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Creatine aids women in outmuscling major depression

Muscle-building supplement vastly improves response time, quality of recovery

SALT LAKE CITY - Women battling stubborn major depression may have a surprising new ally in their fight—the muscle-building dietary supplement creatine.

In a new proof-of-concept study, researchers from three South Korean universities and the University of Utah report that women with major depressive disorder (MDD) who augmented their daily antidepressant with 5 grams of creatine responded twice as fast and experienced remission of the illness at twice the rate of women who took the antidepressant alone. The study, published Aug. 3, 2012, in the American Journal of Psychiatry online, means that taking creatine under a doctor's supervision could provide a relatively inexpensive way for women who haven't responded well to SSRI (selective serotonin reuptake inhibitor) antidepressants to improve their treatment outcomes.

"If we can get people to feel better more quickly, they're more likely to stay with treatment and, ultimately, have better outcomes," says Perry F. Renshaw, M.D., Ph.D., M.B.A, USTAR professor of psychiatry at the U of U medical school and senior author on the study.

If these initial study results are borne out by further, larger trials, the benefits of taking creatine could directly affect many Utahns. The depression incidence in Utah is estimated to be 25 percent higher than the rest of the nation, meaning the state has an even larger proportion of people with the disease. This also brings a huge economic cost to both the state and individuals.

According to numbers recently compiled at the U of U, the state of Utah paid an estimated $214 million in depression-related Medicaid and disability insurance in 2008. Add the costs of inpatient and outpatient treatment, medication, and lost productivity in the workplace, and the total price of depression in Utah reached $1.3 billion in 2008, according to the U estimate. With those large numbers, any treatment that improves outcomes not only could ease the life of thousands of Utah women but also would save millions of dollars.

"There has been a misunderstanding of how crippling and common this disease is in Utah," says Renshaw, who's also medical director of the Mental Illness Research, Education and Clinical Center at the Salt Lake City Veterans Affairs Health Care System. "It begs that we understand it better than we do."

Creatine is an amino acid made in the human liver, kidneys, and pancreas. It also is found in meat and fish. Inside the body it is converted into phosphocreatine and stored in muscle. During high-intensity exercise, phosphocreatine is converted into ATP, an important energy source for cells. For this reason, creatine has become a popular supplement among bodybuilders and athletes who are trying to add muscle mass or improve athletic ability.

How creatine works against depression is not precisely known, but Renshaw and his colleagues suggest that the pro-energetic effect of creatine supplementation, including the making of more phosphocreatine, may contribute to the earlier and greater response to antidepressants.

The eight-week study included 52 South Korean women, ages 19-65, with major depressive disorder. All the women took the antidepressant Lexapro (escitalopram) during the trial. Twenty-five of the women received creatine with the Lexapro and 27 were given a placebo. Neither the study participants nor the researchers knew who received creatine or placebo. Eight women in the creatine group and five in the placebo group did not finish the trial, leaving a total of 39 participants.

Participants were interviewed at the start of the trial to establish baselines for their depression, and then were checked at two, four, and eight weeks to see how they'd responded to Lexapro plus creatine or Lexapro and a placebo. The researchers used three measures to check the severity of depression, with the primary outcomes being measured by the Hamilton Depression Rating Scale (HDRS), a widely accepted test.

The group that received creatine showed significantly higher improvement rates on the HDRS at two and four weeks (32 percent and 68 percent) compared to the placebo group (3.7 percent and 29 percent). At the end of eight weeks, half of those in the creatine group showed no signs of depression compared with one-quarter in the placebo group. There were no significant adverse side effects associated with creatine.

Antidepressants typically don't start to work until four to six weeks. But research shows that the sooner an antidepressant begins to work, the better the treatment outcome, and that's why Renshaw and his colleagues are excited about the results of this first study. "Getting people to feel better faster is the Holy Grail of treating depression," he says.

Study co-author Tae-Suk Kim, M.D., Ph.D., associate professor of psychiatry at the Catholic University of Korea College of Medicine and visiting associate professor of psychiatry at the U of U, already is recommending creatine for some of his female depression patients.

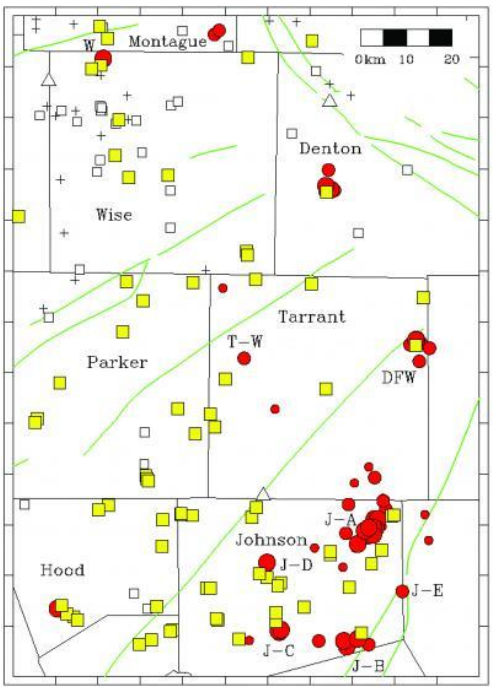
In prior studies, creatine had been shown to be effective only in female rats. But that shouldn't rule out testing the supplement in men as well, according to Renshaw.
U of U researchers expect soon to begin another trial to test creatine in adolescent and college-age females who have not responded to SSRI medications. Principal investigator Douglas G. Kondo, M.D., assistant professor of psychiatry, says he is looking for 40 females between the ages of 13-21. Recruitment of participants will begin as soon as the U of U Institutional Review Board approves the study, which is expected in early July.
After the initial eight weeks of treatment, study participants will be offered a six-month extension of close supervision and monitoring by the research team and board-certified child, adolescent, and adult psychiatrist at no charge.
Those interested in joining the study can call (801) 587-1549; visit the study Web site www.UtahBrain.org; or email Doug.Kondo@hsc.utah.edu.
The first authors on the study are In Kyoon Loo, M.D., Ph.D., professor of the Seoul National University College of Medicine and College of Natural Sciences, Seoul, South Korea, and USTAR research associate professor of psychiatry at the U of U, and Sujung Yoon, M.D., Ph.D., associate professor of psychiatry at the Catholic University of Korea College of Medicine, Seoul, and visiting associate professor of psychiatry at the U of U.
Other authors include Jaeuk Hwang M.D., Ph.D., of the Soonchunhyang University College of Medicine, Seoul; Wangyoun Won, M.D., Catholic University of Korea College of Medicine, Seoul; Jieun E. Kim, M.D., Ph.D., Ewha Womans University Graduate School, Seoul; Sujin Bae, Ph.D., Seoul National University College of Natural Sciences.

http://www.eurekalert.org/pub_releases/2012-08/uota-sfc080312.php

Study finds correlation between injection wells and small earthquakes

Most earthquakes in the Barnett Shale region of north Texas occur within a few miles of one or more injection wells used to dispose of wastes

Most earthquakes in the Barnett Shale region of north Texas occur within a few miles of one or more injection wells used to dispose of wastes associated with petroleum production such as hydraulic fracturing fluids, according to new research from The University of Texas at Austin. None of the quakes identified in the two-year study were strong enough to pose a danger to the public.
The study by Cliff Frohlich, senior research scientist at the university's Institute for Geophysics, appears this week in the journal Proceedings of the National Academy of Sciences.
"You can't prove that any one earthquake was caused by an injection well," says Frohlich. "But it's obvious that wells are enhancing the probability that earthquakes will occur."
Frohlich analyzed seismic data collected between November 2009 and September 2011 by the EarthScope USArray Program, a National Science Foundation-funded network of broadband seismometers from the Canadian border to the Gulf of Mexico. Because of the high density of instruments (25 in or near the Barnett Shale), Frohlich was able to detect earthquakes down to magnitude 1.5, far too weak for people to feel at the surface.



This is a map showing earthquake epicenters determined in this study (red circles), injection wells (squares and + symbols) in use since October 2006, seismograph stations (white triangles), and mapped faults (green lines. Circle sizes indicate quality of epicentral location, with large, medium and small sizes indicating qualities A, B, and C. For injection wells, yellow squares are wells with maximum monthly injection rates exceeding 150,000 barrels of water per month (BWPM); white squares, exceeding 15,000 BWPM; + symbols, exceeding 1,500 BWPM. **Cliff Frohlich/U. of Texas at Austin.**

He found that the most reliably located earthquakes—those which are accurate to within about 0.9 miles (1.5 kilometers)—occurred in eight groups, all within 2 miles (3.2 kilometers) of one or more injection wells.
Before this study, the National Earthquake Information Center had only identified two earthquake groups in the area strongly associated with specific injection wells. This suggests injection-triggered earthquakes are far more common than is generally recognized.
The Barnett Shale is a geological formation in North Texas bearing a large amount of natural gas that was difficult to recover prior to recent technological advances such as hydraulic fracturing. The formation lies beneath Dallas and Fort Worth and extends over several counties, mostly to the west of those cities.
Development of the Barnett Shale and other unconventional plays such as the Bakken Shale in North Dakota

and the Marcellus Shale in Pennsylvania, New York and West Virginia have spurred dramatic growth in domestic natural gas production.

This study comes as some policy makers and members of the public are expressing concern about possible environmental and health impacts of hydraulic fracturing. Most earthquakes identified in the study ranged in magnitude from 1.5 to 2.5, meaning they posed no danger to the public.

"I didn't find any higher risks from disposal of hydraulic fracturing fluids than was thought before," says Frohlich. "My study found more small quakes, nearly all less than magnitude 3.0, but just more of the smaller ones than were previously known. The risk is all from big quakes, which don't seem to occur here."

All the wells nearest to the eight earthquake groups reported high injection rates (maximum monthly injection rates exceeding 150,000 barrels of water). Yet in many other areas where wells had similarly high injection rates, there were no earthquakes. Frohlich tried to address those differences.

"It might be that an injection can only trigger an earthquake if injected fluids reach and relieve friction on a nearby fault that is already ready to slip," says Frohlich. "That just isn't the situation in many places."

Hydraulic fracturing is an industrial process in which water and various chemicals are pumped deep underground in order to fracture rock, allowing oil or gas to more easily flow to a well. As petroleum is produced at the surface, most hydraulic fracturing fluids return to the surface too. Frohlich is careful to point out that he did not evaluate the possible correlation of earthquakes with the actual hydraulic fracturing process, but rather the impacts of disposing of fracturing fluids and other wastes in these injection wells.

Support for this study came from the U.S. Geological Survey and the Jackson School of Geosciences. The author has no financial ties to the hydraulic fracturing industry. Frohlich has consulted for the construction industry on seismic risks for projects including dams, power plants and pipelines. He plans to participate in a future study relating to hydraulic fracturing in the Barnett Shale by the university's Energy Institute.

http://www.americanscientist.org/issues/pub/cracking-with-electricity/1

Cracking with Electricity

Faults seem to give off a warning signal before they slip

Fenella Saunders

Troy Shinbrot is no stranger to research that defies standard beliefs. The Rutgers University biomedical engineer focuses on grains and powders, specifically how they mix and gain electric charges. A few years ago, this specialty led him to work on what's called the Brazil nut effect: In a group of particles of different sizes (such as a container of mixed nuts), shaking makes the larger ones (the Brazil nuts) rise to the top. Common wisdom was that small particles could slip below larger ones, leaving the big ones on top with nowhere to go. Other researchers found that the grains would "convect," rising in the center and sinking at the edges. Large particles would lift up with the whole bed and then get stranded on top, unable to fit into the narrow margins at the sides.

Shinbrot and his colleagues, however, found that large, lightweight particles would sink instead of rising, dubbed the reverse Brazil nut effect—but only when the grains were vibrated above a certain frequency that makes the bed "fluidize." Then the mixture behaves like a liquid with typical buoyancy characteristics, so light objects rise while heavy ones sink.

