in a multi-ethnic environment.

"Most studies on the subject of stereotyping and prejudice look at two (ethnic) groups, usually in isolation. It's always one group against another group," said Correll, a CU graduate who joined the faculty in August after a stint at the University of Chicago.

"But as the country becomes more ethnically diverse, it's more and more important to start thinking about how we process racial and ethnic cues in a multicultural environment," he said.

As with previous studies into the question, data were gathered from subjects playing a "first person shooter" video game, in which figures of varying ethnicity - Caucasian, Asian, Hispanic and African-American - pop up, either "armed" with a weapon or another benign object, such as a cell phone.

Participants - 69 CU-Boulder undergraduates and 254 police officers - had to make quick decisions as to which figures posed a "threat" and shoot them. The police officers were recruited from two-day training seminars in Florida, New Mexico and Washington and represented numerous jurisdictions from 11 states.

The research demonstrates how persistent cultural stereotypes are, Correll said. Even students who displayed little bias when interviewed demonstrated otherwise when faced with a split-second decision.

"I may not believe it personally, but I am exposed to stereotypes constantly through media or social networks ... (such as) the idea that young black men are dangerous," he said. "Those associations can have an influence on my behavior even if I don't believe them."

The study found that police were considerably more accurate than students at correctly identifying a genuinely threatening suspect, as opposed to those brandishing a cell phone or wallet, perhaps a reflection of training. But officers were still influenced by the target's race - an influence that may derive from the officers' "contacts, attitudes and stereotypes," Correll said.

For example, police who endorsed more violent stereotypes about Hispanics and those who overestimated the prevalence of violent crime in their districts demonstrated more bias to shoot Hispanic targets. That raises the question of whether police are responding to real-world threats - and whether that means some ethnic groups really are more likely to be armed and dangerous than others.

"That is a very sensitive question, whether or not (police officers') reactions are based on some kind of truth. Is this police officers responding to reality on the ground? The short answer is, we don't know," Correll said. "But this research almost demands that we ask that question."

The researchers' recent findings were published in the Journal of Social Issues.

Provided by University of Colorado at Boulder

<http://www.sciencedaily.com/releases/2012/10/121025121846.htm>

PFO Closure May Be Superior to Medical Therapy in Preventing Stroke

Trial results show that patent foramen ovale (PFO) closure may be superior to medical therapy in preventing recurrent stroke

ScienceDaily - Results of a large-scale, randomized clinical trial called RESPECT revealed that patent foramen ovale (PFO) closure may be superior to medical therapy in preventing recurrent stroke, according to a presentation of findings today at the Transcatheter Cardiovascular Therapeutics (TCT) conference in Miami.

"In contrast to a previously reported randomized trial for the treatment of cryptogenic stroke, the RESPECT trial enrolled only patients with documented cryptogenic embolic strokes and excluded patients with other potential causes of stroke and/or TIA. The period of follow-up approached nine years and was not restricted to only events within the initial two years of follow-up," said Richard Smalling, M.D., Ph.D., James D. Wood Distinguished Chair in Cardiovascular Medicine at The University of Texas Health Science Center at Houston (UTHealth), who served on the steering committee and as a principal investigator of the trial.

"As a result, the trial enrolled patients at high-risk for recurrent events and followed them for a long period of time, enabling the detection of relatively infrequent recurrent stroke," said Smalling, who is director of interventional cardiovascular medicine at the Memorial Hermann Heart and Vascular Institute. "The totality of evidence in the RESPECT trial clearly demonstrates the superiority of device closure using the Amplatzer PFO Occluder in patients with the above entry criteria compared to standard medical therapy."

According to the National Institutes of Health, a PFO is a hole between the left and right atria (upper chambers) of the heart that fails to close naturally soon after a baby is born. In about one in four people, the hole never closes. The condition is usually not treated unless there are other heart problems or the person has a stroke caused by a blood clot. PFO has been a suspected cause of cryptogenic stroke, meaning a stroke without any identifiable cause usually occurring in people under the age of 55.

The trial enrolled 980 patients from 69 sites over eight years, yielding 2,300 patient-years of data. Medical group regimens were antiplatelet medications or warfarin. All primary endpoint events were recurrent ischemic strokes. As treated, five of the patients in the closure group had a stroke compared to 16 in the medically treated group.

"These patients with cryptogenic stroke are typically young and in the height of the productive period of their lives. Preventing a recurrent, potentially devastating, stroke by implanting a small device with very little risk is a huge potential benefit," Smalling said.

http://www.eurekalert.org/pub_releases/2012-10/usdo-mmd102612.php

Minimizing mining damage with manure

U.S. Department of Agriculture (USDA) research confirms that the time-tested practice of amending crop soils with manure also can help restore soils on damaged post-mining landscapes.

Thousands of acres of land with little or no vegetation, once mined for lead and zinc, remain throughout an area of southwestern Missouri, southeastern Kansas, and northeastern Oklahoma. The mining activities also left behind a legacy of lead-contaminated acidic soils, toxic smelter sites, and large quantities of mine tailings called "chat."

Soil scientist Paul White at the Agricultural Research Service (ARS) Sugarcane Research Unit in Houma, La., was part of a team that studied whether adding beef manure compost to soil at post-mining sites would provide the carbon needed to support a healthy plant cover. The scientists also wanted to determine if the compost could reduce levels of lead and zinc that could contaminate runoff during heavy rain. ARS is USDA's chief intramural scientific research agency.

The team amended soils in experimental plots from the mine sites with 20 or 120 tons of beef manure compost per acre, and established a cover crop of switchgrass on all the plots. Then they took soil samples from the sites five times during the two-year study.

Two years after the study began, soils in the high-compost plots had significant increases in pH, plant-available phosphorus, total nitrogen, carbon and available water. High-compost amendments also increased microbial biomass, enzyme activity and nitrification potential, all of which create and support favorable conditions for plant establishment and growth.

