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Little or no benefit from nutrient additions to vitamin waters and energy drinks

New study reveals nutrient content and on-package marketing are out of tune with dietary needs and conventional nutritional science

A new study by researchers working at the University of Toronto and Ryerson University investigated the nutritional benefits of novel beverages (vitamin waters, energy drinks, and novel juices) sold in Canadian supermarkets by assessing their micronutrient compositions. The findings were published today in the journal Applied Physiology, Nutrition, and Metabolism.

According to the study novel beverages sold in Canadian supermarkets revealed extensive nutrient enrichment.

On-package marketing highlighted nutritional attributes such as immune support and antioxidant properties, and some made claims related to specific nutrients.

In addition, nutrients were often juxtaposed with messages related to performance and emotional well-being, benefits that go beyond conventional nutritional science.

The study found extensive micronutrient additions at levels often well in excess of nutrient requirements. The most commonly found nutrients were vitamins B6, B12, C and niacin. With the exception of vitamin of C, young Canadian adults - the likely target group for these products - are already consuming enough of these nutrients to meet their needs.

Naomi Dachner, a researcher in Nutritional Science as the University of Toronto said, "While our findings suggest that consumers stand to reap little or no benefit from the nutrient additions in novel beverages, most products were being marketed as if they provided a unique benefit to the consumer through the nutrient additions."

After novel beverages began being regulated as foods instead of Natural Health Products, their labels changed to meet food labeling requirements, but there was relatively little change in their nutrient composition or marketing.

Dachner explained, "Most of the nutrients permitted for addition are allowable at levels well above nutrient requirements, and, the new guidance is not designed to steer manufacturers towards the addition of nutrients that would address existing nutrient inadequacies in the population."

"Novel beverages are now required to display Nutrition Facts tables which may facilitate comparisons between products, but this information will not enable consumers to differentiate potentially beneficial nutrient additions from others."

The study raises questions about what measures need to be taken to ensure that consumers of novel beverages are not misled or exposed to unnecessarily high nutrient loads with no potential benefit.

The article titled "An examination of the nutrient content and on-package marketing of novel beverages" was published online today at
http://www.nrcresearchpress.com/doi/abs/10.1139/apnm-2014-0252

http://www.eurekalert.org/pub_releases/2015-01/uoc--rim011215.php

Rise in mass die-offs seen among birds, fish and marine invertebrates

Review of 727 studies points to disease, biotoxicity and other stressors

BERKELEY - An analysis of 727 mass die-offs of nearly 2,500 animal species from the past 70 years has found that such events are increasing among birds, fish and marine invertebrates. At the same time, the number of individuals killed appears to be decreasing for reptiles and amphibians, and unchanged for mammals.

Such mass mortality events occur when a large percentage of a population dies in a short time frame. While the die-offs are rare and fall short of extinction, they can pack a devastating punch, potentially killing more than 90 percent of a population in one shot.

However, until this study, there had been no quantitative analysis of the patterns of mass mortality events among animals, the study authors noted.

"This is the first attempt to quantify patterns in the frequency, magnitude and cause of such mass kill events," said study senior author Stephanie Carlson, an associate professor at the University of California, Berkeley's Department of Environmental Science, Policy and Management.

The study, published today (Monday, Jan. 12) in the Proceedings of the National Academy of Sciences, was led by researchers at UC Berkeley, the University of San Diego and Yale University.

The researchers reviewed incidents of mass kills documented in scientific literature. Although they came across some sporadic studies dating back to the 1800s, the analysis focused on the period from 1940 to the present.

The researchers acknowledged that some of their findings may be due to an increase in the reporting of mass die-offs in recent decades.

But they noted that even after accounting for some of this reporting bias, there was still an increase in mass die-offs for certain animals.

Overall, disease was the primary culprit, accounting for 26 percent of the mass die-offs. Direct effects tied to humans, such as environmental contamination, caused 19 percent of the mass kills.

Biotoxicity triggered by events such as algae blooms accounted for a significant proportion of deaths, and processes directly influenced by climate -- including weather extremes, thermal stress, oxygen stress or starvation -- collectively contributed to about 25 percent of mass mortality events.

The most severe events were those with multiple causes, the study found.

Carlson, a fish ecologist, and her UC Berkeley graduate students had observed such die-offs in their studies of fish in California streams and estuaries, originally piquing their interest in the topic.

"The catastrophic nature of sudden, mass die-offs of animal populations inherently captures human attention," said Carlson. "In our studies, we have come across mass kills of federal fish species during the summer drought season as small streams dry up. The majority of studies we reviewed were of fish. When oxygen levels are depressed in the water column, the impact can affect a variety of species."

The study found that the number of mass mortality events has been increasing by about one event per year over the 70 years the study covered.

"While this might not seem like much, one additional mass mortality event per year over 70 years translates into a considerable increase in the number of these events being reported each year," said study co-lead author Adam Siepielski, an assistant professor of biology at the University of San Diego.

"Going from one event to 70 each year is a substantial increase, especially given the increased magnitudes of mass mortality events for some of these organisms. This study suggests that in addition to monitoring physical changes such as changes in temperature and precipitation patterns, it is important to document the biological response to regional and global environmental change.

The researchers highlighted ways to improve documentation of such events in the future, including the possible use of citizen science to record mass mortality events in real time.

"The initial patterns are a bit surprising, in terms of the documented changes to frequencies of occurrences, magnitudes of each event and the causes of mass mortality," said study co-lead author Samuel Fey, a postdoctoral fellow in ecology and evolutionary biology at Yale.

"Yet these data show that we have a lot of room to improve how we document and study these types of rare events."

Funding from the Environmental Protection Agency and the National Science Foundation helped support this research.

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Researchers identify key substance that protects against pre-term birth

Hyaluronon identified as a critical substance the body makes to protect against premature birth

DALLAS - Researchers at UT Southwestern Medical Center have identified hyaluronon (HA) as a critical substance made by the body that protects against premature births caused by infection. Pre-term birth from infection is the leading cause of infant mortality in many countries according to the World Health Organization. The findings of the study, recently published in the Journal of Clinical Investigation, are the first to identify the specific role that HA plays in the reproductive tract.