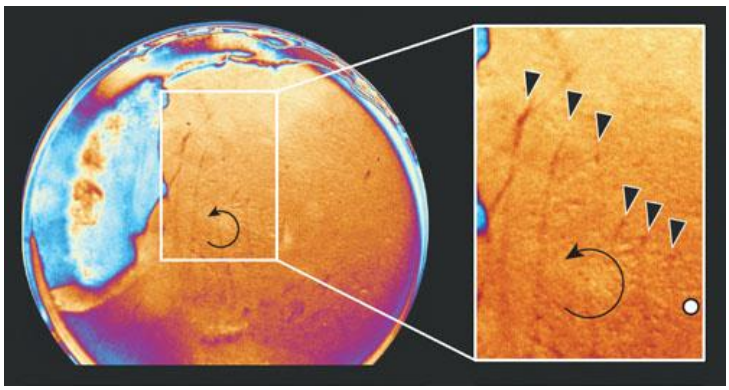
The results were so counterintuitive that reviewers of the paper thought they were impossible. An editor of the journal Physical Review Letters tested it out for himself and confirmed Shinbrot's findings, but was still nervous. "He called me up and wanted to make sure that I wasn't playing a joke on him," Shinbrot says. "He was a little anxious that there was something funny going on that would make him regret publishing the paper."

Two years ago, Shinbrot again succeeded in convincing a journal that his unexpected results in another study were not spurious. In sandstorms, volcanic ash plumes and dust clouds in food, drug or coal processing, the grains spontaneously generate strong electrical charges and can sometime emit flashes or even explode. But the grains themselves are inert, so it's hard to understand how they could charge. Shinbrot and his colleagues proposed a mechanism whereby particles are initially polarized by an external electric field. When they collide in a cloud, the contacting sides cancel their charges, leaving one particle with an overall negative charge and the other with a positive charge. Once they separate, the external field polarizes the grains again, adding one unit of charge to each particle with each collision. But Shinbrot's results went so against accepted theories of electrostatic charging that for several years he considered the results to be unpublishable.

"Most physicists view these problems as solved; they figure the chapter is closed," Shinbrot says. "They don't look at the history and recognize that there are still many open subjects."

Now Shinbrot has made a discovery that he freely admits is very strange and hard to understand, but he is pretty sure his results aren't mistaken.

The problem started with powders destined for pharmaceuticals, which electrostatically charge during processing and stick to surfaces. “So there are problems where you want to mix two powders, and one of them might charge and one of them might not, or they might charge differently,” Shinbrot says. “That can cause them to separate, which is a severe concern when you want to have known amounts of drugs in each tablet.”
2012-09SciObsSaundersFA.jpgClick to Enlarge ImageBecause of his prior interest in dust storms, Shinbrot was aware that electrical discharges from moving powders were possible. He had also heard about visible flashes being reported at the time of earthquakes. “We had this instrumented tumbler, and these instruments for measuring charge,” he says. “To my knowledge nobody had put these two pieces of equipment together, and I just thought ‘well, I wonder what will happen.’”
And he was not expecting what did happen. “It seemed so utterly implausible,” Shinbrot recalls. He and his colleagues reported their results in the June 11 online edition of the Proceedings of the National Academy of Sciences of the U.S.A.
As the powder tumbled, before a large slab of it fractured off in what is called a slip event, the material emitted a detectable negative voltage. In other words, an electric warning signal occurred before the slip happened. Although it’s not a surprise that cracks and slips occur in a tumbling tub of powder, could such signals predict an earthquake, where the soil is also essentially a compacted powder? “We realized there were conceivable connections with geologic events,” says Shinbrot.
To firm up their results, Shinbrot and his colleagues used three different setups: the tumbler, a bed that simply tipped and one that slid from side to side (called a shear cell). In all cases, they tried to control for electrostatic charging in every way possible. “We increased the humidity, we used different materials, we used a static eliminator, we tried to measure in different regions,” he says. “We don’t know exactly how static charging would creep in, but I’m not going to rule it out completely.” However, he is pretty sure the electrical signal is coming from the crack itself, not from some kind of static discharge.



Seen end-on and in false color, a tumbler of powder rotates counterclockwise (circular arrow). A train of defects (black arrowheads) emanates from one point in the tumbler. A voltage signal is emitted shortly before the defects slip, and the signal is strongest if a probe is placed at the point from which the defects emanate (white dot). **Image courtesy of Troy Shinbrot/PNAS.**

One piece of evidence is that the type of bed used seems to affect how far in advance the electrical signal preceded the slip event. The signal seems to be emitted when a precursor defect opens within the material. “If you just take a bucket of powder and tip it, you’ll get a precursor of a half second or so,” Shinbrot says. “If you put it in a tumbler, you might get that same precursor that doesn’t work its way from deep in the bed up to the surface and produce a visible effect for five seconds or so.”
2012-09SciObsSaundersFB.jpgClick to Enlarge ImageAdditionally, the location where the researchers placed the electric probe affected the amount of signal received. “It seems like cracks start at a particular location in the bed, and that’s consistent with our speculation that maybe the cracks are what are producing the voltage,” Shinbrot explains. “But why the cracks start there we have absolutely no clue.”
In the shear cell, which Shinbrot filled with ordinary flour, he and his colleagues could watch the electrical signal happen repeatedly as the cell slid from side to side and the same crack opened and closed. “But it still remains very strange that you can put a powder like flour into a container and get 200 volts out of it,” Shinbrot says.
Although Shinbrot cannot explain why cracks produce voltages, he theorizes that the mechanism is related to the dilation of grains before a slip event. “If you think of a stack of marbles, they’re all sort of interlocked because they’re all sitting against one another,” he explains. “If you try to move one, you actually have to lift it up over a little hump before it can flow.”
The effect, Shinbrot says, seems to be similar to other unusual behavior in everyday materials. It has been reported for some time that when transparent tape is peeled off of its roll, it emits light at the point of separation. Biting a wintergreen Lifesaver also produces a flash, with some of the energy large enough to produce x rays. Shinbrot doesn’t yet know whether the electrical warning signal will be as clear if the grains are not all the same size. When the cracks are of a more jagged shape and less clearly defined, the signal is also affected. Both of these factors might impact the phenomenon’s usefulness for something like earthquake prediction. Shinbrot’s

next move is to size up the test bed to a meter or two, as a first step in determining whether the effect might happen at all on a geologic scale. It's possible that an increased area could decrease the stress on the grains and drop the signal—or the opposite could occur, and with more areas of contact to be broken the result could be magnified.

"If the effect grows with size, then we'll try to collaborate with geophysicists and look at larger scale systems," he says. "If it decreases with size, then we'll just say 'well this was an interesting trip,' and we'll go on with something else."

Assuming there is a relationship between the group's results and seismic events, Shinbrot hopes to coordinate the work with other indicators. For instance, earthquakes are known to emit acoustic signals, and Shinbrot plans to explore any possible connection between them and the electrical discharges.

But he faces some unusual challenges in this area, for which his history of unconventional studies may have prepared him: "If you look up 'earthquake lightning,' you'll find an equal number of websites that talk about it having something to do with UFOs or government conspiracies or whatnot, as authentic scientific research. We don't want to be tarred by the same brush. But it made this topic a very interesting one to study. In the past 10 years there have been some serious scientific studies, and I think there is hope that in the next 10 years this may get on a firmer scientific footing."

It seems likely that no matter what, Shinbrot will persevere in finding the exceptions in physics that show that the field is still full of surprises. As he says, "That's what makes it fun."

http://www.sciencedaily.com/releases/2012/08/120806151246.htm

Epilepsy Drug Reverses Memory Loss in Animal Model of Alzheimer's Disease

Scientists at the Gladstone Institutes have discovered that an FDA-approved anti-epileptic drug reverses memory loss and alleviates other Alzheimer's-related impairments in an animal model of the disease.

ScienceDaily - Scientists in the laboratory of Lennart Mucke, MD, who directs neurological research at Gladstone, conducted the research on mice genetically modified to simulate key aspects of Alzheimer's disease. In the study, they show how levetiracetam -- a drug commonly prescribed for patients who suffer from epilepsy -- suppresses abnormal brain activity and restores memory function in these mice. They are publishing their findings online August 6 in the Proceedings of the National Academy of Sciences.

The news comes at a critical time of renewed focus on this most prevalent of neurodegenerative diseases -- and amid a dearth of medications that prevent, halt or reverse the increasingly common condition. Alzheimer's afflicts 5.4 million people in the United States alone -- a figure expected to nearly triple by 2050.

"For the millions of people suffering from Alzheimer's worldwide, we have no effective drug to prevent or reverse memory loss -- the hallmark symptom of this ultimately fatal disease," said Dr. Mucke, who is also a professor of neurology and neuroscience at the University of California, San Francisco (UCSF), with which Gladstone is affiliated. "This study builds on our earlier findings linking Alzheimer's and epilepsy. It provides new insights into the processes underlying memory loss in Alzheimer's and demonstrates the ability of an anti-epileptic drug to block these processes."

Healthy activity in neuronal networks is critical for essential brain functions such as memory. Alzheimer's wreaks havoc on these brain networks, causing disruptions that occasionally escalate into epileptic seizures. "But whether such neuronal-network disruptions also impair memory was unknown," said Gladstone Postdoctoral Fellow Pascal Sanchez, PhD, who is the paper's lead author. "So we screened seven FDA-approved anti-epileptic medications -- including levetiracetam -- in our Alzheimer's mouse model to see if minimizing these network disruptions could improve memory."

When the Gladstone scientists administered levetiracetam to the mice, they found that abnormal network activity in their brains dropped by 50% in less than a day. After two weeks of treatment, the neurons' ability to communicate with each other improved. The mice also showed better learning and memory in a maze test. Finally, the researchers observed that several proteins that are important for healthy brain function returned to normal levels.

"We are now building on these findings and working to identify the precise mechanism by which this drug reduces brain-network dysfunction and improves memory in our mouse models," said Dr. Sanchez.

The relevance of this discovery to people with Alzheimer's disease is underscored by research that scientists at Johns Hopkins University published just a few months ago. Their study revealed beneficial effects of levetiracetam in a small group of patients with mild cognitive impairment -- a condition that often precedes Alzheimer's. Still, further research is required before the drug is prescribed for Alzheimer's disease.

"Until larger human trials have been completed, we caution against any off-label use of levetiracetam," Dr. Mucke said. "But the consistency between our findings and those just obtained by our colleagues at Johns Hopkins is truly remarkable and, in my opinion, merits additional clinical trials."

Other scientists who participated in this research at Gladstone include Lei Zhu, PhD, Laure Verret, PhD, Keith Vossel, MD, Anna Orr, PhD, Nino Devidze, PhD, Kaitlyn Ho, Gui-Qiu Yu, and Jorge Palop, PhD. John Cirrito, PhD at the Washington University School of Medicine in St. Louis contributed as well. Funding came from a wide variety of sources, including the National Institutes of Health, the National Center for Research Resources, the Alzheimer's Disease Research Center at UCSF and the S.D. Bechtel, Jr. Foundation.

Pascal E. Sanchez, Lei Zhu, Laure Verret, Keith A. Vossel, Anna G. Orr, John R. Cirrito, Nino Devidze, Kaitlyn Ho, Gui-Qiu Yu, Jorge J. Palop, and Lennart Mucke. Levetiracetam suppresses neuronal network dysfunction and reverses synaptic and cognitive deficits in an Alzheimer's disease mode. PNAS, August 6, 2012 DOI: 10.1073/pnas.1121081109

http://www.eurekalert.org/pub_releases/2012-08/nu-tdf080712.php

Thinner diabetics face higher death rate

New-onset diabetics with normal BMI have higher mortality rate than heavier diabetics

CHICAGO --- American adults of a normal weight with new-onset diabetes die at a higher rate than overweight/obese adults with the same disease, according to a new Northwestern Medicine study.

The study, to be published in the Aug. 7 issue of JAMA, found that normal-weight participants experienced both significantly higher total and non-cardiovascular mortality than overweight/obese participants.

Normal-weight adults with type 2 diabetes have been understudied because those who typically develop the disease are overweight or obese. In this study about 10 percent of those with new-onset diabetes were at a normal weight at the time of ascertainment.

Being overweight is a risk factor for developing this disease, but other risk factors such as family history, ethnicity and age may play a role. "It could be that this is a very unique subset of the population who are at a particularly high risk for mortality and diabetes, and it is possible that genetics is a factor with these individuals," said Mercedes R. Carnethon, associate professor of preventive medicine at Northwestern University Feinberg School of Medicine and first author of the study.

Older adults and nonwhite participants are more likely to experience normal-weight diabetes, according to the study. "Many times physicians don't expect that normal-weight people have diabetes when it is quite possible that they do and could be at a high risk of mortality, particularly if they are older adults or members of a minority group," Carnethon said. "If you are of a normal weight and have new-onset diabetes, talk to your doctor about controlling your health risks, including cardiovascular risk factors."