High rates of compost also lowered lead and zinc availability by about 90 percent, which may reduce the amount of lead and zinc that could run off and pollute nearby waterways. Since high levels of bioavailable zinc inhibit plant growth, this binding action also helps to promote the establishment of a vegetative cover that minimizes runoff and soil erosion.

Read more about this study in the October 2012 issue of *Agricultural Research* magazine.

<http://www.ars.usda.gov/is/AR/archive/oct12/soils1012.htm>

http://www.eurekalert.org/pub_releases/2012-10/uol-sr102612.php

'NHS should replace traditional autopsies with non-invasive alternative'

Group chaired by University of Leicester forensic pathology expert recommends Department of Health should create national autopsy imaging service

The NHS should implement a non-invasive alternative to autopsies, according to a Department of Health-commissioned report by leading UK experts within the field of post-mortem cross-sectional imaging.

The NHS Implementation Sub-Group of the Department of Health's Post Mortem, Forensic and Disaster Imaging Group (PMFDI) has called on the NHS to adopt post-mortem cross-sectional imaging for as an adjunct to, and under the right circumstances, a replacement for autopsies.

The group, chaired by Professor Guy Ruty, Chief Forensic Pathologist to the East Midlands Forensic Pathology Unit (EMFPU) at the University of Leicester, made the recommendations in its report *Can Cross-Sectional Imaging as an Adjunct and/or Alternative to the Invasive Autopsy be Implemented within the NHS?*, published today (Friday October 26) by the EMFPU.

The report recommends the NHS introduces a national cross-sectional autopsy imaging service provided by 30 mortuary-based imaging centres in England. This would be a single, integrated service involving radiology and pathology services, based on a single cost no matter what discovering the cause of death involves. This would be supported by transparent costs for each professional group delivering the service.

The group also suggests that a national teaching and training programme for all professionals involved in the service should be funded and developed with sub-speciality recognition for all professions involved in the delivery of the service. The group recommends the need for funded research to produce an evidence base to expand the types of death amenable to the use of non-invasive imaging. The service would be delivered primarily by the Department of Health in collaboration with the Ministry of Justice and local authorities. The Department of Health and Ministry of Justice will now consider the report's recommendations before making a decision on whether to implement the service.

The reports suggests the service should make use of alternative techniques, including post-mortem computed tomography (CT) and magnetic resonance imaging (MRI), for carrying out non-invasive autopsies.

Computed tomography, which can be enhanced by use of injected contrast medium, provides a minimally invasive radiological adjunct and, in the right circumstances, alternative for the investigation of natural and unnatural deaths, for either single cases or mass fatalities. It could also potentially allay qualms from certain faith groups that object to autopsies.

The EMFPU has pioneered research in this area in the UK in relation to the use of computed tomography in the investigation of sudden cardiac death and its application to mass fatality investigations.

Professor Ruttly stated in the report: "There are important religious, cultural and humanitarian benefits offered by non-invasive autopsies and it is recognised that there is no longer the need to undertake invasive autopsy examinations in certain types of death. The current demand by the general public for a non invasive autopsy service is expected to grow."

http://www.eurekalert.org/pub_releases/2012-10/foas-avf102612.php

A Viagra follow-up? Drug used to treat glaucoma actually grows human hair
New research in the FASEB Journal shows how a commonly prescribed glaucoma drug may be effective in treating male pattern baldness and other forms of alopecia

If you're balding and want your hair to grow back, then here is some good news. A new research report appearing online in The FASEB Journal (www.fasebj.org) shows how the FDA-approved glaucoma drug, bimatoprost, causes human hair to regrow. It's been commercially available as a way to lengthen eyelashes, but these data are the first to show that it can actually grow human hair from the scalp.

"We hope this study will lead to the development of a new therapy for balding which should improve the quality of life for many people with hair loss," said Valerie Randall, a researcher involved in the work from the University of Bradford, Bradford, UK. "Further research should increase our understanding of how hair follicles work and thereby allow new therapeutic approaches for many hair growth disorders."

To make this discovery, Randall and colleagues conducted three sets of experiments. Two involved human cells and the other involved mice. The tests on human cells involved using hair follicles growing in organ culture as well as those taken directly from the human scalp. In both of these experiments, the scientists found that bimatoprost led to hair growth. The third set of experiments involved applying bimatoprost to the skin of bald spots on mice. As was the case with human cells, the drug caused hair to regrow.

"This discovery could be the long-awaited follow up to Viagra that middle-aged men have been waiting for," said Gerald Weissmann, MD, editor-in-chief of The FASEB Journal. "Given that the drug is already approved for human use and its safety profile is generally understood, this looks like a promising discovery that has been right in front of our eyes the whole time. On to the front of our scalp!"

http://www.eurekalert.org/pub_releases/2012-10/si-ssf102512.php

Salk study finds diabetes raises levels of proteins linked to Alzheimer's features
Mouse model may provide clues on mechanism linking diabetes and aging to Alzheimer's

Growing evidence suggests that there may be a link between diabetes and Alzheimer's disease, but the physiological mechanisms by which diabetes impacts brain function and cognition are not fully understood. In a new study published in *Aging Cell*, researchers at the Salk Institute for Biological Studies show, for the first time, that diabetes enhances the development of aging features that may underlie early pathological events in Alzheimer's.

Specifically, the Salk team found increases in two hallmarks of Alzheimer's-accumulations of amyloid beta (A β) and tau protein-in the brains of diabetic mice, especially in cells surrounding blood vessels. A β , the misfolded peptide that is thought in part to cause Alzheimer's disease, aggregated inside astrocytes, star-shaped

brain cells that, upon interaction with Abeta, release inflammatory molecules that can destroy neurons. Previously, this had not been shown in mouse models of type 1 diabetes (T1D).