"We found that HA is required to allow the epithelial lining of the reproductive tract to serve as the first line of defense against bacterial infections," said senior author Dr. Mala Mahendroo, an Associate Professor in the Department of Obstetrics and Gynecology's Cecil H. and Ida Green Center for Reproductive Biology Sciences. "Because of this action, HA offers cervical protection against the bacterial infections that cause 25 to 40 percent of pre-term births in women."

Hyaluronon is a natural substance found in many tissues, and is both a lubricant and a beneficial component of eyes, joints, and skin. It has long been thought to play an essential role in increasing the cervix's flexibility during the birth process; however, the study, which was conducted using mouse models, showed that HA is not essential for increased cervical pliability during late pregnancy. Rather, the substance plays an important barrier role in epithelial cells of the lower reproductive tract and in so doing protects against infection-related pre-term birth.

The World Health Organization estimates that 1.09 million children under age 5 die from direct complications of being born prematurely, meaning before the 37th week of pregnancy.

Previous studies by UT Southwestern reproductive biology researchers showed that HA is present in both the cervix and cervical mucus of pregnant women. Next steps include determining the mechanism by which HA affects cervical protection against infection.

"This study demonstrates that HA plays a crucial role in the epithelial barrier as well as the cervix's mucus," said Dr. Yucel Akgul, first author of the study and research scientist in the Department of Obstetrics and Gynecology. "Our next step is to identify exactly how HA protects the cervix, which can have important clinical implications in the effort to reduce infection-mediated pre-term labor."

Other UT Southwestern researchers involved in the study include Dr. R. Ann Word, Professor of Obstetrics and Gynecology. Dr. Word holds the Mary Dees McDermott Hicks Chair in Medical Science.Credit: UT Southwestern

http://www.eurekalert.org/pub_releases/2015-01/lu-dvm011215.php

Do viruses make us smarter?

A new study from Lund University in Sweden indicates that inherited viruses that are millions of years old play an important role in building up the complex networks that characterise the human brain.

Researchers have long been aware that endogenous retroviruses constitute around five per cent of our DNA. For many years, they were considered junk DNA of no real use, a side-effect of our evolutionary journey.

In the current study, Johan Jakobsson and his colleagues show that retroviruses seem to play a central role in the basic functions of the brain, more specifically in the regulation of which genes are to be expressed, and when. The findings indicate that, over the course of evolution, the viruses took an increasingly firm hold on the steering wheel in our cellular machinery. The reason the viruses are activated specifically in the brain is probably due to the fact that tumours cannot form in nerve cells, unlike in other tissues.

"We have been able to observe that these viruses are activated specifically in the brain cells and have an important regulatory role. We believe that the role of retroviruses can contribute to explaining why brain cells in particular are so dynamic and multifaceted in their function. It may also be the case that the viruses' more or less complex functions in various species can help us to understand why we are so different", says Johan Jakobsson, head of the research team for molecular neurogenetics at Lund University.

The article, based on studies of neural stem cells, shows that these cells use a particular molecular mechanism to control the activation processes of the retroviruses. The findings provide us with a complex insight into the innermost workings of the most basal functions of the nerve cells. At the same time, the results open up potential for new research paths concerning brain diseases linked to genetic factors.

"I believe that this can lead to new, exciting studies on the diseases of the brain. Currently, when we look for genetic factors linked to various diseases, we usually look for the genes we are familiar with, which make up a mere two per cent of the genome. Now we are opening up the possibility of looking at a much larger part of the genetic material which was previously considered unimportant. The image of the brain becomes more complex, but the area in which to search for errors linked to diseases with a genetic component, such as neurodegenerative diseases, psychiatric illness and brain tumours, also increases".

http://www.eurekalert.org/pub_releases/2015-01/uom-rum011215.php

Researchers uncover more clues to how drug reverses obesity, diabetes, fatty liver disease

Promising drug for treatment of obesity and related metabolic disorders generates a new signal between fat cells and liver to improve sugar metabolism.

ANN ARBOR--Researchers at the University of Michigan have identified how a promising drug in clinical trials for the treatment of obesity and related metabolic disorders improves the metabolism of sugar by generating a new signal between fat cells and the liver.

In addition to illuminating how the drug, amlexanox, reverses obesity, diabetes and fatty liver disease, the findings suggest a new pathway for future treatments. The research was published Jan.12 in Nature Communications.

Investigators in the lab of Alan Saltiel, the Mary Sue Coleman Director of U-M's Life Sciences Institute, had previously discovered that this drug, which had been used in the treatment of asthma, also has the ability to cause weight loss and improve diabetes in obese mice.

The current study revealed that amlexanox exerts its effects through a specialized type of fat cell by increasing the level of a second messenger molecule called cAMP. In turn, cAMP increases the rate by which cells "burn" fat so that the animal loses weight. But amlexanox also triggers the release of the hormone interleukin-6 from these fat cells, which then travels in the circulation to the liver. In the livers of diabetic mice, interleukin-6 reduces production of glucose, so that overall blood sugar is lowered.

"We know that amlexanox works to reverse obesity and insulin resistance in part by resolving chronic inflammation and increasing energy expenditure, but that's not the whole story of the drug's effects," said Shannon Reilly, first author of the study. "Understanding how the drug also enables crosstalk between fat cells and the liver in obese mice allows us to see more of the amlexanox picture--and also sheds light on communication between different tissues in the body."

The finding is the latest piece of a complex obesity-inflammation-diabetes puzzle that Saltiel lab investigators have been working to solve in order to find new treatments for metabolic disorders.

Obesity leads to a state of chronic, low-grade inflammation in liver and fat tissue, which in turn increases the levels of a pair of kinases: IKK-ε and TBK1. In 2009, the Saltiel lab defined a key role of IKK-ε and TBK1 in the onset of obesity. In 2013, the researchers discovered that amlexanox, an off-patent drug currently prescribed for the treatment of asthma and other uses, reversed obesity, diabetes and fatty liver in mice.

In research published in December 2013, the investigators found that high levels of IKK-ε and TBK1 meant that certain receptors in the fat cells of obese mice were unable to respond to neurotransmitters called catecholamines, which are generated by the sympathetic nervous system and promote "fat-burning." High levels of IKK-ε and TBK1 also resulted in lower levels of cAMP. Amlexanox reduces IKK-ε and TBK1, leading to higher cAMP, increased sensitivity to catecholamines and increased energy expenditure by the fat cells.