Researchers analyzed data from five cohort studies and identified 2,625 U.S. men and women over the age of 40 who were determined to have diabetes at the start of the studies. Some of these individuals already knew they were diabetic, and others found out through their participation in the studies.

Diabetes determination was based on a fasting glucose of 126 mg/dL or greater or newly initiated diabetes medication with concurrent measurements of body mass index (BMI). A participant of normal weight had a BMI of 18.5 to 24.99, while overweight/obese participants had a BMI of 25 or greater.

With the aging and diversification of the population, cases of normal weight diabetes likely will be on the rise, Carnethon said. Future studies should focus on factors such as fat distribution and genetic types in normal-weight people with diabetes, she said.

http://www.eurekalert.org/pub_releases/2012-08/plos-dod080712.php

Doctors often don't disclose all possible risks to patients before treatment

Doctors may "routinely underestimate the importance of a small set of risks that vex patients

Most informed consent disputes involve disagreements about who said what and when, not stand-offs over whether a particular risk ought to have been disclosed. But doctors may "routinely underestimate the importance of a small set of risks that vex patients" according to international experts writing in this week's PLOS Medicine.

Increasingly, doctors are expected to advise and empower patients to make rational choices by sharing information that may affect treatment decisions, including risks of adverse outcomes. However, authors from Australia and the US led by David Studdert from the University of Melbourne argue that doctors, especially surgeons, are often unsure which clinical risks they should disclose and discuss with patients before treatment.

To understand more about the clinical circumstances in which disputes arise between doctors and patients in this area, the authors analyzed 481 malpractice claims and patient complaints from Australia involving allegations of deficiencies in the process of obtaining informed consent.

The authors found that 45 (9%) of the cases studied were disputed duty cases—that is, they involved head-to-head disagreements over whether a particular risk ought to have been disclosed before treatment. Two-thirds of these disputed duty cases involved surgical procedures, and the majority (38/45) of them related to five specific outcomes that had quality of life implications for patients, including chronic pain and the need for re-operation. The authors found that the most common justifications doctors gave for not telling patients about particular risks before treatment were that they considered such risks too rare to warrant discussion or the specific risk was covered by a more general risk that was discussed.

However, nine in ten of the disputes studied centered on factual disagreements—arguments over who said what, and when. The authors say: "Documenting consent discussions in the lead-up to surgical procedures is particularly important, as most informed consent claims and complaints involved factual disagreements over the disclosure of operative risks."

The authors say: "Our findings suggest that doctors may systematically underestimate the premium patients place on understanding certain risks in advance of treatment."

They conclude: "Improved understanding of these situations helps to spotlight gaps between what patients want to hear and what doctors perceive patients want—or should want—to hear. It may also be useful information for doctors eager to avoid medico-legal disputes."

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

Citation: Bismark MM, Gogos AJ, Clark RB, Gruen RL, Gawande AA, et al. (2012) Legal Disputes over Duties to Disclose Treatment Risks to Patients: A Review of Negligence Claims and Complaints in Australia. PLoS Med 9(8): e1001283. doi:10.1371/journal.pmed.1001283

http://www.eurekalert.org/pub_releases/2012-08/uocm-gjl080312.php

Grapefruit juice lets patients take lower dose of cancer drug

A glass a day of grapefruit juice lets patients derive the same benefits from an anti-cancer drug as they would get from more than three times as much of the drug by itself, according to a new clinical trial.

The combination could help patients avoid side effects associated with high doses of the drug and reduce the cost of the medication. Researchers at the University of Chicago Medicine study the effects that foods can have on the uptake and elimination of drugs used for cancer treatment. In a study published in August in Clinical Cancer Research, they show that eight ounces a day of grapefruit juice can slow the body's metabolism of a drug called sirolimus, which has been approved for transplant patients but may also help many people with cancer. Patients who drank eight ounces a day of grapefruit juice increased their sirolimus levels by 350 percent. A drug called ketoconazole that also slows drug metabolism increased sirolimus levels by 500 percent.

"Grapefruit juice, and drugs with a similar mechanism, can significantly increase blood levels of many drugs," said study director Ezra Cohen, MD, a cancer specialist at the University of Chicago Medicine, "but this has long been considered an overdose hazard. Instead, we wanted to see if grapefruit juice can be used in a controlled fashion to increase the availability and efficacy of sirolimus."

Grapefruit juice's pharmaceutical prowess stems from its ability to inhibit enzymes in the intestine that break down sirolimus and several other drugs. The effect begins within a few hours of what the researchers refer to as "grapefruit juice administration." It wears off gradually over a few days.

Cohen and colleagues organized three simultaneous phase-1 trials of sirolimus. Patients received only sirolimus, sirolimus plus ketoconazole, or sirolimus plus grapefruit juice. They enrolled 138 patients with incurable cancer and no known effective therapy.

The first patients started with very low sirolimus doses, but the amounts increased as the study went on, to see how much of the drug was required in each setting to reach targeted levels, so that patients got the greatest anti-cancer effect with the least side effects.

The optimal cancer-fighting dose for those taking sirolimus was about 90 mg per week. At doses above 45 mg, however, the drug caused serious gastrointestinal problems, such as nausea and diarrhea, so patients taking sirolimus alone switched to 45 mg twice a week. The optimal doses for the other two groups were much lower. Patients taking sirolimus plus ketoconazole, needed only 16 mg per week to maintain the same levels of drug in the blood. Those taking sirolimus plus grapefruit juice, needed between 25 and 35 mg of sirolimus per week.

"This is the first cancer study to harness this drug-food interaction," the authors note.
No patients in the study had a complete response, but about 30 percent of patients in the three trials had stable disease, meaning a period when their cancers did not advance. One patient receiving grapefruit juice had a partial response—significant tumor shrinkage—that lasted for more than three years.
Although ketoconazole produced a slightly stronger drug-retention effect, grapefruit juice has the advantage that it is non-toxic, with no risk of overdose. "Therefore," the authors wrote, "we have at our disposal an agent that can markedly increase bioavailability (in this study by approximately 350%) and, critically in the current environment, decrease prescription drug spending on many agents metabolized by P450 enzymes."
Sirolimus was the first of a series of drugs, known as mTOR inhibitors, that were developed to prevent rejection of transplanted organs but that also have anti-cancer effects. As the first of its class, it was also the first to come off patent, making it less costly. "Further cost savings," the authors suggest, could be realized "by combining the drug with agents that inhibit its metabolism." Because different people produce varied amounts of the enzymes that break down sirolimus, the effect of grapefruit juice can vary, but tests of enzyme levels may be able to predict how an individual patient will respond.
"The variation in potency of the grapefruit juice itself may be far greater than the variation in the enzymes that break down sirolimus," Cohen said. An early version of the study used canned grapefruit juice, generously donated by a Chicago-based grocery chain. But tests of the product found it lacked the active ingredients. So the researchers shifted to a frozen concentrate product supplied by the Florida Department of Citrus.
This study was supported by the National Institutes of Health—and not by a pharmaceutical company. Dose-finding studies are "not necessarily profitable" for drug makers, the authors note, especially if the study results in lower recommended doses after the drug has been approved and priced.
Additional authors of this study include Kehua Wu, Christine Hartford, Masha Kocherginsky, Yuanyuan Zha, Anitha Nallari, Michael Maitland, Kammi Fox-Kay, Kristin Moshier, Larry House, Jacqueline Ramirez, Samir Undevia, Gini Fleming, Thomas Gajewski and Mark Ratain of the University of Chicago, and Kimberly Eaton of the University of Texas Medical School at Houston.

http://nyti.ms/P7wtQp

Paid Sick Leave May Reduce Work Injuries

A new study suggests that offering paid sick leave might reduce the rate of nonfatal injury among workers and improve the bottom line at the same time.

By NICHOLAS BAKALAR

Using data on about 38,000 workers from a national survey conducted by the Centers for Disease Control and Prevention, researchers found that from 2005 to 2008 the injury rate per 100 workers among those with paid sick leave was 2.59, compared with 4.18 among those without.
The availability of sick leave and the probability of injury varies by industry, sex, education level and geography. But even after accounting for these and other variables, the researchers found that the odds of a nonfatal injury were 28 percent lower among workers with paid sick leave.
The authors, writing online in The American Journal of Public Health, acknowledge that the data does not establish a causal relationship between paid leave and the lower incidence of injury, and a firm conclusion that paid sick leave is cost-effective cannot yet be drawn.
Still, the lead author, Abay Asfaw, a senior service fellow at the C.D.C., said that providing paid sick leave may benefit both employers and workers.
“We can infer,” Mr. Asfaw said, “that lower injury rates mean lower levels of workers’ compensation payments. In the long term, paid sick leave might help employers to reduce cost and increase profit.”

http://phys.org/news/2012-08-seeds-defense-stress-triggers-widespread.html

Planting the seeds of defense

Study finds stress triggers widespread epigenetic changes that aid in disease resistance

It was long thought that methylation, a crucial part of normal organism development, was a static modification of DNA that could not be altered by environmental conditions. New findings by researchers at the Salk Institute for Biological Studies, however, suggest that the DNA of organisms exposed to stress undergo changes in DNA methylation patterns that alter how genes are regulated.
The scientists found that exposure to a pathogenic bacteria caused widespread changes in a plant's epigenetic code, an extra layer of biochemical instructions in DNA that help control gene expression. The epigenetic changes were linked to the activity of genes responsible for coordinating a plant's response to stress, suggesting that the epigenome may help organisms develop resistance to pathogens and other environmental stressors.
"This means the epigenome may not just be a static set of instructions, but also a way of rewriting those instructions based on experience," says Joseph Ecker, a professor in Salk's Genomic Analysis Laboratory, who

led the research team. "Our findings, combined with other researchers' findings, build the case that life experiences leave an imprint on our DNA."
In the study, published online June 25 in the Proceedings of the National Academy of Sciences, Ecker and his colleagues studied how DNA methylation regulates the immune system of the Arabidopsis thaliana plant. Methylation is a biochemical process that, among other things, suppresses the expression of "jumping genes" called transposons that have been incorporated into the genome over time. Using genome-wide sequencing technologies, the researchers found a wide range of methylation changes in the plant's response to a bacterial infection and performed a variety of analyses to determine how these methylation changes alter gene expression.
"From previous studies, we know that the expression of a few genes is coupled to methylation changes in response to stress," says first author Robert Dowen, who worked on the project at Salk with Ecker and is now with Massachusetts General Hospital in Boston. "Our findings, however, show that exposing a plant to stress triggers a multitude of methylation changes that help the plant defend against invading pathogens."
Plants use a sophisticated series of defense mechanisms to restrict the growth of parasitic bacteria upon infection by stimulating various hormonal signals that trigger alterations in gene expression networks. The Salk findings and other recent studies suggest that these cellular defense responses engage the DNA methylation machinery to impart control over gene expression networks. Epigenetic changes in the genetic material, including changes in DNA methylation patterns and modifications to histones (proteins which play a key role in gene regulation), can alter the expression of a gene without changing its DNA sequence. In addition, molecules called small interfering RNAs (siRNAs) are intimately connected with DNA methylation, especially at the jumping genes, where these siRNAs direct the methylation process. Surprisingly, the researchers found that the levels of these siRNAs also change during infection at specific transposons and correspond to activation of these mobile DNA fragments. These findings illustrate the dynamic nature of the epigenome in response to stress.
The Salk findings may have broad implications for agriculture, including engineering the DNA methylation patterns of plants to generate pathogen-resistant crops and minimize pesticide exposure. These application technologies are of intense interest, as more than 30 to 40 percent of annual crops are lost to pathogens each year at a cost of some $500 billion.
A recent study published in Plant Physiology suggests that memory of environmental conditions may be passed transgenerationally, as plant defenses are primed in the progeny of plants whose parents have already been exposed to pathogens. "While this phenomenon is poorly understood, it is of wide interest and is being intensively studied in the field," says Dowen. "We think our findings may provide a framework for directly testing whether the methylation changes that we observed are passed to the progeny or whether a similar mechanism may be occurring in human cells."

http://www.sciencedaily.com/releases/2012/08/120807194047.htm

New Non-Toxic Disinfectant Could Tackle Hospital Infections

Akwaton works at extremely low concentrations and can be used in healthcare settings to help control persistent hospital-acquired infections.