"Our study supports and extends the links between diabetes, aging and Alzheimer's," says senior author Pamela Maher, a senior staff scientist in Salk's Laboratory of Cellular Neurobiology. "We show that type 1 diabetes increases vascular-associated amyloid beta buildup in the brain and causes accelerated brain aging."

The findings suggest that the neurovascular system may be a good candidate for new therapeutic targets to treat Alzheimer's in the early stages of the disease.

Alzheimer's and diabetes are two diseases that are increasing at an alarming rate within the U.S. population. Alzheimer's affects one in 10 Americans over 65 years of age and nearly 50 percent of those over 85. Similarly, more than 8 percent of Americans (approximately 26 million people) have diabetes, with the vast majority of those individuals being over 60.

Maher says her team is uncertain of the precise mechanism behind the increase in Abeta and tau in the mouse brain, but their data suggest that changes in astrocytes, as well as other pro-inflammatory processes and the bonding of proteins with sugar molecules (called non-enzymatic glycation), may contribute.

"Astrocytes play a key role in maintaining nerve cells in the brain," says lead study author Antonio Currais, a postdoctoral researcher at Salk. "Both chronic peripheral inflammation and increased non-enzymatic glycation are associated with diabetes, and these changes may act on the brain to alter astrocyte function, which eventually leads to Alzheimer's-like changes."

All nerve cells are closely connected to blood vessels, as they need nutrients - especially glucose (sugar) and oxygen - provided by the blood in order to function. Astrocytes facilitate the transfer of nutrients between blood vessels and cells. The buildup of Abeta at sites where astrocytes interact with blood vessels suggest that this could impair the transfer of nutrients. The type of Abeta localization seen in Maher's mouse models is also found in human Alzheimer's patients

To examine the contributions of diabetes to Alzheimer's-related pathology in the aged brain, the Salk researchers induced T1D in two sets of mouse models. One set, known as SAMP8 mice, undergo accelerated aging and develop early deterioration in learning and memory, as well as a number of brain alterations similar to those found in Alzheimer's. The other set, SAMR1 mice, which in this study came from the same gene pool as the SAMP8 mice, age normally. Using these mice, Maher and her colleagues addressed how T1D interacts with age to contribute to Alzheimer's-related pathology. They showed that T1D elicits a wide range of pathological changes in the brains of both strains of mice, which are exacerbated by premature aging.

The Salk study is the first to show that these modifications are similar to those seen in old nondiabetic SAMP8 mice and to identify unique pathological changes, such as increases in markers for inflammation, in aged, T1D SAMP8 mice. Unlike most mouse studies of Alzheimer's, Maher's mice were not engineered to produce high levels of human Abeta or tau, so all of their observations came from naturally occurring Abeta and tau.

Other researchers on the study were Marguerite Prior and Professor David Schubert, from Salk's Laboratory for Cellular Neurobiology; David Lo, from Salk's Laboratory of Neuronal Structure and Function; and Corinne Jolivald of the University of California, San Diego.

The work was supported by the National Institutes of Health, the Fritz B. Burns Foundation, the Bundy Foundation, Fundação para a Ciência e a Tecnologia and the Alzheimer's Association.

<http://www.sciencedaily.com/releases/2012/10/121026084350.htm>

Penis Worms Show the Evolution of the Digestive System

A team of scientists has revealed that the enigmatic marine penis worms (priapulids) develop their intestine as humans, fish or starfish.

ScienceDaily - This surprising finding shows that very different animals share a common way of forming a gut.

A research team led by Dr. Andreas Hejnol from the Sars International Centre for Marine Molecular Biology in Norway, examined the formation of the gut and the expression of genes needed to form the mouth and the anus in priapulid embryos. Priapulids are an obscure group of marine worms that live in shallow waters.

"Surprisingly, priapulids form the gut like humans, fish, frogs, starfish and sea urchins - and all of them even use the same genes. It does not mean that these penis worms are now closely related to humans. Instead the fact that different animals share a common way of forming the gut suggests that the embryological origins of the human intestine and how it develops are much older than previously thought -- most likely over 500 million years, when the first bilaterally symmetric animals appeared on Earth" remarks Hejnol.



Adult Priapulid caudatus. Bruno Vellutini, Sars International Centre for Marine Molecular Biology

The study, featured online on the 25th of October in the journal *Current Biology*, represents the first description of the entire embryonic development of these enigmatic animals.

"Priapulids are important for understanding the evolution of animals, because they are thought to be among the first bilaterally symmetric animals and have changed very little since the Earth's Cambrian Period" says first author Dr José M. Martín-Durán.

Bilaterally symmetric animals (99% of all animals) are those with a left and right body side. Historically, they have been divided into two large groups based on major differences in how the gut develops in the embryo. The intestine is an essential organ, and that is why it is present in nearly all animal species. The gut develops very early, when some cells move towards the inside of the embryo, usually at a defined region that is called the 'blastopore'.

"The important point is that in some animals this region becomes the mouth, while in others it becomes the anus. For more than a century, this difference has captivated scientists, but there is not a completely satisfactory explanation for it yet" explains Hejnol.

The work shows how important it is to study the vast diversity of animals found in the oceans. "Priapulids still hide a lot of secrets to unravel, which will have a great influence on our understanding of the origin of other major organs, such as the brain, blood or legs" concludes Hejnol.

They reproduce in winter time, so the scientists have to travel regularly to the west coast of Sweden during the ice-cold season to get a hold of them. "We sail the fjords dredging in areas where they are abundant, collecting animals and later getting embryos from them in the lab. Although thrilling, sometimes the collection trips turn into real adventures, with low temperatures, snow or even frozen waters" says Martín-Durán.