The U-M study explains how increased cAMP in fat cells promotes the secretion of the hormone interleukin-6, which signals the liver to stop producing glucose--thus improving overall blood sugar levels in obese diabetic mice.

Saltiel is also the John Jacob Abel Collegiate Professor in the Life Sciences and a professor of internal medicine and molecular and integrative physiology at the U-M Medical School. Other authors of the study were Louise Chang, Maeran Uhm, BreAnne Poirier, Danielle Krause and Xiaoling Peng of the U-M Life Sciences Institute; Maryam Ahmadian, Ruth Yu, Michael Downes and Ronald Evans of the Gene Expression Laboratory, Salk Institute for Biological Sciences; Christopher Liddle of the Gene Expression Laboratory, Salk Institute for Biological Sciences, and the Storr Liver Unit, Westmead Millennium Institute and University of Sydney, Westmead Hospital; Brian Zamarron of the U-M Program in Immunology; Evgenia Korytnaya, Adam Neidert and Elif Oral of the U-M Department of Internal Medicine, Metabolism, Endocrine and Diabetes Division; and Carey Lumeng of the U-M Department of Pediatrics and Communicable Diseases.

Support for the research was provided by the National Institutes of Health and the Leona M. and Harry B. Helmsley Charitable Trust.

http://www.eurekalert.org/pub_releases/2015-01/jhm-sms010815.php

Sound mind, strong heart: Same protein sustains both

Possible biochemical explanation for connection between mental and physical vitality

A Roman philosopher was the first to note the relationship between a sound mind and a sound body. Now the findings of a new Johns Hopkins study reveal a possible biochemical explanation behind this ancient observation.

The research, published ahead of print Jan. 12 in the Proceedings of the National Academy of Sciences, reveals that a protein already known to act as a natural antidepressant, enhance learning and memory, power nerve cell growth, and nourish blood vessels is also a central player in maintaining heart muscle vitality. The team's experiments, conducted in mice and lab-grown heart cells, show this multi-tasking protein, a nerve-growth factor called BDNF (brain-derived neurotrophic factor), helps sustain the ability of heart muscle cells to contract and relax properly. The results reveal that either BDNF deficiency or cell insensitivity to BDNF's presence can precipitate heart muscle dysfunction, particularly under conditions of chronic or repeated physical stress on the heart, such as endurance training or high blood pressure. Specifically, the researchers tracked BDNF's role in a cascade of molecular signaling events in heart cells, the disruption of which led to heart muscle failure.

If confirmed in humans, the research team says, the findings could pave the way to new treatments for certain forms of heart failure, a disorder that affects nearly 6 million Americans and more than 23 million people worldwide.

In addition, because of BDNF's well-known antidepressant effects and its role as a booster of nerve cell health, the research teams says the results suggest a possible biochemical link between depression and heart disease, two disorders that tend to occur in concert but whose relationship remains poorly understood.

"Our results are not only a vivid reminder of the astounding complexity of the heart's chemistry and physiology, but also a striking example of the ability of a single protein to act on multiple fronts and affect many organs and functions," says lead investigator Ning Feng, M.D., Ph.D., a cardiology fellow at the Johns Hopkins University School of Medicine.

The findings also can help clarify the biological means behind recent -- and unexplained observations -- that heart failure patients whose cardiac function worsens during physical exertion have low levels of BDNF in the blood.

"Our observation that BDNF directly controls the ability of heart muscle cells to 'beat' properly offers one possible explanation behind the declining cardiac function seen in people with heart failure, especially during exercise," says senior author Nazareno Paolocci, M.D., Ph.D., assistant professor of medicine at the Johns Hopkins University School of Medicine.

In an initial set of experiments, the scientists isolated cardiac cells from rodents with either normal or failing hearts in a lab dish and exposed the cells to BDNF. The normal heart cells responded by contracting and relaxing vigorously in the presence of BDNF, a phenomenon marked by peaks of contraction-triggering calcium flow into the cells. However, cells obtained from failing hearts, even when awash in BDNF, responded weakly or not at all. To determine why, the team homed in on BDNF's receptor, a molecule called TrkB, located on the surface of cells and responsible for receiving BDNF's chemical signals and transmitting them inside the cell. Compared with cardiac cells from mice with normal hearts, the failing heart cells had a slightly different version of the TrkB receptor, one that produces less of a catalyst protein responsible for triggering critical signaling inside the cardiac cell. This slightly sub-performing version of the receptor was less responsive to BDNF, rendering the heart cell less sensitive to it. While this TrkB variant is fairly common and does not necessarily portend disease, it may render the heart cells of those who carry the altered version less capable of using BDNF, the researchers say. Mice engineered to lack TrkB

receptors in their heart cells developed impaired cardiac function. Their hearts contracted poorly, pumped blood less efficiently and took longer to relax after each beat.

"Taken together, these findings show that any abnormality in the way BDNF communicates with its receptor appears to unlock a cascade of chemical glitches that eventually leads to poor cardiac function," Feng says.

The investigators say that disruptions in proper BDNF-TrkB signaling can even explain what drives chemotherapy-induced heart failure, a serious and well-established side effect of certain cancer treatments. Such treatments include chemicals that block multiple growth-factor receptors, TrkB among them, to halt tumor growth. And while this approach is critical to stave off cancer progression, it can also inadvertently lead to heart failure by interfering with the ability of cardiac cells to respond to the BDNF circulating in the body.

Another important finding, the researchers say, is that mice with missing BDNF receptors remained sensitive to adrenaline, the neurotransmitter released during fight-or-flight situations to infuse the heart with extra energy needed for peak cardiac performance during bouts of intense physical or emotional activity. The finding, the scientists say, means that BDNF affects cardiac function independently and separately from adrenaline by providing continuous, low-level fuel for heart contraction under normal conditions or prolonged periods of slightly elevated cardiac output, such as endurance training.

"Just like a constant low flame can keep a pot on slow simmer, constant levels of BDNF seem to maintain heart muscle vitality," Paolocci says.

The researchers point out that low levels of BDNF by themselves may not be enough to cause immediate heart disease, but chronic BDNF deficiency or insensitivity, compounded by additional physiologic or pathologic stressors, is a main culprit in fueling the disease.

"In the absence of chronic stressors, such as hypertension or an elevated workload of the heart muscle, BDNF deficiency may not cause full-blown disease, but it could be the proverbial straw that leads to a 'broken heart,'" Paolocci says.