ScienceDaily - A new disinfectant, Akwaton, that works at extremely low concentrations could be used in healthcare settings to help control persistent hospital-acquired infections such as Clostridium difficile. The study is reported online in the Journal of Medical Microbiology.
Researchers from the Université de Saint-Boniface in Winnipeg, Canada tested the new compound, Akwaton, against bacterial spores that attach to surfaces and are difficult to destroy. Previous work by the group has shown Akwaton is also effective at low concentrations against strains of Meticillin-resistant Staphylococcus aureus and Escherichia coli.
Spore-forming bacteria include C. difficile -- a common bacterium found in healthcare settings whose spores can survive on surfaces for long periods of time. Spores are heat-tolerant and can survive a number of years in a dehydrated state before they are reactivated. Most chemical disinfectants control or prevent spore growth rather than irreversibly destroying them.
The present study showed that Akwaton was able to destroy Bacillus subtilis bacterial spores, suspended in water and attached to stainless steel or glass surfaces, at concentrations well below 1% after just 90 seconds' treatment. It was equally as effective at more dilute concentrations (below 0.1%) if left to act for longer periods.
Lead researcher Dr Mathias Oulé, explained the advantages over other chemical compounds currently used against bacterial spores. "Most disinfectants have to be applied at much higher concentrations -- typically between 4-10% -- to properly get rid of bacterial spores. Unfortunately such high levels of these compounds

may also be harmful to humans and other animals. Akwaton is non-corrosive, non-irritable, odourless and is effective at very low concentrations," he said.
"Bacterial spores demonstrate a remarkable resistance to physical and chemical agents as well as ordinary antiseptics. On top of this micro-organisms are becoming increasingly resistant to disinfectants as well as antibiotics.. Our latest study shows Akwaton is effective at destroying these spores as well as bacteria that are known problems in healthcare environments"
Akwaton is fast-acting and non-toxic for humans at low concentrations. Other studies have shown that the compound is also environmentally safe. "All these properties make it an ideal disinfectant for hospitals and laboratories. It may also have great value in the food industry to tackle spore-forming food pathogens such as Bacillus cereus and Clostridium perfringens," explained Dr Oulé.
Mathias Oulé et al. Akwaton, Polyhexamethylene-Guanidine Hydrochloride-Based Sporicidal Disinfectant: A Novel Tool to Fight Bacterial Spores and Nosocomial Infections. Journal of Medical Microbiology, 2012 DOI: 10.1099/jmm.0.0047514-0

http://www.eurekalert.org/pub_releases/2012-08/s-sdt080812.php

Scientists discover the truth behind Colbert's 'truthiness'

A picture inflates the perceived truth of true and false claims

Trusting research over their guts, scientists in New Zealand and Canada examined the phenomenon Stephen Colbert, comedian and news satirist, calls "truthiness"—the feeling that something is true. In four different experiments they discovered that people believe claims are true, regardless of whether they actually are true, when a decorative photograph appears alongside the claim. The work is published online in the Springer journal, Psychonomic Bulletin & Review.
"We wanted to examine how the kinds of photos people see every day—the ones that decorate newspaper or TV headlines, for example—might produce "truthiness," said lead investigator Eryn J. Newman of Victoria University of Wellington, New Zealand. "We were really surprised by what we found."
In a series of four experiments in both New Zealand and Canada, Newman and colleagues showed people a series of claims such as, "The liquid metal inside a thermometer is magnesium" and asked them to agree or disagree that each claim was true. In some cases, the claim appeared with a decorative photograph that didn't reveal if the claim was actually true—such as a thermometer. Other claims appeared alone. When a decorative photograph appeared with the claim, people were more likely to agree that the claim was true, regardless of whether it was actually true.
Across all the experiments, the findings fit with the idea that photos might help people conjure up images and ideas about the claim more easily than if the claim appeared by itself. "We know that when it's easy for people to bring information to mind, it 'feels' right," said Newman.
The research has important implications for situations in which people encounter decorative photos, such as in the media or in education. "Decorative photos grab people's attention," Newman said. "Our research suggests that these photos might have unintended consequences, leading people to accept information because of their feelings rather than the facts."
Newman EJ et al (2012). Nonprobative photographs (or words) inflate truthiness. Psychonomic Bulletin & Review; DOI 10.3758/s13423-012-0292-0

http://www.eurekalert.org/pub_releases/2012-08/uotw-eha080812.php

Early human ancestors had more variable diet

Scientists reconstruct dietary preferences of 3 groups of hominins in South Africa

An international team of researchers, including Professor Francis Thackeray, Director of the Institute for Human Evolution at Wits University, will be publishing their latest research on what our early ancestors ate, online in the prestigious journal, Nature, on Wednesday, the 8th of August 2012 at 19:00 (SAST).
The paper titled Evidence for diet but not landscape use in South African early hominins was authored by Vincent Balter from the Ecole Normale Supérieure in Lyon, France; Jose´ Braga from the Université de Toulouse Paul Sabatier in Toulouse in France; Philippe Te´louk from the Ecole Normale Supérieure in Lyon in France; and Thackeray from the University of the Witwatersrand in Johannesburg in South Africa. The paper has been selected for Advance Online Publication (AOP) on www.nature.com
The latest research sheds more light on the diet and home ranges of early hominins belonging to three different genera, notably Australopithecus, Paranthropus and Homo – that were discovered at sites such as Sterkfontein, Swartkrans and Kromdraai in the Cradle of Humankind, about 50 kilometres from Johannesburg.
Australopithecus existed before the other two genera evolved about 2 million years ago. The scientists conducted an analysis of the fossil teeth, indicating that Australopithecus, a predecessor of early Homo, had a more varied diet than early Homo. Its diet was also more variable than the diet of another distant human relative

known as Paranthropus. According to Thackeray, the results of the study show that Paranthropus had a primarily herbivorous-like diet, while Homo included a greater consumption of meat.
Signatures of essential chemical elements have been found in trace amounts in the tooth enamel of the three fossils genera, and the results are indicators of what South African hominins ate and what their habitat preferences were.
Strontium and barium levels in organic tissues, including teeth, decrease in animals higher in the food chain. The scientists used a laser ablation device, which allowed them to sample very small quantities of fossil material for analysis. Since the laser beam was pointed along the growth prisms of dental enamel, it was possible to reconstruct the dietary changes for each hominin individual.
Thackeray states that the greater consumption of meat in the diet of early forms of Homo could have contributed to the increase in brain size in this genus. Australopithecus probably ate both meat and the leaves and fruits of woody plants. The composition of this diet may have varied seasonally. Apart from the dietary differences, the new results indicate that the home-range area was of similar size for species of the three hominin genera.
The scientists have also measured the strontium isotope composition of dental enamel. Strontium isotope compositions are free of dietary effects but are characteristic of the geological substrate on which the animals lived. According to the results all the hominids lived in the same general area, not far from the caves where their bones and teeth are found today.
Professor Vincent Balter of the Geological Laboratory of Lyon in France, suggests that up until two millions years ago in South Africa, the Australopithecines were generalists, but gave up their broad niche to Paranthropus and Homo, both being more specialised than their common ancestor.

http://bit.ly/RHk9qq

Fossils confirm three early humans roamed Africa

Few treasure hunts last 40 years. Fewer still end with the unearthing of three bits of broken bone that could help untangle the roots of our family tree.

18:00 08 August 2012 by Douglas Heaven

In 1972, the skull of an early human – known as KNM-ER 1470 – was found in Koobi Fora in northern Kenya. Homo habilis, an early member of our own genus, was thought to have had the plains of Africa to itself 2 million years ago, but the 1.9-million-year-old skull didn't quite fit with the known remains of that species. Some were convinced this was a tantalising glimpse of a whole new species, dubbed Homo rudolfensis. Others attributed the differences in shape between this skull and others belonging to Homo habilis to geographical or sexual variation within the species – the unusually large 1470 skull perhaps belonged to a male H. habilis. Without any other specimens to decide either way, the debate rolled on.
Meave Leakey and her colleagues have now discovered three new fossils that share many of the distinctive features of the anomalous skull. The finds finally look set to confirm that the 1470 skull is not an anomalous oddity, but belonged to a distinct species, which will probably continue to be called Homo rudolfensis.
Given the paucity of previous specimens, the three new fossils – a well-preserved face, a complete lower jaw, and part of a lower jaw – are a rich haul. To find such complete fragments is very unusual, Leakey says.
The new face is smaller than 1470 and belonged to a juvenile, but it has the same long, flat form that has bugged Leakey ever since 1972. "It's been a long search," she says.
Unlike the 1470 skull, the new face still has many of its teeth, making it possible to work out the probable shape of the lower jaw – another feature lacking in the 1470 skull. Both of the new jaws are a likely fit for the species.
Together, the finds confirm that the differences between Homo habilis and Homo rudolfensis are too great to imply they are male and female members of the same species. No modern ape shows such an extreme level of difference between male and female members of the species.
The fossil record actually suggests there were three roughly contemporaneous species of Homo around 2 million years ago. "The specimens can be readily divided into a Homo erectus group, and two others: one including 1470 and the new specimens, and the other including everything else," Leakey says.
However, this still might not tie things up completely. In a commentary piece published alongside the new paper, Bernard Wood at George Washington University in Washington DC notes that some researchers have suggested that our evidence for Homo habilis and Homo rudolfensis stretches the definition of the genus Homo too far. While it now seems certain that these fossils belong to two distinct species, we may yet find that they are not in fact part of the same lineage that led to Homo sapiens.
Journal reference: Nature, DOI: 10.1038/nature11322

http://phys.org/news/2012-08-low-cost-device-purify-human-compost.html

Engineer builds low-cost device to purify human waste, make compost and generate electricity

The inexpensive green latrine can be deployed throughout places such as rural Africa

Phys.org - Caitlyn Shea Butler, a civil engineering professor at the University of Massachusetts Amherst, has designed and is now field-testing a new "green latrine" that purifies human waste, turning it into compost for farming and generating electricity. Her multipurpose invention is called a "Microbial Fuel Cell Latrine."

Butler believes her inexpensive green latrine can be deployed throughout places such as rural Africa, transforming the way human waste is treated in areas where sanitation facilities are poor or nonexistent. At the same time, the device can play a key role in preventing waterborne diseases, including diarrhea.

"You get a lot out of this system," says Butler. "The latrine produces electricity. It makes compost. And you protect the ground water source. So you get a lot back for a small investment."

Butler traveled to Ghana in May to install a pilot version of her device. Working with graduate students Cynthia Castro and Joe Goodwill, collaborators Mark Henderson and Brad Rogers from Arizona State University, and residents of the small village of Agona Nyakrom, they installed the first working model of her Microbial Fuel Cell Latrine.

She says the pilot model can immediately address two issues faced by the village. First, when human waste leaches into underground water, deadly pathogens that cause waterborne diseases such as diarrhea spread throughout the aquifer. High nitrogen concentrations contained in the waste can also damage healthy water systems as well as cause nitrate poisoning in infants and the elderly. Butler's microbial latrine prevents that from happening. The second problem is that many rural areas of Africa have limited electricity, and Butler's fuel cell would generate enough electricity to power a light within the latrine, thus allowing villagers access throughout the night. "This is a centralized resource that will benefit the whole community," says Butler.

Butler's latrine works like a battery. It has an anode and a cathode and is similar to a fuel cell where a fuel, for example hydrogen, is oxidized at the anode, and an oxidant, such as oxygen, is reduced at the cathode. In this case, the organic waste matter is the fuel and nitrate is the oxidant. After solid wastes are first filtered in a composting chamber, dissolved waste organic matter is oxidized in an anode chamber. The oxidation of organic matter is assisted by bacteria on the anode surface and uses the anode as an electron acceptor to complete their metabolic reaction. Electrons released in this biological process are conveyed through a load-bearing circuit, producing electricity, to the cathode compartment. There a different community of bacteria uses the cathode as an electron donor, capturing the energy from the electrons, to reduce harmful nitrates in the waste stream.

The primary nitrogen compound found in human waste is ammonium, which can be broken down by oxidation, or nitrification. In Butler's latrine, nitrification takes place thanks to bacteria living in an intermediate chamber that separates the anode and cathode chambers. The result is effluent water that is quite low in organic matter and nutrients, minimizing pathogen persistence in the environment.