José M. Martín-Durán, Ralf Janssen, Sofía Wennberg, Graham E. Budd, Andreas Hejnol. *Deuterostomic Development in the Protostome Priapulid caudatus*. *Current Biology*, 2012; DOI: 10.1016/j.cub.2012.09.037

<http://www.wired.com/wiredscience/2012/10/early-dinosaur-feathers/>

Dinosaurs Sprouted Wings Earlier Than Thought Dinosaurs still walk - and fly - among us: We call them birds.

By Michael Balter, ScienceNOW

Most paleontologists think birds descended from a group of winged dinosaurs, and thus dinos never went completely extinct. But where did the wings come from? New discoveries from Canada suggest that both wings and feathers arose earlier in dinosaur evolution than previously thought, possibly to attract members of the opposite sex or to protect hatching baby dinos.

Although many details of the origins of birds and winged flight are fiercely debated, researchers generally agree that birds belong to a group of dinosaurs called maniraptorans, some of which had feathers and wings and could probably fly. *Microraptor*, discovered in China, is a leading example of such a dino flyer. Indeed, almost all feathered dinosaurs have been found in the Liaoning and Inner Mongolia regions of northeastern China, where finely grained lake deposits provide excellent preservation of dinosaur fossils; the few exceptions come mostly from Germany.



Artistic reconstruction of early feathered ornithomimid dinosaurs. Image: Julius Csotonyi

But the restriction of these discoveries to such a limited geographical area has left a gap in the fossil record, leaving paleontologists to wonder whether wings and feathers might have evolved in dinosaur groups older than the maniraptorans. A team led by Darla Zelenitsky, a geoscientist at the University of Calgary in Canada decided to take a closer look at three specimens of a dinosaur called *Ornithomimus edmontonicus* housed at the Royal Tyrrell Museum of Paleontology near Drumheller, Canada. Two of the specimens, encased in hard blocks of coarse-grained sandstone, were found by a resident of Drumheller in 2008 and 2009; the third had been in the museum's collections since the 1990s.

O. edmontonicus belongs to a group of dinosaurs called ornithomimosaur, which look something like ostriches but were not previously known to have feathers. They first appear in the fossil record millions of years before maniraptorans. But when Zelenitsky's team began slowly chipping away at the sandstone blocks with a small pneumatic tool called an air scribe, it found hundreds of traces of filaments along the bodies and limbs of the specimens, which closely resembled the feather filaments from maniraptoran specimens in China.

Moreover, as the team reports in this week's issue of *Science*, while one of the two adult skeletons showed evidence of possessing a pennibrachium - a forelimb bearing long feathers that form a winglike surface - the

third specimen, a juvenile dinosaur about 1-year-old, lacked this structure, although it still had numerous feathers along its body. This marks the first time that wings and feathers have been identified in ornithomimosaurs. And because this group evolved earlier than maniraptorans, it suggests that wings arose earlier in dinosaur evolution than previously realized, the team concludes.

“Our specimens are currently the most primitive dinosaur to show winglike structures,” Zelenitsky says. And because ornithomimosaurs were fairly large, weighing 150 kilograms or more, “these earliest wings did not initially evolve for flight - they were obviously not flyers or gliders,” she adds. Moreover, *O. edmontonicus* does not appear to have developed its full plumage until it reached the adult stage, leading the team to suggest that the wings and feathers served some sort of adult reproductive function “such as courtship and brooding,” Zelenitsky says.

Lawrence Witmer, a paleontologist and early bird expert at Ohio University in Athens, calls the new finds “incredibly exciting,” in part because the identification of feathers in coarse-grained river sediments means that feathery structures might preserve more easily than previously thought. That means that many more feathered dinosaurs are probably waiting in the wings, ready to be discovered. Just as importantly, Witmer says, the finds “push the evolution of definitive feathers further back in time.” Witmer says the discoveries support what he calls the “semaphore model” of wing evolution, “in which showy flags appear early on, and later in evolution smaller species exploit the aerodynamic properties that these flags also provide.”

This story provided by ScienceNOW, the daily online news service of the journal Science.

<http://news.discovery.com/tech/living-bacteria-cables-121026.html#mkcpgn=rssnws1>

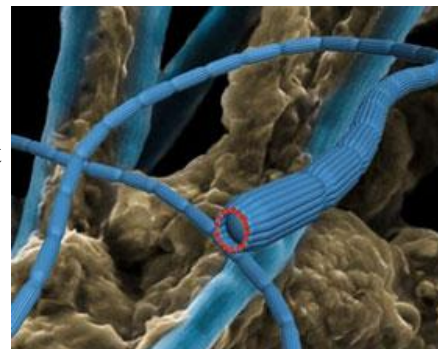
Living Power Cables Made from Bacteria

A tiny section of bacterium contains a bundle of insulated wires that carries an electric current.

Content provided by George Dvorsky, iO9

Three years ago, scientists discovered electric currents running through the seabed -- but they had no idea what was causing them. But now, researchers from Denmark and the United States believe they have the answer: bacteria that function as living electrical cables. In a remarkable case of biological engineering, scientists have confirmed that each tiny section of the bacteria contains a bundle of insulated wires that leads an electric current from one end to the other. The discovery could lead to an entirely new class of organic electronics -- including devices that could be implanted in the human body.

According to Nils Risgaard-Petersen, Christian Pfeffer, and their colleagues at Aarhus University, they started to suspect that something was up when they noticed the appearance of a previously unknown type of long, multi-cellular bacteria. These bacteria were always present when electric currents were around. Moreover, they could disrupt the currents when they pulled a thin wire through the seabed -- a possible indication of broken connections.