The research was funded in part by the American Heart Association under grant number GRNT17070027 and by the National Institutes of Health under grant number T32HL-0227, with additional funding support from the Magic That Matters Fund of the Division of Cardiology at Johns Hopkins.

Other investigators involved in the research included Sabine Huke, Guangshuo Zhu, Carlo Tocchetti, Sa Shi, Takeshi Aiba, Nina Kaludercic, Donald Hoover, Sarah Beck, Joseph Mankowski, Gordon Tomaselli, Donald Bers and David Kass.

http://www.eurekalert.org/pub_releases/2015-01/uoc--hm011215.php

Hybrid 'super mosquito' resistant to insecticide-treated bed nets

Interbreeding of two malaria mosquito species in the West African country of Mali has resulted in a "super mosquito" hybrid that's resistant to insecticide-treated bed nets.

"It's 'super' with respect to its ability to survive exposure to the insecticides on treated bed nets," said medical entomologist Gregory Lanzaro of UC Davis, who led the research team. The research, published Jan. 6 in the Proceedings of the National Academy of Sciences, "provides convincing evidence indicating that a man-made change in the environment -- the introduction of insecticides -- has altered the evolutionary relationship between two species, in this case a breakdown in the reproductive isolation that separates them," said Lanzaro, who is director of the Vector Genetics Laboratory and professor in the Department of Pathology, Microbiology and Immunology in the School of Veterinary Medicine.

"What we provide in this new paper is an example of one unusual mechanism that has promoted the rapid evolution of insecticide resistance in one of the major malaria mosquito species." Anopheles gambiae, a major malaria vector, is interbreeding with isolated pockets of another malaria mosquito, A. coluzzii. Entomologists initially considered them as the "M and S forms" of Anopheles gambiae. They are now recognized as separate species. Interbreeding of two malaria mosquito species in the West African country of Mali has resulted in a "super mosquito" hybrid that's resistant to insecticide-treated bed nets.

"It's 'super' with respect to its ability to survive exposure to the insecticides on treated bed nets," said medical entomologist Gregory Lanzaro of UC Davis, who led the research team. "What we provide in this new paper is an example of one

unusual mechanism that has promoted the rapid evolution of insecticide resistance in one of the major malaria mosquito species."

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The insecticide resistance came as no surprise. "Growing resistance has been observed for some time," Lanzaro said. "Recently it has reached a level at some localities in Africa where it is resulting in the failure of the nets to provide meaningful control, and it is my opinion that this will increase."

Lanzaro credits insecticide-treated nets with saving many thousands, probably tens of thousands of lives in Mali alone. The World Health Organization's World Malaria Report indicates that deaths from malaria worldwide have decreased by 47 percent since 2000. Much of that is attributed to the insecticide-treated bed nets. However, it was just a matter of time for insecticide resistance to emerge, medical entomologists and epidemiologist agree.

Now there's "an urgent need to develop new and effective malaria vector control strategies," Lanzaro said. A number of new strategies are in development, including new insecticides, biological agents -- including mosquito-killing bacteria and fungi -- and genetic manipulation of mosquitoes aimed at either killing them or altering their ability to transmit the malaria parasite.

First author on the paper is Laura Norris, a postdoctoral scholar in the UC Davis Department of Entomology and Nematology who was supported by a National Institutes of Health training grant awarded to Lanzaro. She has since accepted a position with the President's Malaria Initiative in Washington, D.C.

Other co-authors include, at UC Davis, Anthony Cornel, Yoosook Lee, Bradley Main and Travis Collier; and Abdrahamane Fofana of the Malaria Research and Training Center at the University of Bamako, Mali. Three grants from the National Institutes of Health funded the research.

http://www.eurekalert.org/pub_releases/2015-01/pfan-bw011215.php

$375 billion wasted on billing and health insurance-related paperwork annually: Study

Medical billing paperwork and insurance-related red tape cost the U.S. economy approximately $471 billion in 2012, 80 percent of which is waste due to the inefficiency of the nation's complex, multi-payer way of financing care, a group of researchers say.

The researchers - physicians and health policy researchers with ties to the University of California, San Francisco, the City University of New York School of Public Health, and Harvard Medical School - note that a simplified, single-payer system of financing health care similar to Canada's or the U.S. Medicare program could result in savings of approximately $375 billion annually, or more than $1 trillion over three years.

Such savings could be used to cover everyone who is currently uninsured and to upgrade coverage for the tens of millions of Americans who now have inadequate policies with no increase in national health spending, they say. The four-member research team reports its findings in the peer-reviewed journal BMC Health Services Research. Their article was published in final form this week.

Aliya Jiwani, the article's lead author, said, "Our team reviewed and combined all existing studies of the costs of billing and insurance-related administrative tasks across multiple health care sectors.

"Using a standard definition of 'billing and insurance-related costs,' or what we call BIR, we found that physician practices spent about $70 billion in 2012 on bureaucratic paperwork. Hospitals spent an estimated $74 billion on BIR, and other institutions, such as nursing homes, home health care agencies, prescription drug and medical supply companies, spent an estimated $94 billion on these money-chasing tasks. She continued: "Private insurers spent $198 billion on BIR, whereas public insurers, e.g. Medicare and other government-sponsored programs, spent $35 billion on such activities.

"Most significant," Jiwani said, "is our finding that were the U.S. to adopt a simplified health care financing system - either along the lines of Canada's system or our Medicare program - 80 percent of those itemized expenditures would disappear. That's how much administrative waste is embedded in our fragmented, dysfunctional system of paying for care."

Jiwani, who obtained her master's degree from Yale and is currently pursuing doctoral studies in public health at George Washington University, said that necessary administrative tasks such as patient scheduling and writing chart notes were excluded from the BIR totals.

Senior author Dr. James G. Kahn, who teaches and conducts health economics research at the Philip R. Lee Institute for Health Policy Studies at UC San Francisco, said that the study is the first scientific article to provide a comprehensive portrayal of the costs of BIR in the U.S. health care system. "Synthesizing costing data on BIR costs from existing studies, using a uniform yardstick for defining BIR, and comparing those results with costs in simplified insurance systems in other countries, we see the true magnitude of administrative bloat in U.S. health care," he said.