Butler says, "My research objectives focus on developing energy-efficient treatment strategies for both water and wastewater treatment. I examine bioelectrochemical systems where biofilms, capable of using either an anode as an electron acceptor or cathode as an electron donor, remediate environmental pollutants and concurrently produce electricity." Butler's project and her Ghana trip were funded by a $100,000 grant from the Grand Challenges Exploration program supported by the Bill & Melinda Gates Foundation in this collaborative project between engineers from UMass Amherst and Arizona State. *Provided by University of Massachusetts Amherst*

http://phys.org/news/2012-08-grey-parrots-inferential.html

Researchers find Grey parrots able to use inferential reasoning

Researchers have found that Grey parrots are capable of inferential reasoning on a level that is superior to virtually all other animals save great apes and humans

Phys.org - A team of German and Austrian researchers has found that Grey parrots are capable of inferential reasoning on a level that is superior to virtually all other animals save great apes and humans. In lab experiments involving choosing which box contains food, the researchers describe, in their paper published in the journal Proceedings of the Royal Society B, how the birds were able to infer through auditory clues, which box contained a hidden food treat.

In this new experiment, the team built on prior research that had shown that African Grey parrots when presented with two boxes they couldn't see through, chose the box with the food in it after finding the first empty. Such an experiment showed either that the birds were avoiding the empty box, or fully believed food was hidden in the second. To get a better reading, they tried a similar experiment using sound instead of sight clues.

In the second experiment, the team showed the birds two opaque boxes, one of which contained food. The researchers then shook the boxes allowing the birds to hear that something was inside just one of them. The birds then guessed correctly which box had the food in it, walked over and tipped it over and ate their treat. Next, however, the researchers tried shaking just the empty box, producing no sound. This time, the birds were able to infer that the food must be in the other box and ran to it when given the chance, accomplishing a feat the team says, humans can't handle until the age of three. They also say that dogs and monkeys failed when given the same test and that it seems that other than the birds, only great apes and human are known to be capable of such inferential thinking.

To find out just how good the birds were at their inferential thinking, the team resorted to some trickery, they attached tiny speakers to their wrists and played recorded sounds of boxes with food being shaken instead of letting the food make the actual sound. In such cases, they found the birds could not be fooled, they picked the box with food in it only when the sound matched the boxes as they would were they to come naturally.

The researchers also found something else interesting, the birds did better when the boxes were shaken side to side, rather than up and down, likely they say, because the up and down motions of the box distracted the birds because it's very similar to the way the birds normally bob their heads when interacting with one another.

Abstract

Our ability to make logical inferences is considered as one of the cornerstones of human intelligence, fuelling investigations of reasoning abilities in non-human animals. Yet, the evidence to date is equivocal, with apes as the prime candidates to possess these skills. For instance, in a two-choice task, apes can identify the location of hidden food if it is indicated by a rattling noise caused by the shaking of a baited container. More importantly, they also use the absence of noise during the shaking of the empty container to infer that this container is not baited. However, since the inaugural report of apes solving this task, to the best of our knowledge, no comparable evidence could be found in any other tested species such as monkeys and dogs. Here, we report the first successful and instantaneous solution of the shaking task through logical inference by a non-ape species, the African grey parrot. Surprisingly, the performance of the birds was sensitive to the shaking movement: they were successful with containers shaken horizontally, but not with vertical shaking resembling parrot head-bobbing. Thus, grey parrots seem to possess ape-like cross-modal reasoning skills, but their reliance on these abilities is influenced by low-level interferences.

More information: Grey parrots use inferential reasoning based on acoustic cues alone, PNAS, Published online before print August 8, 2012, doi: 10.1098/rspb.2012.1292

http://www.eurekalert.org/pub_releases/2012-08/uof-urd080812.php

UF researchers discover earliest use of Mexican turkeys by ancient Maya

A new University of Florida study shows the turkey, one of the most widely consumed birds worldwide, was domesticated more than 1,000 years earlier than previously believed.

Writer: Danielle Torrent

GAINESVILLE, Fla. --- Researchers say discovery of the bones from an ancient Mayan archaeological site in Guatemala provides evidence of domestication, usually a significant mark of civilization, and the earliest evidence of the Mexican turkey in the Maya world. The study appears online in PLoS ONE today.

The discovery of the turkey bones is significant because the Maya did not use a lot of domesticated animals. While they cultivated domesticated plants, most of their animal protein came mostly from wild resources, said lead author Erin Thornton, a research associate at the Florida Museum of Natural History on the UF campus and Trent University Archaeological Research Centre.

"We might have gotten the timing of the introduction of this species to the ancient Maya wrong by a significant chunk of time," Thornton said. "The species originates from central Mexico, outside the Maya cultural area. This is the species the Europeans brought back with them to Europe -- all domestic turkeys originated from Mexico."

Mayans had great passion for food. Corn, squash, beans formed the staple of food for Mayans. Having said that Mayans were not vegetarians. Mayans loved cuisines made of turkey, chicken and pigs.

Using archaeological evidence, comparisons of bone structure and ancient DNA analysis, scientists determined the turkey fossils belonged to the non-local species Meleagris gallopavo gallopavo, which is native to central and northern Mexico. The Mexican turkey is the ancestor of all domestic turkeys consumed in the world today and Mesoamerica's only indigenous domesticated animal. The discovery of the bones south of the turkey's natural range shows animal exchange occurred from northern Mesoamerica to the Maya cultural region during the Late Preclassic period from 300 B.C. to A.D. 100.

"This research has consequences for understanding Maya subsistence because they would have had access to a controlled, managed resource," Thornton said. "The turkey bones came from right within the ceremonial precinct of the site, so these are probably the remains of some sort of elite sacrifice, meal or feast."
The bones were recovered from the El Mirador archaeological site, one of the largest and most developed Preclassic locations found in the Maya lowlands. The site contains massive temple complexes, some of the largest Maya architecture ever constructed.
"Plant and animal domestication suggests a much more complex relationship between humans and the environment -- you're intentionally modifying it and controlling it," Thornton said.
Researchers assumed turkey bones previously recovered from Maya sites belonged to the native ocellated turkey, Meleagris ocellata. The new evidence means researchers may need to re-examine previously recovered bones, said Florida State University anthropology professor emeritus Mary Pohl.
"This study is extremely significant and I think it opens up a whole new perspective on the Maya and animal domestication," Pohl said. "I find it especially interesting that these turkey bones are in this very special pyramid context because people often think of turkeys as something to eat, but they were probably making some sort of special offerings of them, which would go along with the fact that they brought them in from a long distance."
Florida Museum researchers hope a new two-year, $185,000-grant from the National Science Foundation will help answer some of the questions the study has raised about the history of turkey rearing and domestication in Mesoamerica.
"The turkeys were brought in, they weren't local, but we don't know if they were brought in and then killed shortly after, used as a trade item or bred on-site after an even earlier introduction," Thornton said. "The El Mirador study is really just a tantalizing piece of the puzzle and we still have a lot left to learn and explore."
While the fossils were originally excavated in the 1980s, they were displayed in the Brigham Young University Museum of Peoples and Cultures until being sent to Thornton for identification in 2004.
Study co-authors include Kitty Emery and David Steadman of the Florida Museum of Natural History, Camilla Speller and Dongya Yang of Simon Fraser University, and Ray Matheny of Brigham Young University.

http://www.sciencedaily.com/releases/2012/08/120808121918.htm

Protein That Boosts Longevity May Protect Against Diabetes: Sirtuins Help Fight Off Disorders Linked to Obesity

A protein that slows aging in mice and other animals also protects against the ravages of a high-fat diet, including diabetes, according to a new MIT study.

Anne Trafton

ScienceDaily - MIT biology professor Leonard Guarente '74 discovered SIRT1's longevity-boosting properties more than a decade ago and has since explored its role in many different body tissues. In his latest study, appearing in the Aug. 8 print edition of the journal Cell Metabolism, he looked at what happens when the SIRT1 protein is missing from adipose cells, which make up body fat. When put on a high-fat diet, mice lacking the protein started to develop metabolic disorders, such as diabetes, much sooner than normal mice given a high-fat diet.
"We see them as being poised for metabolic dysfunction," says Guarente, the Novartis Professor of Biology at MIT. "You've removed one of the safeguards against metabolic decline, so if you now give them the trigger of a high-fat diet, they're much more sensitive than the normal mouse." The finding raises the possibility that drugs that enhance SIRT1 activity may help protect against obesity-linked diseases.
Guarente first discovered the effects of SIRT1 and other sirtuin proteins while studying yeast in the 1990s. Since then, these proteins have been shown to coordinate a variety of hormonal networks, regulatory proteins and other genes, helping to keep cells alive and healthy.
In recent years, Guarente and his colleagues have deleted the gene from organs such as brain and liver to pinpoint its effects more precisely. Their previous work has revealed that in the brain, SIRT1 protects against the neurodegeneration seen in Alzheimer's, Huntington's and Parkinson's diseases. SIRT1 is a protein that removes acetyl groups from other proteins, modifying their activity. The possible targets of this deacetylation are numerous, which is likely what gives SIRT1 its broad range of protective powers, Guarente says.
In the Cell Metabolism study, the researchers analyzed the hundreds of genes that were turned on in mice lacking SIRT1 but fed a normal diet, and found that they were almost identical to those turned on in normal mice fed a high-fat diet. This suggests that in normal mice, development of metabolic disorders is a two-step process. "The first step is inactivation of SIRT1 by the high-fat diet, and the second step is all the bad things that follow that," Guarente says.

The researchers investigated how this occurs and found that in normal mice given a high-fat diet, the SIRT1 protein is cleaved by an enzyme called caspase-1, which is induced by inflammation. It's already known that high-fat diets can provoke inflammation, though it's unclear exactly how that happens, Guarente says. "What our study says is that once you induce the inflammatory response, the consequence in the fat cells is that SIRT1 will be cleaved," he says.

That finding "provides a nice molecular mechanism to understand how inflammatory signals in adipose tissue could lead to rapid derangement of metabolic tissue," says Anthony Suave, an associate professor of pharmacology at Weill Cornell Medical College, who was not part of the research team.

Drugs that target that inflammatory process, as well as drugs that enhance sirtuin activity, might have some beneficial therapeutic effect against obesity-related disorders, Suave says.

The researchers also found that as normal mice aged, they were more susceptible to the effects of a high-fat diet than younger mice, suggesting that they lose the protective effects of SIRT1 as they age. Aging is known to increase inflammation, so Guarente is now studying whether that age-related inflammation also provokes SIRT1 loss.

This research was funded by the National Institutes of Health, the Glenn Medical Foundation and the American Heart Association.

Angeliki Chalkiadaki, Leonard Guarente. ***High-Fat Diet Triggers Inflammation-Induced Cleavage of SIRT1 in Adipose Tissue To Promote Metabolic Dysfunction. Cell Metabolism****, 2012; 16 (2): 180 DOI: 10.1016/j.cmet.2012.07.003*

http://www.eurekalert.org/pub_releases/2012-08/cru-sdh080712.php

Scientists discover how iron levels and a faulty gene cause bowel cancer

High levels of iron could raise the risk of bowel cancer by switching on a key pathway in people with faults in a critical anti-cancer gene

HIGH LEVELS of iron could raise the risk of bowel cancer by switching on a key pathway in people with faults in a critical anti-cancer gene, according to a study published in Cell Reports* today (Thursday).

Cancer Research UK scientists, based at the University of Birmingham and the Beatson Institute for Cancer Research in Glasgow, found bowel cancers were two to three times more likely to develop in mice with a faulty APC gene that were fed high amounts of iron compared to mice who still had a working APC gene.

In contrast, mice with a faulty APC gene fed a diet low in iron did not develop bowel cancer at all.

Study author Professor Owen Sansom, deputy director of the Cancer Research UK Beatson Institute for Cancer Research in Glasgow, said: "We've made a huge step in understanding how bowel cancer develops. The APC gene is faulty in around eight out of 10 bowel cancers but until now we haven't known how this causes the disease. "It's clear that iron is playing a critical role in controlling the development of bowel cancer in people with a faulty APC gene. And, intriguingly, our study shows that even very high levels of iron in the diet don't cause cancer by itself, but rely on the APC gene."