The bacteria, which is a hundred times thinner than a human hair, contain nanoscale strings that are enclosed in a membrane -- just like insulated wires. Mingdong Dong, Jie Song and Nils Risgaard-Petersen

Looking at it more closely, they noticed that the bacteria, which is a hundred times thinner than a human hair, contained nanoscale strings that were enclosed by a membrane. They concluded that the entire organism functions as a virtual electric cable -- insulating wires and all. And indeed, the researchers note that the structure is very similar to the electric cables that we use on a daily basis.

The researchers theorize that the adaptation gives the bacterium a distinct advantage over other oceanic microbes. Collectively, when they sit in an undisturbed seabed, they extend tens of thousands of kilometers of cable within a single square meter (10.76 square feet). Their ability to conduct a current allows them to pull in vast amounts of energy that's put out through seabed decomposition. And in fact, a single teaspoon of mud can contain as much of one kilometer of living electric cables.

Another unique characteristic of the bacteria is that it can maintain efficient combustion in the oxygen-free part of the seabed. It does this by forming a chain where one individual bacterium extends out into the oxygen-rich area of the seawater; all that's required is a few millimeters. When the combustion happens, there is a transfer of the electrons of the food to oxygen. The bacteria manage this transfer over a distance of about a centimeter.

And like any electric cable, any disturbance can lead to a fatal breakage -- and an end to the current.

Looking to the future, the new insight could inspire developments in the nascent field of organic electronics. Assuming that a similar kind of bacteria (or other microorganisms) can be engineered, these biological systems could be used to conduct currents in advanced electronic devices, or even in prosthetic devices for humans.

[Check out the entire study in Nature.](#)

<http://www.sciencedaily.com/releases/2012/10/121026125021.htm>

Autism Early Intervention Found to Normalize Brain Activity in Children as Young as 18 Months

Intensive early intervention therapy that improves very young autistic children's cognition and language skills normalizes their brain activity, decreases autism symptoms and improves their social skills too

ScienceDaily - An intensive early intervention therapy that is effective for improving cognition and language skills among very young children with autism also normalizes their brain activity, decreases their autism symptoms and improves their social skills, a nationwide study has found. The researchers said the study is the first to demonstrate that an autism early intervention program can normalize brain activity.

"We know that infant brains are quite malleable and previously demonstrated that this therapy capitalizes on the potential of learning that an infant brain has in order to limit autism's deleterious effects," said study author Sally Rogers, professor of psychiatry and behavioral sciences and a researcher with the UC Davis MIND Institute.

"The findings on improved behavioral outcomes and the ability to normalize brain activity associated with social activities signify that there is tremendous potential for the brains of children with autism to develop and grow more normally," Rogers said.

Published online October 26 in the Journal of the American Academy of Child & Adolescent Psychiatry, the randomized, case-controlled, multi-centered study titled "Early behavioral intervention is associated with normalized brain activity in young children with autism," found that the children who received the intervention exhibited greater brain activation when viewing faces rather than objects, a response that was typical of the normal children in the study, and the opposite of the children with autism who received other intervention. The U.S. Centers for Disease Control and Prevention estimates that 1 in 88 children born today will be diagnosed with autism spectrum disorder. Hallmarks of the neurodevelopmental condition include persistent deficits in social communication and relatedness, and repetitive or restrictive patterns of interest that appear in early childhood and impair everyday functioning.

Named the Early Start Denver Model (ESDM), the intervention method was developed by Rogers and Geraldine Dawson, chief science officer of the research and advocacy organization Autism Speaks. The therapy fuses a play-based, developmental, relationship-based approach and the teaching methods of applied behavioral analysis.

"This may be the first demonstration that a behavioral intervention for autism is associated with changes in brain function as well as positive changes in behavior," said Thomas R. Insel, director of the National Institute of Mental Health, which funded the study. "By studying changes in the neural response to faces, Dawson and her colleagues have identified a new target and a potential biomarker that can guide treatment development." For the present study, the researchers recruited 48 diverse male and female children diagnosed with autism between 18 and 30 months in Sacramento, Calif., and in Seattle, as well as typically developing case controls. The ratio of male-to-female participants was more than 3-to-1. Autism is five times more common among boys than girls.

Approximately half of the children with autism were randomly assigned to receive the ESDM intervention for over two years. The participants received ESDM therapy for 20 hours each week, and their parents also were trained to deliver the treatment, a core feature of the intervention. The other participants with autism received similar amounts of various community-based interventions as well as evaluations, referrals, resource manuals and other reading materials.

At the study's conclusion, the participants' brain activity was assessed using electroencephalograms (EEGs) that measured brain activation while viewing social stimuli -- faces -- and non-social stimuli -- toys. Earlier studies have found that typical infants and young children show increased brain activity when viewing social stimuli rather than objects, while children with autism show the opposite pattern.

Twice as many of the children who received the ESDM intervention showed greater brain activation when viewing faces rather than when viewing objects -- a demonstration of normalized brain activity. Eleven of the 15 children who received the ESDM intervention, 73 percent, showed more brain activation when viewing faces than toys. Similarly, 12 of the 17 typically developing children, or 71 percent, showed the same pattern. But the majority -- 64 percent -- of the recipients of the community intervention showed the opposite, "autistic" pattern, i.e., greater response to toys than faces. Only 5 percent showed the brain activation of typical children. Further, the children receiving ESDM who had greater brain activity while viewing faces also had fewer social-pragmatic problems and improved social communication, including the ability to initiate interactions, make eye contact and imitate others, said MIND Institute researcher Rogers. Use of the ESDM intervention has been

shown to improve cognition, language and daily living skills. A study published in 2009 found that ESDM recipients showed more than three times as much gain in IQ and language than the recipients of community interventions.