Kahn continued: "Money spent on such unnecessary bureaucratic tasks is money that could and should be spent on patient care. "The potential savings of adopting a single-payer system is striking: at least $375 billion annually," he said. "Such a

system would enjoy powerful economies of scale, sharply reduce the burdens of claims processing, and obviate the need for marketing, advertising and underwriting expenses. Our nation's patients, our physicians, and the U.S. economy all stand to gain from such a shift."

The two other team members, Dr. David U. Himmelstein and Dr. Steffie Woolhandler, are practicing internists who teach and conduct health services research at CUNY's School of Public Health at Hunter College and who lecture in medicine at Harvard Medical School. They are co-founders of Physicians for a National Health Program.

Billing and insurance-related administrative costs in United States' health care: synthesis of micro-costing evidence. Aliya Jiwani, M.P.H., David U. Himmelstein, M.D., Steffie Woolhandler, M.D., M.P.H., James G. Kahn, M.D. BMC Health Services Research, 2014, 14:556 doi:10.1186/s12913-014-0556-7.

A PDF of the full article is available here: http://www.biomedcentral.com/content/pdf/s12913-014-0556-7.pdf

http://www.eurekalert.org/pub_releases/2015-01/ssoe-sco010915.php

Social cost of climate change too low, Stanford scientists say

The 'social cost' of carbon dioxide emissions may not be $37, as previously estimated by a recent US government study, but $220.

The economic damage caused by a ton of CO2 emissions-often referred to as the "social cost of carbon-could actually be six times higher than the value that the United States uses to guide current energy regulations, and possibly future mitigation policies, Stanford scientists say.

A recent U.S. government study concluded, based on the results of three widely used economic impact models, that an additional ton of CO2 emitted in 2015 would cause US$37 worth of economic damages. These damages are expected to take various forms, including decreased agricultural yields and harm to human health related to climate change.

But according to a new study, published online this week in the journal Nature Climate Change, the actual cost could be much higher. "We estimate that the social cost of carbon is not $37, as previously estimated, but $220," said study coauthor Frances Moore, a PhD candidate in the Emmett Interdisciplinary Program in Environment and Resources in Stanford's School of Earth Sciences. Based on the findings, countries may want to increase their efforts to curb greenhouse gas emissions, said study coauthor Delavane Diaz, a PhD candidate in the Department of Management Science and Engineering. "If the social cost of carbon is higher, many more mitigation measures will pass a cost-benefit analysis," Diaz said. "Because carbon emissions are so harmful to society, even costly means of reducing emissions would be worthwhile."

For their study, Moore and Diaz modified a well-known model for calculating the economic impacts of climate change, known as an integrated assessment model, or IAM. Their alternative formulation incorporated recent empirical findings suggesting that climate change could substantially slow economic growth rates, particularly in poor countries.

IAMs are important policy tools. Because they include both the costs and benefits of reducing emissions, they can inform governments about the optimal level of investment in emission reduction. The U.S. Environmental Protection Agency, for example, uses the $37 average value from three IAMs to evaluate greenhouse gas regulations. Canada, Mexico, the United Kingdom, France, Germany and Norway have also used IAMs to analyze climate and energy policy proposals.

While useful, IAMs have to make numerous simplifying assumptions. One limitation, for example, is that they fail to account for how the damages associated with climate change might persist through time. "For 20 years now, the models have assumed that climate change can't affect the basic growth-rate of the economy," Moore said. "But a number of new studies suggest this may not be true. If climate change affects not only a country's economic output, but also its growth, then that has a permanent effect that accumulates over time, leading to a much higher social cost of carbon."

In the new study, Moore and Diaz took a widely used IAM, called the Dynamic Integrated Climate-Economy (DICE) model, and modified it in three ways: they allowed climate change to affect the growth rate of the economy; they accounted for adaptation to climate change; and they divided the model into two regions to represent high- and low-income countries.

"There have been many studies that suggest rich and poor countries will fare very differently when dealing with future climate change effects, and we wanted to explore that," Diaz said.

One major finding of the new study is that the damages associated with reductions in economic growth rates justify very rapid and very early mitigation that is sufficient to limit the rise of global temperature to two degrees Celsius above pre-industrial levels. This is the target that some experts say is necessary to avert the worst effects of global warming.

"This effect is not included in the standard IAMs," Moore said, "so until now it's been very difficult to justify aggressive and potentially expensive mitigation measures because the damages just aren't large enough."

The pair's IAM also shows that developing countries may suffer the most from climate change effects. "If poor countries become less vulnerable to climate change as they become richer, then delaying some emissions reductions until they are more fully developed may in fact be the best policy," Diaz said. "Our model shows that this is a major uncertainty in mitigation policy, and one not explored much in previous work."

The pair notes two important caveats to their work, however. First, the DICE model's representation of mitigation is limited. It doesn't take into account, for example, the fact that low-carbon technologies take time to develop and deploy. Secondly, while it explores the effects of temperature on economic growth, the model does not factor in the potential for mitigation efforts to also impact growth. "For these two reasons, the rapid, near-term mitigation level found in our study may not necessarily be economically optimal", Diaz said. "But this does not change the overall result that if temperature affects economic growth-rates, society could face much larger climate damages than previously thought, and this would justify more stringent mitigation policy."

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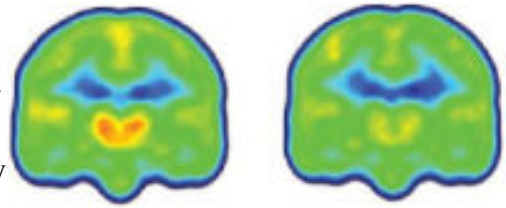
Imaging study finds first evidence of neuroinflammation in brains of chronic pain patients

First evidence of neuroinflammation in key regions of the brains of patients with chronic pain

A new study from Massachusetts General Hospital (MGH) investigators has found, for the first time, evidence of neuroinflammation in key regions of the brains of patients with chronic pain. By showing that levels of an inflammation-linked protein are elevated in regions known to be involved in the transmission of pain, the study published online in the journal Brain paves the way for the exploration of potential new treatment strategies and identifies a possible way around one of the most frustrating limitations in the study and treatment of chronic pain - the lack of an objective way to measure the presence or intensity of pain.