Co-author Dr Chris Tselepis, a Cancer Research UK scientist at the University of Birmingham, said: "Our results also suggest that iron could be raising the risk of bowel cancer by increasing the number of cells in the bowel with APC faults. The more of these cells in the bowel, the greater the chance that one of these will become a starting point for cancer. "We're now planning to develop treatments that reduce the amount of iron in the bowel and so could lower the risk of developing bowel cancer. We hope to start using these in trials in the next few years in people who are at a greater risk."

The study could also explain why foods such as red meat, which have high levels of iron, are linked to an increased risk of bowel cancer.

When the APC gene is deleted, two proteins are switched on that cause iron to build up in bowel cells. When this happens, a key cancer signalling pathway called wnt is switched on, causing cells to grow out of control.

In mice fed a diet with no iron, cells with a faulty APC gene were killed and bowel cancers did not develop.

Mice with a fully functioning APC gene did not develop bowel cancers, even when fed a diet high in iron. In these bowel cells, the iron accumulation proteins are turned off and wnt signalling remains inactive.

Dr Julie Sharp, senior science information manager at Cancer Research UK, said: "Bowel cancer is the third most common cancer in the UK. These findings suggest a potentially effective way of reducing the chances of bowel cancer developing in people who are at high risk. Finding ways of 'mopping up' the iron that is in the bowel could have a real impact on the number of people who develop the disease.

"This research is a great example of scientists coming together and sharing their different expertise to find new ways of understanding and potentially preventing cancer."

Radulescu, S et al. Luminal iron levels govern intestinal tumourigenesis following Apc loss in vivo Cell Reports (2012)

http://www.eurekalert.org/pub_releases/2012-08/sri-sri080912.php

Scripps Research Institute scientists show copper facilitates prion disease

The research provides new clue to 'mad cow' and related conditions

LA JOLLA, CA - Many of us are familiar with prion disease from its most startling and unusual incarnations—the outbreaks of "mad cow" disease (bovine spongiform encephalopathy) that created a crisis in the global beef industry. Or the strange story of Kuru, a fatal illness affecting a tribe in Papua New Guinea known for its cannibalism. Both are forms of prion disease, caused by the abnormal folding of a protein and resulting in progressive neurodegeneration and death.

While exactly how the protein malfunctions has been shrouded in mystery, scientists at The Scripps Research Institute now report in the journal Proceedings of the National Academy of Sciences (PNAS) that reducing copper in the body delays the onset of disease. Mice lacking a copper-transport gene lived significantly longer when infected with a prion disease than did normal mice.

"This conclusively shows that copper plays a role in the misfolding of the protein, but is not essential to that misfolding," said Scripps Research Professor Michael Oldstone, who led the new study. "We've known for many years that prion proteins bind copper," said Scripps Research graduate student Owen Siggs, first author of the paper with former Oldstone lab member Justin Cruite. "But what scientists couldn't agree on was whether this was a good thing or a bad thing during prion disease. By creating a mutation in mice that lowers the amount of circulating copper by 60 percent, we've shown that reducing copper can delay the onset of prion disease."

Zombie Proteins

Unlike most infections, which are caused by bacteria, viruses, or parasites, prion disease stems from the dysfunction of a naturally occurring protein. "We all contain a normal prion protein, and when that's converted to an abnormal prion protein, you get a chronic nervous system disease," said Oldstone. "That occurs genetically (spontaneously in some people) or is acquired by passage of infectious prions. Passage can occur by eating infected meat; in the past, by cannibalism in the Fore population in New Guinea through the ingestion or smearing of infectious brains; or by introduction of infectious prions on surgical instruments or with medical products made from infected individuals."

When introduced into the body, the abnormal prion protein causes the misfolding of other, normal prion proteins, which then aggregate into plaques in the brain and nervous system, causing tremors, agitation, and failure of motor function, and leads invariably to death.

A Delicate Balance

The role of copper in prion disease had previously been studied using chelating drugs, which strip the metals from the body—an imprecise technique. The new study, however, turned to animal models engineered in the lab of Nobel laureate Bruce Beutler while at The Scripps Research Institute. (Beutler is currently director of the Center for the Genetics of Host Defense at UT Southwestern.)

The Beutler lab had found mice with mutations disrupting copper-transporting enzyme ATP7A. The most copper-deficient mice died in utero or soon after birth, but those with milder deficiency were able to live normally. "Copper is something we can't live without," said Siggs. "Like iron, zinc, and other metals, our bodies can't produce copper, so we absorb small amounts of it from our diet. Too little copper prevents these enzymes from working, but too much copper can also be toxic, so our body needs to maintain a fine balance. Genetic mutations like the one we describe here can disrupt this balance."

Death Delayed

In the new study, both mutant and normal mice were infected with Rocky Mountain Laboratory mouse scrapie, which causes a spongiform encephalopathy similar to mad cow disease. The control mice developed illness in about 160 days, while the mutant mice, lacking the copper-carrying gene, developed the disease later at 180 days. Researchers also found less abnormal prion protein in the brains of mutant mice than in control mice, indicating that copper contributed to the conversion of the normal prion protein to the abnormal disease form. However, all the mice eventually died from disease.

Oldstone and Siggs note the study does not advocate for copper depletion as a therapy, at least not on its own. However, the work does pave the way for learning more about copper function in the body and the biochemical workings of prion disease.

In addition to Siggs, Cruite, Beutler, and Oldstone, authors of the paper "Disruption of copper homeostasis due to a mutation of Atp7a delays the onset of prion disease," are Xin Du formerly of Scripps Research and currently of the University of California, San Diego (UCSD); Sophie Rutschmann, formerly of Scripps Research and currently of Imperial College London; and Eliezer Masliah of UCSD. For more information, see http://www.pnas.org/content/early/2012/08/03/1211499109.abstract.

This work was supported by the National Institutes of Health (award numbers HHSN272200700038C, AG04342, AG18440, AG022074, and NS057096) and by the General Sir John Monash Foundation.

http://www.eurekalert.org/pub_releases/2012-08/uoc--usd080912.php

UCLA scientist discovers plate tectonics on Mars

For years, many scientists had thought that plate tectonics existed nowhere in our solar system but on Earth.

Now, a UCLA scientist has discovered that the geological phenomenon, which involves the movement of huge crustal plates beneath a planet's surface, also exists on Mars.

"Mars is at a primitive stage of plate tectonics. It gives us a glimpse of how the early Earth may have looked and may help us understand how plate tectonics began on Earth," said An Yin, a UCLA professor of Earth and space sciences and the sole author of the new research.

Yin made the discovery during his analysis of satellite images from a NASA spacecraft known as THEMIS (Time History of Events and Macroscale Interactions during Substorms) and from the HIRISE (High Resolution Imaging Science Experiment) camera on NASA's Mars Reconnaissance Orbiter. He analyzed about 100 satellite images — approximately a dozen were revealing of plate tectonics.

Yin has conducted geologic research in the Himalayas and Tibet, where two of the Earth's seven major plates divide.

"When I studied the satellite images from Mars, many of the features looked very much like fault systems I have seen in the Himalayas and Tibet, and in California as well, including the geomorphology," said Yin, a planetary geologist.

For example, he saw a very smooth, flat side of a canyon wall, which can be generated only by a fault, and a steep cliff, comparable to cliffs in California's Death Valley, which also are generated by a fault. Mars has a linear volcanic zone, which Yin said is a typical product of plate tectonics.

"You don't see these features anywhere else on other planets in our solar system, other than Earth and Mars," said Yin, whose research is featured as the cover story in the August issue of the journal Lithosphere.

The surface of Mars contains the longest and deepest system of canyons in our solar system, known as Valles Marineris (Latin for Mariner Valleys and named for the Mariner 9 Mars orbiter of 1971□, which discovered it). It is nearly 2,500 miles long — about nine times longer than the Earth's Grand Canyon. Scientists have wondered for four decades how it formed. Was it a big crack in Mars' shell that opened up?

"In the beginning, I did not expect plate tectonics, but the more I studied it, the more I realized Mars is so different from what other scientists anticipated," Yin said. "I saw that the idea that it is just a big crack that opened up is incorrect. It is really a plate boundary, with horizontal motion. That is kind of shocking, but the evidence is quite clear.

"The shell is broken and is moving horizontally over a long distance. It is very similar to the Earth's Dead Sea fault system, which has also opened up and is moving horizontally."

The two plates divided by Mars' Valles Marineris have moved approximately 93 miles horizontally relative to each other, Yin said. California's San Andreas Fault, which is over the intersection of two plates, has moved about twice as much — but the Earth is about twice the size of Mars, so Yin said they are comparable.

Yin, whose research is partly funded by the National Science Foundation, calls the two plates on Mars the Valles Marineris North and the Valles Marineris South.

"Earth has a very broken 'egg shell,' so its surface has many plates; Mars' is slightly broken and may be on the way to becoming very broken, except its pace is very slow due to its small size and, thus, less thermal energy to drive it," Yin said. "This may be the reason Mars has fewer plates than on Earth."

Mars has landslides, and Yin said a fault is shifting the landslides, moving them from their source.

Does Yin think there are Mars-quakes?

"I think so," he said. "I think the fault is probably still active, but not every day. It wakes up every once in a while, over a very long duration — perhaps every million years or more."

Yin is very confident in his findings, but mysteries remain, he said, including how far beneath the surface the plates are located.

"I don't quite understand why the plates are moving with such a large magnitude or what the rate of movement is; maybe Mars has a different form of plate tectonics," Yin said. "The rate is much slower than on Earth."

The Earth has a broken shell with seven major plates; pieces of the shell move, and one plate may move over another. Yin is doubtful that Mars has more than two plates.

"We have been able to identify only the two plates," he said. "For the other areas on Mars, I think the chances are very, very small. I don't see any other major crack."

Did the movement of Valles Marineris North and Valles Marineris South create the enormous canyons on Mars? What led to the creation of plate tectonics on Earth?
Yin, who will continue to study plate tectonics on Mars, will answer those questions in a follow-up paper that he also plans to publish in the journal Lithosphere.

http://bit.ly/Tz8eLc

Researcher accused of misleading pregnant women

Freedom of information requests have revealed that pregnant women may not have been given all the facts before taking an experimental treatment to prevent female fetuses from being masculinised as a result of a rare genetic disorder.

17:35 09 August 2012 by Sara Reardon

Research has provided some evidence that dexamethasone, a drug normally prescribed to relieve inflammation, can prevent girls with a rare hormonal disease from developing male genitalia and same-sex attraction if they are treated as fetuses. But as yet, no clinical studies show that this treatment is safe, says Alice Dreger of Northwestern University in Evanston, Illinois. She claims that researchers have misled an unknown number of pregnant women into taking the experimental treatment without properly informing them of its risks.
Since the 1980s, Maria New of Mount Sinai School of Medicine in New York has studied and popularised the idea of prescribing dexamethasone "off-label" to women at risk of having foetuses with congenital adrenal hyperplasia (CAH). The treatment is now taught as standard practice in medical schools. But because the drug must be given very early in pregnancy before the fetus' gender or CAH status is known, many fetuses are treated unnecessarily. A child with two carrier parents has a one-in-four chance of having the disease, and the treatment only works for girls.
There is little research available on the effects of dexamethasone, which mimics a steroid hormone. And because dexamethasone doesn't cure CAH but only prevents masculinisation of girls, it can be difficult to distinguish possible effects of the drug from other treatments the children receive after birth.

Developmental problems

However, some evidence suggests that the drug may be harmful to foetuses early in development. A recent study of 43 children in Sweden who did not have CAH but had been treated with dexamethasone as fetuses found that 20 per cent of them had some sort of developmental problem. (Journal of Clinical Endocrinology and Metabolism, DOI: 10.1210/jc.2012-1222).
Through freedom of information requests to Mount Sinai School of Medicine, Dreger and colleagues documented what they see as attempts by New's group to circumvent proper patient consent procedures for experimental use of the drug.
The researchers allege that, according to New's grant applications, she skipped important steps in patient consent, promoting treatment as "safe and effective" without informing parents that the claim is controversial. Years later, New's group then followed up a fraction of the patients to ask about side effects.
Because New doesn't have a financial stake in a drug company, the US Food and Drug Administration says that she is free to promote the treatment as safe and effective.
New declined to be interviewed, but in a statement from Mount Sinai, spokesperson Ian Michaels said the claims are "unfounded" because New's practices have previously been cleared by federal agencies and that the FDA has waived the need for dexamethasone to be approved as an "investigational new drug".
Journal reference: Bioethical Inquiry, DOI 10.1007/s11673-012-9384-9

http://www.sciencedaily.com/releases/2012/08/120809133805.htm

Neolithic Man: The First Lumberjack?