"This is the first case-controlled study of an intensive early intervention that demonstrates both improvement of social skills and normalized brain activity resulting from intensive early intervention therapy," said Dawson, the study's lead author and professor of psychiatry at the University of North Carolina, Chapel Hill. "Given that the American Academy of Pediatrics recommends that all 18- and 24-month-old children be screened for autism, it is vital that we have effective therapies available for young children as soon as they are diagnosed."

"For the first time," Dawson continued, "parents and practitioners have evidence that early intervention can alter the course of brain and behavioral development in young children. It is crucial that all children with autism have access to early intervention which can promote the most positive long-term outcomes."

Rogers, Dawson and Laurie A. Vismara, also a researcher with the MIND Institute, have authored two books on the intervention. One for professionals is titled "Early Start Denver Model for Young Children with Autism: Promoting Language, Learning, and Engagement" and one for parents titled "An Early Start for Your Child with Autism: Using Everyday Activities to Help Kids Connect, Communicate, and Learn."

The ESDM intervention is available in Sacramento through the MIND Institute clinic and in a number of locations throughout the U.S. and other nations. Training in delivering the ESDM method is provided through the MIND Institute and the University of Washington.

Other study authors include Emily J.H. Jones, Kaitlin Venema, Rachel Lowy, Susan Faja, Dana Kamara, Michale Murias, Jessica Greenson, Jamie Winter, Milani Smith and Sara J. Webb, all of the University of Washington, and Kristen Merkle of Vanderbilt University.

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Geraldine Dawson, Emily J.H. Jones, Kristen Merkle, Kaitlin Venema, Rachel Lowy, Susan Faja, Dana Kamara, Michael Murias, Jessica Greenson, Jamie Winter, Milani Smith, Sally J. Rogers, Sara J. Webb. Early Behavioral Intervention Is Associated With Normalized Brain Activity in Young Children With Autism. Journal of the American Academy of Child & Adolescent Psychiatry, 2012; 51 (11): 1150 DOI: 10.1016/j.jaac.2012.08.018

<http://www.sciencedaily.com/releases/2012/10/121026125125.htm>

Bean Used in Chinese Food Could Protect Against Sepsis

A bean commonly used in Chinese cuisine protects against the life-threatening condition sepsis

ScienceDaily - Researchers at The Feinstein Institute for Medical Research have discovered that a bean commonly used in Chinese cuisine protects against the life-threatening condition sepsis. These findings are published in the current issue of Evidence-based Complementary and Alternative Medicine (eCAM).

It has been found that a deoxyribonucleic acid (DNA) protein, HMGB1, mediates inflammation. Inflammation is necessary for maintaining good health -- without inflammation, wounds and infections would never heal. However, persistent and constant inflammation can damage tissue and organs, and lead to diseases such as sepsis. Sepsis affects approximately 750,000 Americans each year, 28 to 50 percent of whom die from the condition, and costs the nation's healthcare system nearly \$17 billion annually. It is a potentially life-threatening complication of an infection or injury, and occurs when chemicals released into the bloodstream to fight the infection trigger inflammation throughout the body. The result is that organs become damaged, including liver, heart, lungs, kidney, and brain. If excessive damage occurs, it may be irreversible. Therefore, it is important to identify ways in which persistent and constant inflammation can be halted.

Neutralizing the protein HMGB1 protects against persistent and constant inflammation that results in damage to tissue and organs. Haichao Wang, PhD, and his colleagues, including Shu Zhu, MD and PhD, and Andrew E. Sama, MD, at the Feinstein Institute found that extract from mung bean (*Vigna radiata*), a bean native to India and commonly used in Chinese food and traditional medicine, reduced the release of HMGB1, thereby increasing survival rates in mice from 29.4 percent to 70 percent ($P < 0.05$).

"Many traditional medicinal herbs have been successfully developed into effective therapies for various inflammatory ailments, and now we have validated the therapeutic potential of another medicinal product, mung bean extract," said Dr. Wang. "Demonstrating that mung bean extract has a positive effect on septic mice shows promise that this bean can also have a positive effect on septic humans -- of course, additional studies are required to prove the safe and effective use in humans."

The Feinstein Institute and its parent company, the North Shore-LIJ Health System, have been dedicated to studying and treating sepsis. In 2010, the Feinstein Institute hosted an international Merinoff Symposium dedicated to sepsis. This symposium attracted researchers, policymakers and other opinion leaders from around the world who identified that sepsis should be categorized as a medical emergency treatable with fluids and

antibiotics within one hour of recognition. The health system mounted an aggressive sepsis prevention and early identification initiative that has reduced the health system's sepsis mortality rate by 35 percent in the last four years, which translates into thousands of saved lives.

Shu Zhu, Wei Li, Jianhua Li, Arvin Jundoria, Andrew E. Sama, Haichao Wang. It Is Not Just Folklore: The Aqueous Extract of Mung Bean Coat Is Protective against Sepsis. Evidence-Based Complementary and Alternative Medicine, 2012; 2012: 1 DOI: 10.1155/2012/498467

<http://www.sciencedaily.com/releases/2012/10/121026172943.htm>

Inhaled Anesthesia Affects Children's Brains More Than Intravenous Anesthetic, Study Shows

Researchers find children's brains are more affected by inhaled anesthetic than intravenous anesthetic with increased levels of brain lactate

ScienceDaily - Stony Brook University School of Medicine researchers have found that children's brains are more affected by an inhaled anesthetic than an intravenous anesthetic with increased levels of brain lactate. Lactate increases brain activation and may lead to metabolic changes associated with anxiety and delirium. Reported in the November issue of *Anesthesiology*, the findings provide new clues to metabolic changes within the brains of children undergoing anesthesia and could help researchers understand why general anesthesia may be potentially harmful to the developing brain.