Images created by averaging PET scan data from chronic pain patients (left) and healthy controls (right) reveals higher levels of inflammation-associated translocator protein (orange/red) in the thalamus and other brain regions of chronic pain patients.
Marco Loggia, PhD, Martinos Center for Biomedical Imaging, Massachusetts General Hospital

"Finding increased levels of the translocator protein in regions like the thalamus - the brain's sensory gateway for pain and other stimuli - is important, since we know that this protein is highly expressed in microglia and astrocytes, the immune cells of the central nervous system, when they are activated in response to some pathologic event," says Marco Loggia, PhD, of the MGH-based Martinos Center for Biomedical Imaging, lead author of the report.

Demonstrating glial activation in chronic pain suggests that these cells may be a therapeutic target, and the consistency with which we found glial activation in chronic pain patients suggests that our results may be an important step towards developing biomarkers for pain conditions."

While numerous studies have clearly associated glial activation with persistent pain in animal models, none have previously documented glial activation in the brain of humans with chronic pain. The current study initially enrolled 19 patients with chronic lower back pain and 25 healthy control participants. In a subset of 10 patients and 9 pain-free controls - carefully selected from the initial larger group based on sex, age and genetic characteristics - brain imaging studies were conducted with one of the Martinos Center's integrated PET/MR scanners using a new radiopharmaceutical that binds to the translocator protein (TSPO). Loggia and colleagues found that the levels of the protein in the thalamus and other brain regions were significantly higher in patients than in controls.

The PET signal increases were so remarkably consistent across participants, Loggia notes, that it was possible to spot which were the patients and which were the controls just by looking at the individual images prior to detailed statistical analysis of the data.

Another interesting finding was that among patient participants, who had been asked to report their current levels of pain during the imaging session, those with the highest levels of TSPO had reported lower levels of pain. Loggia explains, "While upregulation of TSPO is a marker of glial activation, which is an inflammatory state, animal studies have suggested that the protein actually limits the magnitude of glial response after its initiation and promotes the return to a pain-free, pre-injury status. This means that what we are imaging may be the process of glial cells trying to 'calm down' after being activated by the pain. Those participants with less pain-related upregulation of TSPO may have a more exaggerated neuroinflammatory response that ultimately leads to more inflammation and pain. While larger studies would be needed to further support this interpretation, this evidence suggests that drugs called TSPO agonists, which intensify the action of TSPO, may benefit pain patients by helping to limit glial activation."

An assistant professor of Radiology at Harvard Medical School, Loggia notes that the ability to image glial activation could identify patients for whom the drugs targeting the process would be most appropriate. Future studies should investigate whether the same glial activation patterns are seen in patients with other forms of chronic pain or whether particular "glial signatures" may differentiate specific syndromes or pathologic mechanisms.

Additional co-authors of the Brain paper include senior author Jacob Hooker, PhD, and Bruce Rosen, MD, PhD, of the Martinos Center. Support for the study includes grants from the National Institute of Neurological Disorders and Stroke, National Center for Advancing Translational Science and the National Center for Research Resources.

http://www.eurekalert.org/pub_releases/2015-01/e-dop011315.php

Development of psychosis: Gray matter loss and the inflamed brain

Progressive reduction of cortical brain tissue thickness as psychosis develops

Philadelphia, PA, The thickness of cortical brain tissue progressively reduces as individuals develop psychosis, according to researchers of a large, multi-site study of young adults at clinical high risk.

Onset of psychosis typically occurs during the transition from adolescence to early adulthood, a period of time when the brain is also maturing. Brain tissue is commonly divided by its appearance on magnetic resonance imaging (MRI) into gray matter, the component of cortical tissue containing nerve cell bodies, and white matter, the component of cortical tissue containing the axons or projections from these nerve cell bodies.

Prior neuroimaging research has established that individuals who convert to psychosis have more rapid and more pronounced gray matter loss, compared to non-converters and healthy individuals. However, since the long-term effects of antipsychotic medications on cortical gray matter are not well understood and nearly all patients are treated with these medications, it has been difficult to distinguish the effects of antipsychotic drug treatment from the progression of schizophrenia.

Dr. Tyrone Cannon, Professor of Psychology and Psychiatry at Yale University, and his collaborators in the North American Prodrome Longitudinal Study Consortium have now provided important new insights into cortical changes associated with the development of psychosis. Their work is published in the current issue of Biological Psychiatry.

They conducted a longitudinal MRI study across 8 U.S. sites. They recruited 274 individuals at clinical high risk for psychosis and 135 healthy controls. Each participant received an initial (baseline) scan and a second scan either one year later or at the time of conversion to psychosis.

Thirty-five individuals ultimately converted to psychosis and they showed a steeper rate of thinning in prefrontal cortex compared with those who did not convert and the healthy control group. Importantly, this tissue loss was not explained by exposure to antipsychotic drugs.

"Because this differential rate of tissue loss was observed among subjects who had never been exposed to psychiatric drugs, we can conclude that the brain changes are part of the natural course of the disorder rather than being a consequence of treatment," explained Cannon.

Interestingly, the tissue loss observed in the converters was correlated with levels of proinflammatory cytokines in plasma, suggesting the presence of systemic neuroinflammation.

"The findings are also important in showing that markers of proinflammatory cytokines at the baseline assessment predicted the rate of gray matter loss among the individuals who converted to psychosis, suggesting that activation of microglia was involved in the tissue loss," he added. "This could mean that psychosis is associated with an abnormal acceleration in the processes underlying normal synaptic pruning during late adolescence/early adulthood, or that some kind of immune-related process is involved in psychosis onset, or both."

"Inflammation is increasingly recognized as a contributing factor to the emergence of progression of disease in every organ in the body," said Dr. John Krystal, Editor of Biological Psychiatry. "This report suggests that neuroinflammation may be a process that in some cases 'tips people over' from the at-risk state into psychosis."