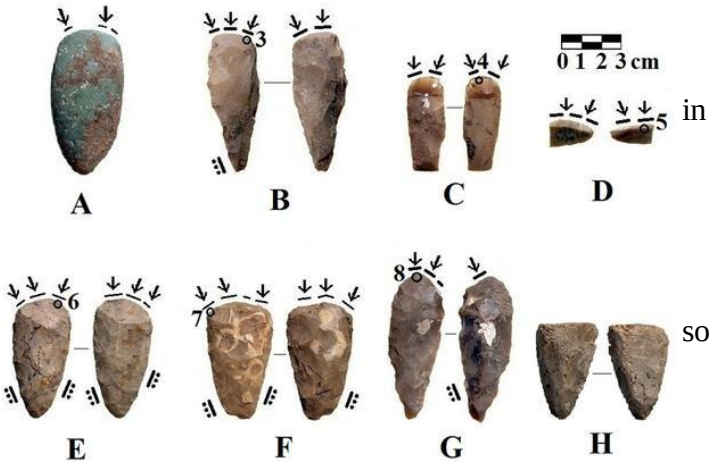
Now Dr. Ran Barkai of Tel Aviv University has shed new light on this milestone in human evolution, demonstrating a direct connection between the development of an agricultural society and the development of woodworking tools.

ScienceDaily - During the Neolithic Age (approximately 10000-6000 BCE), early man evolved from hunter-gatherer to farmer and agriculturalist, living in larger, permanent settlements with a variety of domesticated animals and plant life. This transition brought about significant changes in terms of the economy, architecture, man's relationship to the environment, and more.
Now Dr. Ran Barkai of Tel Aviv University's Department of Archaeology and Ancient Near Eastern Civilizations has shed new light on this milestone in human evolution, demonstrating a direct connection between the development of an agricultural society and the development of woodworking tools.
"Intensive woodworking and tree-felling was a phenomenon that only appeared with the onset of the major changes in human life, including the transition to agriculture and permanent villages," says Dr. Barkai, whose

research was published in the journal PLoS One. Prior to the Neolithic period, there is no evidence of tools that were powerful enough to cut and carve wood, let alone fell trees. But new archaeological evidence suggests that as the Neolithic age progressed, sophisticated carpentry developed alongside agriculture.

Evolution of axes

The use of functional tools in relation to woodworking over the course of the Neolithic period has not been studied in detail until now. Through their work at the archaeological site of Motza, a neighbourhood in the Judean Hills, Dr. Barkai and his fellow researchers, Prof. Rick Yerkes of Ohio State University and Dr. Hamudi Khalaily of the Israel Antiquity Authority, have unearthed evidence that increasing sophistication terms of carpentry tools corresponds with increased agriculture and permanent settlements.



The early part of the Neolithic age is divided into two distinct eras -- Pre-Pottery Neolithic A (PPNA) and Pre-Pottery Neolithic B (PPNB). Agriculture and domesticated plants and animals appear only in PPNB, the transition between these two periods is a watershed moment in human history. And these changes can be tracked in the woodworking tools which belong to each period, says Dr. Barkai.

Some utilized Bifaces and a tranchet spall from EPPNB layer VI at Motza. Ventral face to the left, dorsal face to the right, black lines show the extent of the wood-working microwear traces, arrows show the orientation of the polish and striations, lines with dots show location of hafting traces. (A) Polished greenstone axe from SN 2, Locus 2136, Basket 40013, made of green stone, with weakly-developed wood working traces and slight edge damage along distal edge. (B) flint tranchet axe, SN 32, Locus 4050, Basket 41007. Circle shows the location of Fig. 3 Right. (C) flint tranchet chisel N19c, SN 14, Locus 4014, Basket 40211. Circle shows the location of Fig. 4 Right. (D) tranchet spall, SN 26, Basket 40309. Circle shows the location of Fig. 5. (E) flint tranchet axe resharpened by polishing, SN 15, Locus 5016, Basket 50135. Circle shows the location of Fig. 6. (F) flint tranchet axe, SN 34, Locus 5040, Basket 50437. Circle shows the location of Fig. 7. (G) flint tranchet axe K17c from Motza, SN 11, Locus 5040, Basket 50479. Circle shows the location of Fig. 8. (H) base of a recycled flint axe, SN 33, Locus 5067, Basket 50730 with worn lateral edges and worn dorsal and ventral faces. Some of these surfaces have large patches of stone-on-stone polish. It seems to have been re-used as a stone polishing tool. (Credit: Yerkes et al, PLoS One, doi:10.1371/journal.pone.0042442.g002)

Within PPNA, humans remained gatherers but lived in more permanent settlements for the first time, he says. Axes associated with this period are small and delicate, used for light carpentry but not suited for felling trees or other massive woodworking tasks. In PPNB, the tools have evolved to much larger and heavier axes, formed by a technique called polishing. The researchers' in-depth analysis of these tools shows that they were used to cut down trees and complete various building projects.

"We can document step by step the transition from the absence of woodworking tools, to delicate woodworking tools, to heavier woodworking tools," Dr. Barkai says, and this follows the "actual transition from the hunter-gatherer lifestyle to agriculture." He also identifies a trial-and-error phase during which humans tried to create an axe strong enough to undertake larger woodworking tasks. Eventually, they succeeded in creating a massive ground stone axe in PPNB.

Home makeover

Whether the transition to an agricultural society led to the development of major carpentry tools or vice versa remains to be determined, says Dr. Barkai, who characterizes it as a "circular argument." Whatever the answer, the parallel changes led to a revolution in lifestyle.

Beyond the change from a hunter-gatherer to an agricultural economy, a new form of architecture also emerged. Not only did people begin to live in permanent villages, but the buildings in which they lived literally took a different shape. The round and oval structures of earlier domiciles were replaced by rectangular structures in PPNB, explains Dr. Barkai. "Evidence tells that us that for each home, approximately 10 wooden beams were needed. Prior to this, there were no homes with wooden beams." In addition, humans began to produce limestone-based plaster floors for their homes -- which also represented a growing use of wood, since plaster is manufactured by heating limestone.

These architectural developments, along with building pens and fences for domesticated animals, also necessitated the felling of trees in large quantities.

Richard W. Yerkes, Hamudi Khalaily, Ran Barkai. Form and Function of Early Neolithic Bifacial Stone Tools Reflects Changes in Land Use Practices during the Neolithization Process in the Levant. PLoS ONE, 2012; 7 (8): e42442 DOI: 10.1371/journal.pone.0042442

http://www.eurekalert.org/pub_releases/2012-08/bawh-gnm081012.php

Good news: Migraines hurt your head but not your brain

According to new research from Brigham and Women's Hospital, migraines are not associated with cognitive decline

Boston, MA—Migraines currently affect about 20 percent of the female population, and while these headaches are common, there are many unanswered questions surrounding this complex disease. Previous studies have linked this disorder to an increased risk of stroke and structural brain lesions, but it has remained unclear whether migraines had other negative consequences such as dementia or cognitive decline. According to new research from Brigham and Women's Hospital (BWH), migraines are not associated with cognitive decline. This study is published online by the British Medical Journal (BMJ) on August 8, 2012. "Previous studies on migraines and cognitive decline were small and unable to identify a link between the two. Our study was large enough to draw the conclusion that migraines, while painful, are not strongly linked to cognitive decline," explained Pamela Rist ScD, a research fellow in the Division of Preventive Medicine at BWH, and lead author on this study.

The research team analyzed data from the Women's Health Study, a cohort of nearly 40,000 women, 45 years and older. In this study, researchers analyzed data from 6,349 women who provided information about migraine status at baseline and then participated in cognitive testing during follow-up. Participants were classified into four groups: no history of migraine, migraine with aura (transient neurology symptoms mostly of the visual field), migraine without aura, and past history of migraine. Cognitive testing was carried out in two year intervals up to three times.

"Compared with women with no history of migraine, those who experienced migraine with or without aura did not have significantly different rates of cognitive decline," explained Rist. "This is an important finding for both physicians and patients. Patients with migraine and their treating doctors should be reassured that migraine may not have long term consequences on cognitive function."

There is still a lot that is unknown about migraines. However this study offers promising evidence for patients and their treating physicians. More research needs to be done to understand the consequences of migraine on the brain and to establish strategies to influence the course of the disease in order to optimize treatment strategies.

This research was supported by The Women's Health Study is supported by grants from the National Heart, Lung, and Blood Institute (HL-043851, HL-080467, HL-099355) and the National Cancer Institute (CA-47988). The cognitive substudy of the Women's Health Study was supported by a grant from the National Institute of Aging (AG-15933). PMR was supported by a training grant from the National Institute of Aging (AG-00158). TK is supported in part by a Chair of Excellence grant of the French National Research Agency (Agence Nationale de la Recherche, R09177DD).

http://www.sciencedaily.com/releases/2012/08/120810083611.htm

Security Risk: Sensitive Data Can Be Harvested from a PC Even If It Is in Standby Mode, Experts Say

When you switch off your computer any passwords you used to login to web pages, your bank or other financial account evaporate into the digital ether, right? Not so fast!

ScienceDaily - Researchers in Greece have discovered a security loophole that exploits the way computer memory works and could be used to harvest passwords and other sensitive data from a PC even if it is in standby mode. Writing in a forthcoming issue of the International Journal of Electronic Security and Digital Forensics, Christos Georgiadis of the University of Macedonia in Thessaloniki and colleagues Stavroula Karayianni and Vasilios Katos at the Democritus University of Thrace in Xanthi explain how their discovery could be used by information specialists in forensic science for retrieving incriminating evidence from computers as well as exploited by criminals to obtain personal data and bank details.

The researchers point out that most computer users assume that switching off their machine removes any data held in random access memory (RAM), this type of fast memory is used by the computer to temporarily hold data currently used by a given application. RAM is often referred to as volatile memory, because anything contained in RAM is considered lost when a computer is switched off. Indeed, all data is lost from RAM when the power supply is disconnected; so it is volatile in this context.

However, Georgiadis and colleagues have now shown that data held in RAM is not lost if the computer is switched off but the mains electricity supply not interrupted. They suggest that forensics experts and criminals might thus be able to access data from the most recently used applications. They point out that starting a new

memory-intensive application will overwrite data in RAM while a computer is being used, but simply powering off the machine leaves users vulnerable in terms of security and privacy.
"The need to capture and analyse the RAM contents of a suspect PC grows constantly as remote and distributed applications have become popular, and RAM is an important source of evidence," the team explains, as it can contain telltale traces of networks accessed and the unencrypted forms of passwords sent to login boxes and online forms.
The team tested their approach to retrieving data from RAM after a computer had been switched off following a general and common usage scenario involving accessing Facebook, Gmail, Microsoft Network (MSN) and Skype. They carried out RAM dumps immediately after switch off at 5, 15 and 60 minutes. They then used well-known forensic repair tools to piece together the various fragments of data retrieved from the memory dumps.
The team was able to reconstruct login details from the memory dumps for several popular services being used in the Firefox web browser including Google Mail (GMail), Facebook, Hotmail, and the WinRar file compression application. "We can conclude that volatile memory loses data under certain conditions and in a forensic investigation such memory can be a valuable source of evidence," the team says.
Christos Georgiadis, Stavroula Karayianni and Vasilios Katos. A framework for password harvesting from volatile memory. International Journal of Electronic Security and Digital Forensics, 2012

http://www.sciencedaily.com/releases/2012/08/120810112915.htm

'Theranostic' Imaging Offers Means of Killing Prostate Cancer Cells

Experimenting with human prostate cancer cells and mice, cancer imaging experts at Johns Hopkins say they have developed a method for finding and killing malignant cells while sparing healthy ones.