In "Metabolomic Profiling of Children's Brains Undergoing General Anesthesia with Sevoflurane and Propofol," 59 children ages two-to-seven years old were administered one of two routinely used anesthetics for an MRI procedure. One group received sevoflurane (inhaled) and the other received propofol (intravenous). The parietal cortex of the children's brains was imaged one hour after being administered anesthesia. The Stony Brook team, led by Zvi Jacob, MD, and Helene Benveniste, MD, PhD, mapped the metabolic patterns of the children's brains by using non-invasive proton magnetic resonance spectroscopy (HMRS), an imaging method that tracks metabolic processes and defines chemical fingerprints that cellular processes leave behind. The imaging revealed that approximately twice the amount of lactate and 20 percent more glucose were present in the parietal cortex of sevoflurane-anesthetized children compared to propofol-anesthetized children. "Lactate increases when the brain is activated, and therefore the higher level of lactate in the brain of a child administered sevoflurane compared to propofol is likely the result, in part, of more neuronal firing during the unconscious state, which means more activity in the brain," said Dr. Benveniste, Professor of Anesthesiology and Radiology, and Vice Chair for Research, Department of Anesthesiology. "This activity resulting in lactate 'flooding' in the setting of anesthesia may be disadvantageous and increase the chance of children becoming anxious and/or delirious during emergence from anesthesia or in the immediate post-operative period." The research team documented that children who emerged from anesthesia with more agitation and dissociative behavior also had the highest levels of brain lactate. During emergence from anesthesia, each child was assessed for emergence delirium by a recovery room nurse using the Pediatric Anesthesia Emergence Delirium Scale (PAED). The PAED score was significantly higher in the children anesthetized with sevoflurane compared to propofol.

Additionally, the children who emerged with more agitation and cognitive disassociation -- regardless of the anesthetic form used -- had a higher PAED score and higher lactate and glucose concentrations, but lower concentrations of creatine, in the brain. "It is important to point out that the results do not suggest that either of the anesthetics cause long-term effects," emphasized Dr. Benveniste.

The children involved in the study did not differ in age, weight or gender between the two groups. Children with acute brain trauma and other conditions that increased intracranial pressure were excluded from the study. All were anesthetized for MRI procedures only, and therefore post-surgical pain did not contribute to the mental or emotional status of patients. All children recovered without complications from the anesthesia. The recovery time was shorter with propofol compared to sevoflurane.

The Stony Brook research team used prior knowledge of simulated spectral signatures of brain metabolites to access the data. Numerous metabolites were measured, including lactate, glucose, creatine, glutamine, and lipids. The study results also translated and validated previous findings by the research team. In a rodent model, they found that inhaled anesthesia led to lactate and glucose brain levels two times higher than anesthetization with propofol.

Dr. Benveniste said that the research team will expand its studies by including younger children and increasing the overall numbers in order to investigate if the findings are age-dependent.

Zvi Jacob, Haifang Li, Rany Makaryus, Shaonan Zhang, Ruth Reinsel, Hedok Lee, Tian Feng, Douglas L. Rothman, Helene Benveniste. Metabolomic Profiling of Children's Brains Undergoing General Anesthesia with Sevoflurane and Propofol. Anesthesiology, 2012; 117 (5): 1062 DOI: 10.1097/ALN.0b013e31826be417

http://www.eurekalert.org/pub_releases/2012-10/hasf-ivm102212.php

Influenza vaccine may reduce risk of heart disease and death

Flu shot may reduce risk of a major cardiac event by 50 percent and cardiac deaths by 40 percent

Getting a flu shot may not only protect you from getting sick, it might also prevent heart disease.

Two Toronto-based researchers presented studies at the 2012 Canadian Cardiovascular Congress which found that the influenza vaccine could be an important treatment for maintaining heart health and warding off cardiovascular events like strokes and heart attacks.

Dr. Jacob Udell, a cardiologist at Women's College Hospital and the University of Toronto, and his team from the TIMI Study Group and Network for Innovation in Clinical Research looked at published clinical trials on this subject, dating back to the 1960s. "For those who had the flu shot, there was a pretty strong risk reduction," says Dr. Udell.

The flu vaccine provided an approximate 50 per cent reduction in the risk of a major cardiac event (heart attack, stroke, or cardiac death) compared with placebo after one year of follow-up. A similar trend was seen for the flu vaccine reducing death from any cause (approximately 40 per cent). The influenza vaccine reduced cardiovascular events and cardiovascular death in people with or without heart disease.

The combined studies examined a total of 3,227 patients, with an almost equal split between patients with and without established heart disease. Half of the participants were randomly assigned to receive flu vaccine and those that did not typically received a placebo vaccine.

Dr. Udell says these results provide support for current guideline recommendations for influenza vaccination of individuals with a prior heart attack, but for a different reason than simply reducing flu risk. And although it was encouraging to see a reduction in non-fatal cardiac events, he believes a large, lengthier multi-national study would comprehensively demonstrate the vaccine's effectiveness to reduce fatal cardiac events and save lives. "A large study that was international in scope and representative of patients such as those in North America and Canada in particular could help answer this question," he says.

This research could also potentially boost use of the vaccine, which Udell believes is still woefully low. "The use of the vaccine is still much too low, less than 50 per cent of the general population; it's even poorly used among health care workers," he says. "Imagine if this vaccine could also be a proven way to prevent heart disease."

An Ipsos Reid survey conducted by B.C. and Quebec Lung Associations this year found that 36 per cent of Canadians reported having received a flu shot in 2011. And according to the Public Health Agency of Canada's National Advisory Committee on Immunization (NACI), the 2008 Adult National Immunization Coverage Survey found that vaccination rates for adults 18 to 64 years of age with a chronic medical condition is low at 35 per cent. It also found that non-institutionalized seniors aged 65 and older have higher coverage, at 66 per cent.