The authors recommend that future work be conducted to evaluate whether inflammation precedes and perhaps even predicts such gray matter loss, or whether it is a consequence of such loss.The article is "Progressive Reduction in *Cortical Thickness as Psychosis Develops: A Multisite Longitudinal Neuroimaging Study of Youth at Elevated Clinical Risk" by Tyrone D. Cannon, Yoonho Chung, George He, Daqiang Sun, Aron Jacobson, Theo G.M. van Erp, Sarah McEwen, Jean Addington, Carrie E. Bearden, Kristin Cadenhead, Barbara Cornblatt, Daniel H. Mathalon, Thomas McGlashan, Diana Perkins, Clark Jeffries, Larry J. Seidman, Ming Tsuang, Elaine Walker, Scott W. Woods, and Robert Heinssen, on behalf of North American Prodrome Longitudinal Study Consortium (doi: 10.1016/j.biopsych.2014.05.023). The article appears in Biological Psychiatry, Volume 77, Issue 2 (January 15, 2015), published by Elsevier.*

http://bit.ly/1E9J5Ob

Time for a 'Completely Different' Haemophilia Treatment?

A promising therapy curtails clotting inhibitors rather than replacing proteins that promote blood clotting

Dec 16, 2014 |By Cassandra Willyard

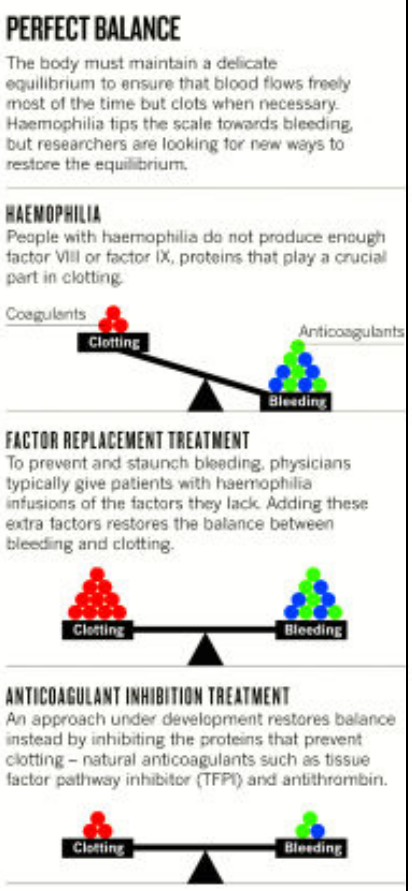
The control of blood clotting treads a fine line between promotion and inhibition. Kanjaksha Ghosh has seen more than a thousand people with haemophilia since he became a physician. But he has always wondered why some patients bleed spontaneously and develop crippling joint damage whereas others barely seem to be affected.

Ghosh, who heads the National Institute of Immunohaematology in Mumbai, India, remembers a soldier who had been fighting insurgents in the northeast of

the country. The man's brother was almost bedridden by haemophilia, but the soldier's symptoms were so mild that he did not even realize that he had the disease until he was shot on the battlefield.

In the 1990s, Ghosh began trying to work out why such discrepancies existed by studying families like the soldier's. When he delved into the genomes of those with a milder disease, he often saw not just a mutation in the affected clotting-factor gene, but also a mutation in another gene—the first causing haemophilia, the tendency to bleed, and the second causing thrombophilia, the tendency to clot. Ghosh's research leads to the conclusion that a patient with haemophilia who co-inherits a thrombophilic gene bleeds less than one without that mutation.

Blood coagulation is regulated by one set of proteins that causes clotting and another set that prevents it. Too little clotting ability leads to bleeding disorders. Too much leads to vessel-blocking clots that can cause strokes and heart attacks. Existing haemophilia treatments tip the balance towards clotting by adding what the body lacks—the clotting factor that is missing or defective. But natural human experiments such as Ghosh's soldier suggest an alternative strategy to treat the disease. Rather than boosting the factors that promote clotting, researchers might instead disable the anticoagulation machinery that prevents clotting.



In the past few years, three drug companies have moved compounds aimed at inhibiting anticoagulation into clinical trials. The hope is that these therapies will be as effective as existing treatments and much more convenient. Rather than receiving multiple infusions of protein replacement each week, patients might be able to control their bleeding with long-lasting injections.

Target practice

The complex cascade that results in the formation of a clot begins when a blood vessel is injured. Several proteins hold the process in check to prevent clots from forming where they are not needed. One such protein, tissue factor pathway inhibitor (TFPI), impedes the initiation of coagulation. Studies published over the past two decades suggest that blocking this protein can promote clotting, which could curb bleeding in people with haemophilia.

The Danish pharmaceutical company Novo Nordisk in Bagsvaerd began working on an antibody designed to inhibit TFPI in the 1990s. Its researchers showed that this antibody could speed up clot formation in blood plasma from people with haemophilia. They also found that it could shorten bleeding time and hasten clotting in rabbits with induced haemophilia. These results seemed promising, but Novo Nordisk began pursuing other strategies to treat haemophilia, and research to develop an anti-TFPI antibody was halted.

In 2006, Novo Nordisk decided to look for therapies that could be injected under the skin and revived the programme. By 2010, the company had launched a clinical trial in Europe and Asia to test the safety of an anti-TFPI monoclonal antibody called concizumab. The researchers administered the antibody either intravenously or subcutaneously to 28 healthy volunteers and 24 people with haemophilia. Preliminary results presented in 2013 at the International Society on Thrombosis and Haemostasis meeting in Amsterdam suggest that concizumab is safe, and that it can improve coagulation. Participants did not report any severe adverse events, although one of the healthy volunteers in the group receiving the highest dose of concizumab developed a small blood clot that disappeared on its own.

The company hopes to launch a second study in mid-2015 to determine the appropriate dose before moving on to test the efficacy of the treatment. “We have liked TFPI as a target for a long time,” says Ida Hilden, scientific director of Novo Nordisk's concizumab project.

Drug company Baxter International, based in Deerfield, Illinois, sells recombinant clotting factors for treating haemophilia and also has its sights on TFPI. In the same year that Novo Nordisk launched its concizumab trial, Baxter struck a deal to purchase a suite of haemophilia-related assets from the former therapeutics company Archemix. Those assets included a therapy designed to inhibit TFPI that had already entered a safety study in the United Kingdom. This therapy was an aptamer, a small strand of nucleotides designed to inhibit TFPI's activity by binding to it, much like an antibody.

The compound, known as BAX 499, performed well in animal studies but failed to deliver in humans. In 2012, Baxter halted the trial due to an increased number of bleeding events. The failure came as a shock. “We did extensive safety studies in monkeys,” says Fritz Scheiflinger, vice-president of research and innovation at Baxter BioScience in Vienna. “We gave huge amounts of aptamer over six months”, yet there were no signs that the compound was unsafe, he says.