ScienceDaily The method, called theranostic imaging, targets and tracks potent drug therapies directly and only to cancer cells. It relies on binding an originally inactive form of drug chemotherapy, with an enzyme, to specific proteins on tumor cell surfaces and detecting the drug's absorption into the tumor.The binding of the highly specific drug-protein complex, or nanoplex, to the cell surface allows it to get inside the cancerous cell, where the enzyme slowly activates the tumor-killing drug.
Researchers say their findings, published in the journal American Chemical Society Nano online Aug. 6, are believed to be the first to show that chemotherapies can be precisely controlled at the molecular level to maximize their effectiveness against tumors, while also minimizing their side effects.
Senior study investigator Zaver Bhujwalla, Ph.D., a professor at the Johns Hopkins University School of Medicine and its Kimmel Cancer Center, notes that a persistent problem with current chemotherapy is that it attacks all kinds of cells and tissues, not just cancerous ones.
In the theranostic imaging experiments, overseen by Bhujwalla and study co-investigator Martin Pomper, M.D., Ph.D., investigators directed drugs only to cancer cells, specifically those with prostate-specific membrane antigen, or PSMA cell surface proteins.
"Our results show a non-invasive imaging approach to following and delivering targeted therapy to any cancer that expresses PSMA," says Bhujwalla, who also serves as director of the Johns Hopkins In Vivo Cellular and Molecular Imaging Center (ICMIC), where the theranostic imaging studies were developed.
Bhujwalla says the new technique potentially will work against any cancer in which tumors elevate production of certain cell surface proteins.Examples would include breast cancers with HER-2/neu and CXCR4 proteins, and some liver, lung and kidney cancers also known to express particular proteins. She notes that PSMA is expressed in the vessels of most solid tumors, suggesting that the nanoplex reported in the latest study could be used in general to image and treat a variety of cancers.
In their latest series of experiments, primarily in mice injected with human prostate tumor cells, Bhujwalla and the Johns Hopkins team tested their ability to track with imaging devices the delivery of anti-cancer drugs directly to tumors.Some of the tumors were composed of cells with PSMA, while other so-called control tumors had none.Included in the drug nanoplex were small strands of RNA, cell construction acids that can be used instead to block and turn down production of a well-known enzyme, choline kinase, whose levels usually rise with tumor growth.All nanoplex components were imaged inside the tumor, in addition to dropping choline kinase production, which decreased by 80 percent within 48 hours of nanoplex absorption into cells with ample PSMA.When researchers used antibodies to block the action of PSMA, down went the level of nanoplex uptake and drug activation in cancerous cells as measured by dimming of the image.
Different concentrations of the drug nanoplex, tagged with radioactive and fluorescent molecules, were mixed in the lab with prostate cancer tissue cells, some of which had extra PSMA and others which had none.Only

those cells with extra PSMA showed nanoplex uptake, as measured by image intensity, which later decreased when PSMA-blocking chemicals were added (back to levels seen in cells with almost no PSMA).
Additional experiments involving injections of three different concentrations of the drug nanoplex showed no damage to other vital mouse organs, such as the kidney and liver, nor any uptick in the mouse immune system response.
"Our theranostic imaging approach shows how the best methods of detection and treatment can be combined to form highly specialized, more potent and safer forms of chemotherapy," says Pomper, a professor at Johns Hopkins, who also serves as an associate director at ICMIC.
He says that an important goal for theranostic imaging is to move it beyond standard chemotherapy that attacks one target molecule at a time."With theranostic imaging, we can attack multiple tumor targets, making it harder for the tumor to evade drug treatment," says Pomper, who is already working with colleagues at Johns Hopkins to identify other molecular targets.
The most recent studies were performed at Johns Hopkins over two years, starting in 2010, with funding support from the National Cancer Institute, part of the National Institutes of Health.The corresponding grant numbers are P50-CA103175, RO1-CA138515 and RO1-CA134675.
In addition to Bhujwalla, and Pomper, other Johns Hopkins researchers from the Russell H. Morgan Department of Radiology involved in this imaging study were lead investigators Zhihang Chen, Ph.D., and Mary-France Penet, Ph.D.Additional study co-investigators were Sridhar Nimmagadda, Ph.D.; Li Cong, Ph.D.; Sangeeta Banerjee, Ph.D.; Paul Winnard Jr., Ph.D.; Dmitri Artemov, Ph.D.; and Kristine Glunde, Ph.D.
Zhihang Chen, Marie-France Penet, Sridhar Nimmagadda, Cong Li, Sangeeta R. Banerjee, Paul T. Winnard, Dmitri Artemov, Kristine Glunde, Martin G. Pomper, Zaver M. Bhujwalla. PSMA-Targeted Theranostic Nanoplex for Prostate Cancer Therapy. ACS Nano, 2012; : 120809154716000 DOI: 10.1021/nn301725w

http://www.eurekalert.org/pub_releases/2012-08/nu-sas081012.php

Smelling a skunk after a cold

Brain changes after a stuffed nose protect the sense of smell

CHICAGO --- Has a summer cold or mold allergy stuffed up your nose and dampened your sense of smell? We take it for granted that once our nostrils clear, our sniffers will dependably rebound and alert us to a lurking neighborhood skunk or a caramel corn shop ahead.
That dependability is no accident. It turns out the brain is working overtime behind the scenes to make sure the sense of smell is just as sharp after the nose recovers.
A new Northwestern Medicine study shows that after the human nose is experimentally blocked for one week, brain activity rapidly changes in olfactory brain regions. This change suggests the brain is compensating for the interruption of this vital sense. The brain activity returns to a normal pattern shortly after free breathing has been restored.
Previous research in animals has suggested that the olfactory system is resistant to perceptual changes following odor deprivation. This new paper focuses on humans to show how that's possible. The study is published in the journal Nature Neuroscience.
"You need ongoing sensory input in order for your brain to update smell information," said Keng Nei Wu, the lead author of the paper and a graduate student in neuroscience at Northwestern University Feinberg School of Medicine. "When your nostrils are blocked up, your brain tries to adjust to the lack of information so the system doesn't break down. The brain compensates for the lack of information so when you get your sense of smell back, it will be in good working order."
For the study, Wu completely blocked the nostrils of 14 participants for a week while they lived in a special low-odor hospital room. At night, participants were allowed to breathe normally while they slept in the room.
After the smell deprivation, researchers found an increase in activity in the orbital frontal cortex and a decrease of activity in the piriform cortex, two regions related to the sense of smell.
"These changes in the brain are instrumental in maintaining the way we smell things even after seven days of no smell," Wu said.
When unrestricted breathing was restored, people were immediately able to perceive odors. A week after the deprivation experience, the brain's response to odors had returned to pre-experimental levels, indicating that deprivation-caused changes are rapidly reversed.
Such a rapid reversal is quite different from other sensory systems, such as sight, which typically have longer-lasting effects due to deprivation. The olfactory system is more agile, Wu suggested, because smell deprivation due to viral infection or allergies is common.

This study also has clinical significance relating to upper respiratory infection and sinusitis, especially when such problems become chronic, at which point ongoing deprivation could cause more profound and lasting changes, Wu noted.
"It also implies that deprivation has a significant impact on the brain, rather than on the nose itself," Wu said. "More knowledge about how the system reacts to short-term deprivation may provide new insights into how to deal with this problem in a chronic context."
Other Northwestern authors include Bruce K. Tan, James D. Howard, David B. Conley and Jay A. Gottfried, the senior author. The research was supported by grants R01DC010014 and K08DC007653 from the National Institute on Deafness and Other Communication Disorders of the National Institutes of Health and grant M01-RR00048 from the National Center for Research Resources of the National Institutes of Health.

http://www.sciencedaily.com/releases/2012/08/120813074015.htm

Fruity Science Halves Fat in Chocolate

It may not make chocolate one of your five a day -- but scientists have found a way to replace up to 50 per cent of its fat content with fruit juice.

ScienceDaily - University of Warwick chemists have taken out much of the cocoa butter and milk fats that go into chocolate bars, substituting them with tiny droplets of juice measuring under 30 microns in diameter.
They infused orange and cranberry juice into milk, dark and white chocolate using what is known as a Pickering emulsion.
Crucially, the clever chemistry does not take away the chocolatey 'mouth-feel' given by the fatty ingredients. This is because the new technique maintains the prized Polymorph V content, the substance in the crystal structure of the fat which gives chocolate its glossy appearance, firm and snappy texture but which also allows it to melt smoothly in the mouth. The final product will taste fruity -- but there is the option to use water and a small amount of ascorbic acid (vitamin C) instead of juice to maintain a chocolatey taste.
Dr Stefan Bon from the Department of Chemistry at the University of Warwick was lead author on the study published in the Journal of Materials Chemistry. He said the research looked at the chemistry behind reducing fat in chocolate, but now it was up to the food industry to use this new technique to develop tasty ways to use it in chocolate.
Dr Bon said: "Everyone loves chocolate -- but unfortunately we all know that many chocolate bars are high in fat. "However it's the fat that gives chocolate all the indulgent sensations that people crave -- the silky smooth texture and the way it melts in the mouth but still has a 'snap' to it when you break it with your hand. "We've found a way to maintain all of those things that make chocolate 'chocolatey' but with fruit juice instead of fat. "Our study is just the starting point to healthier chocolate -- we've established the chemistry behind this new technique but now we're hoping the food industry will take our method to make tasty, lower-fat chocolate bars."
The scientists used food-approved ingredients to create a Pickering emulsion, which prevents the small droplets from merging with each other.
Moreover, their chocolate formulations in the molten state showed a yield stress which meant that they could prevent the droplets from sinking to the bottom. The new process also prevents the unsightly 'sugar bloom' which can appear on chocolate which has been stored for too long.
Thomas S. Skelhon, Nadia Grossiord, Adam R. Morgan, Stefan A. F. Bon. Quiescent Water-in-Oil Pickering Emulsions as a Route toward Healthier Fruit Juice Infused Chocolate Confectionary. Journal of Materials Chemistry, 2012; DOI: 10.1039/C2JM34233B

http://www.sciencedaily.com/releases/2012/08/120813074130.htm

'Harmless' Condition Shown to Alter Brain Function in Elderly

Leukoaraiosis, tiny areas in the brain that have been deprived of oxygen appearing as bright white dots on MRI scans, is not a harmless part of the aging process, but rather a disease that alters brain function in the elderly

ScienceDaily - Researchers at the Mayo Clinic say a common condition called leukoaraiosis, made up of tiny areas in the brain that have been deprived of oxygen and appear as bright white dots on MRI scans, is not a harmless part of the aging process, but rather a disease that alters brain function in the elderly. Results of their study are published online in the journal Radiology.
"There has been a lot of controversy over these commonly identified abnormalities on MRI scans and their clinical impact," said Kirk M. Welker, M.D., assistant professor of radiology in the College of Medicine at Mayo Clinic in Rochester, Minn. "In the past, leukoaraiosis has been considered a benign part of the aging process, like gray hair and wrinkles."
Leukoaraiosis, also called small vessel ischemia and often referred to as unidentified bright objects or "UBOs" on brain scans, is a condition in which diseased blood vessels lead to small areas of damage in the white matter

of the brain. The lesions are common in the brains of people over the age of 60, although the amount of disease varies among individuals.

"We know that aging is a risk factor for leukoaraiosis, and we suspect that high blood pressure may also play a role," Dr. Welker said.

Dr. Welker's team performed functional MRI (fMRI) scans on cognitively normal elderly participants recruited from the Mayo Clinic Study of Aging between 2006 and 2010. In 18 participants, the amount of leukoaraiosis was a moderate 25 milliliters, and in 18 age-matched control participants, the amount of disease was less than five milliliters.

The patients were imaged in an MRI scanner as they performed a semantic decision task by identifying word pairs and a visual perception task that involved differentiating straight from diagonal lines. fMRI is a special type of magnetic resonance imaging that measures metabolic changes in an active part of the brain.

Although both groups performed the tasks with similar success, the fMRI scans revealed different brain activation patterns between the two groups. Compared to members of the control group, patients with moderate levels of leukoaraiosis had atypical activation patterns, including decreased activation in areas of the brain involved in language processing during the semantic decision task and increased activation in the visual-spatial areas of the brain during the visual perception task.

"Different systems of the brain respond differently to disease," Dr. Welker explained. "White matter damage affects connections within the brain's language network, which leads to an overall reduction in network activity."

He pointed out that identifying leukoaraiosis in the brain is important, both for individual patients undergoing brain mapping for surgery or other treatments and for research studies.

For improved neurological health, Dr. Welker said efforts should be taken to prevent leukoaraiosis from occurring.

"Our results add to a growing body of evidence that this is a disease we need to pay attention to," he said. "Leukoaraiosis is not a benign manifestation of aging but an important pathologic condition that alters brain function."

Kirk Welker et al. Altered Functional MR Imaging Language Activation in Elderly Individuals with Cerebral Leukoaraiosis. Radiology, 2012 (in press)