According to the NACI, rates for both groups have declined somewhat since their 2006 survey and fall short of the 80 per cent national targets for influenza vaccine coverage in adults under age 65 with chronic conditions and in seniors. People with ICDs who get the shot have fewer adverse events. The second study, conducted by cardiologists Drs. Ramanan Kumareswaran and Sheldon Singh from Sunnybrook Health Sciences Centre examined the use of the influenza vaccine in patients with implantable cardiac defibrillators or ICDs.

"Anecdotes suggest that patients have more ICD shocks during flu season. We were trying to figure out what we can do to reduce the amount of shocks in (our clinic's) ICD population during the flu season," says Dr. Kumareswaran.

Patients with ICDs that had appointments at the Sunnybrook Hospital ICD clinic between September 1st 2011 and November 31st 2011 completed a survey that identified their demographics, health status, if they received a flu shot in the past year and opinions towards the vaccine.

The patients' health charts were reviewed to determine all ICD therapies in five months preceding the 2010 flu season (June to October) and for three months during the 2010-2011 flu season (December to March).

A total of 230 patients with an average age between 70 and 74 completed surveys with 179 (78 per cent) patients reported receiving the vaccination in the previous year. Just over 20 per cent did not receive the vaccine.

The patients who did not receive the flu vaccine had a trend toward experiencing more ICD therapies on average. Specifically, 10.6 per cent of patients who received the vaccine received at least one ICD therapy during flu season compared to 13.7 per cent of patients who did not receive the influenza vaccine.

"What is interesting is that if this is consistent over time, it could be of significant benefit to our patient population who already have compromised survival to start with," says Dr. Singh.

"We would like to look at this on a larger scale to determine whether or not our results can be replicated. We're in the process to determine how best to do that." An ICD is a small battery-powered electrical impulse generator implanted in patients who are at risk of sudden cardiac death.

The device is programmed to detect cardiac arrhythmia and correct it by delivering a jolt of electricity or increasing the heart rate to restore a healthy rhythm once an irregular beat has been detected.

About 5,000 Canadians get ICDs every year and there are about 100,000 Canadians who currently have them. (Most Canadians with advanced heart disease are potential candidates for ICDs.)

Heart and Stroke Foundation spokesperson Dr. Beth Abramson says these studies strengthen National Advisory Committee for Immunization recommendations for the use of the influenza vaccine in those at high risk of developing influenza related complications, such as patients with heart disease or diabetes, and those who have close contact with those at high risk of developing complications. "In addition to leading a heart healthy life, having an annual flu shot could be another easy way to help prevent cardiac events," she says.

Dr. Abramson notes that the Heart and Stroke Foundation recommends an influenza vaccination for those at high risk of influenza-related complications or hospitalization (including people with heart conditions, those with diabetes, people over 65 years of age, people with a BMI at or above 40 and children or adults treated with ASA). It is also recommended for people who are most likely to transmit influenza to high risk individuals (family members, friends, coworkers, healthcare provider and caregivers).

http://www.eurekalert.org/pub_releases/2012-10/fccc-dit102512.php

Drop in testosterone tied to prostate cancer recurrence

Fox Chase researchers find that men whose testosterone falls after radiation are more likely to experience a rise in PSA

BOSTON, MA - Men whose testosterone drops following radiation therapy for prostate cancer are more likely to experience a change in PSA levels that signals their cancer has returned, according to new research from Fox Chase Cancer Center. The findings will be presented on October 29 at the American Society for Radiation Oncology's 54th Annual Meeting.

Specifically, men whose testosterone fell following various forms of radiation therapy were more likely to experience an increase in prostate-specific antigen (PSA) - often the first indication the cancer has recurred.

"The men who had a decrease in testosterone also appear to be the men more likely to see an increase in PSA after treatment," says study author Jeffrey Martin, MD, resident physician in the Department of Radiation Oncology at Fox Chase. In theory, doctors may one day be able to use testosterone levels to guide treatment decisions, says Martin. "For men with a decrease in testosterone, doctors might intervene earlier with other medications, or follow their PSA more closely than they would otherwise, to spot recurrences at an earlier time."

Martin and his colleagues decided to conduct the study because there is limited information regarding testosterone levels after radiation treatment and what it means for prognosis. To investigate whether a decrease in testosterone has any clinical effects, Martin and his colleagues reviewed medical records from nearly 260 men who received radiation therapy for prostate cancer between 2002 and 2008. The men were treated with either brachytherapy, in which doctors insert radioactive seeds in the prostate, or intensity modulated radiation therapy (IMRT), in which an external beam of radiation is directed at the prostate.

The researchers found that testosterone levels tended to decrease following both forms of radiation therapy. And men who experienced a post-radiation drop in testosterone - particularly a significant drop - were more likely to see their PSA levels rise during the follow-up period.

Still, an increase in PSA - known as biochemical failure - was relatively rare, the authors found. "Only 4% of patients with low-risk prostate cancer had biochemical failure at five years," says Martin.

Even though researchers have seen testosterone decrease following another form of radiation, these latest findings are still somewhat surprising, says Martin, because testosterone is believed to drive prostate cancer. In fact, some patients with advanced forms are prescribed hormone therapy that attempts to knock down testosterone. "Seeing that a drop in testosterone is tied to recurrence is kind of a surprising result," says Martin. "We don't necessarily know what this means yet. I think the relationship between testosterone levels following radiation therapy and prognosis needs more study, and until then it's premature to say this is something patients should ask their doctors about."

This was a small study that needs to be validated in a larger group of men before doctors begin basing their predictions of recurrence on patients' testosterone levels, he cautions. "I think the link between testosterone and PSA needs more study, in a larger set of patients."

Martin's co-authors include Dennis Sopka, Karen Ruth, Mark Buyounouski, Alexander Kutikov, Mark Sobczak, David Y. T. Chen, and Eric Horwitz from Fox Chase.