Scheiflinger and his colleagues think that they now have an explanation for this strange effect. TFPI lasts no more than a couple of hours in the bloodstream, but BAX 499 has a longer half-life. When BAX 499 binds to TFPI, it allows the protein to persist for longer and, over time, to accumulate. And although the drug binds to TFPI, it does not completely deactivate it. So, as partially active TFPI piles up, the balance eventually tips from a pro-clotting effect to an anti-clotting effect. The problem seems to be confined to this particular compound, but nonetheless, the company has shifted its focus away from aptamers.

Baxter is now concentrating on peptides—short strings of amino acids that can be tailored to block part of the TFPI protein—a strategy that Scheiflinger and his colleagues first considered in 2005. The company has identified several promising candidates, but has not yet decided whether it will move them into clinical trials.

TFPI is not the only target for companies hoping to hamper the anticoagulant system. Alnylam Pharmaceuticals in Cambridge, Massachusetts, has set its sights on antithrombin—a protein produced by the liver that hinders clotting.

"Antithrombin is probably one of the most potent natural anticoagulants we have in the body," says Benny Sorensen, medical director of clinical research and development at Alnylam. But rather than inhibiting antithrombin's activity, the company plans to block its expression by using short strands of RNA to silence the messenger RNA that carries the code for antithrombin—an approach called RNA interference.

The company is testing its therapy, called ALN-AT3, in a safety study, and the initial results were presented at the World Federation of Haemophilia annual meeting in Melbourne, Australia, in May. After giving healthy volunteers a single low dose of the drug, expression of antithrombin was reduced by 28–32%—an outcome that Sorensen says left the researchers "very surprised". They had thought that it would take higher doses to achieve such a result.

But Sorensen believes that they can do even better. In that first phase, the researchers were not allowed to exceed a 40% reduction in antithrombin because of the safety risks to healthy volunteers. The next phase of the study will include people with haemophilia, and there will not be the same limitation. So the researchers plan to administer multiple doses of the drug. Sorensen thinks that if they can achieve a 50–80% reduction in antithrombin, ALN-AT3 may be able to control bleeding in people with haemophilia without infusions of clotting factor.

Cautious optimism

All of these therapies have one major advantage over protein replacement: antibodies, peptides and RNA can be effective even when injected under the skin, in part because they are so much smaller than the proteins used for factor-replacement therapy. Novo Nordisk envisages putting its antibody into a 'pen' like the one that people with diabetes use to administer insulin. This would be much more convenient than the intravenous infusions required for existing therapies. "Haemophilia patients are pestered from when they are one or two years old for the rest of their lives with intravenous injections," Sorensen says. "If we can achieve a correction of this haemostatic imbalance that would prevent spontaneous bleeds, then we've really offered an unbelievable change in the lives of these haemophilia patients."

If compounds such as concizumab and ALN-AT3 prove effective, they will undoubtedly be a boon for at least one group of people with haemophilia: those who develop inhibitory antibodies against the blood-clotting factors VIII and IX, and who can no longer receive this standard therapy. Roughly 5% of those with haemophilia B fall into this category, and 30% of those with haemophilia A (see page S12). Baxter, Novo Nordisk and Alnylam think that their products will appeal to other people with haemophilia. But whether these therapies will be safe and effective enough to replace infusions of clotting factor "is the million-dollar question", Scheiflinger says. Sorensen is the most optimistic. He speculates that a once-a-month dose of ALN-AT3 might control bleeding without the need for prophylactic infusions of clotting factor. Even if patients cannot completely forgo factor replacement, he adds, ALN-AT3 might allow them to use less, which could reduce the risk of developing inhibitors.

But many of the physicians who treat patients with haemophilia are not convinced. "The common thinking among haemophilia treaters is that these new strategies can never replace treatment with factor VIII and IX in non-inhibitor patients," says Erik Berntorp, a haematologist at Lund University in Malmö, Sweden. David Ginsburg, a geneticist at the University of Michigan, Ann Arbor, is equally cautious. "In the case of a genetic deficiency, it's pretty hard to improve on replacing the missing factor," he says.

Kenneth Mann, a biochemist at the University of Vermont in Burlington, does not doubt that blocking these anticoagulant pathways will increase the production of thrombin, a key protein in clotting, but he does not think that these therapies will necessarily work for everyone. People with haemophilia "are more heterogeneous than we'd like to admit," he says. And companies will have to work out how to stratify patients on the basis of their real bleeding risk to determine who will benefit from these new approaches. "I don't mean to throw a wet blanket on this," he says, "but caution is required."

One risk is that these therapies will work too well, tipping the balance towards clotting. In a person without haemophilia, Ginsburg says, a total lack of antithrombin "seems to be disastrous". Mice that lack either antithrombin or TFPI die in utero. Although the antithrombin-based therapies for haemophilia are not

designed to completely block their targets, “knocking them down is not without risk”, he says. And as the failure of BAX 499 shows, the risks posed by any new medication can be hard to predict.

Jakob Back, vice-president of the concizumab project at Novo Nordisk, understands the scepticism. Protein replacement has been the go-to therapy for haemophilia for decades. Concizumab and similar therapies represent “a completely different way of approaching haemophilia compared to anything we've been doing for the last 50 years”, he says. “We are moving into unknown territory.”

Cassandra Willyard is a freelance writer in Madison, Wisconsin.

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http://bit.ly/158Kf10

Human brains have a groovy feature that chimps' don't

Could a lopsided gap help set us apart from our primate cousins? Our brains and chimps' are built differently in the areas that give us our social skills and language.

20:00 12 January 2015 by Clare Wilson

The human brain has a 4.5-centimetre-long groove running deeper along the right side than the left. Chimp brains lack this asymmetry, as François Leroy of the French National Institute of Health and Medical Research in Saclay, and colleagues, have discovered. The groove's function is unknown, but its location suggests it played a role in the evolution of our communication abilities. "One day this will help us understand what makes us tick," says Colin Renfrew of the University of Cambridge, who was not involved in the study.

Although our brain is about three times the size of a chimp's, anatomical features that only the human brain possesses are surprisingly hard to find. One known difference is in a region called Broca's area, which is also involved in speech and is larger in humans than chimps.

The asymmetrical groove in humans was also known, but the new study, in which 177 people and 73 chimps had brain scans, revealed it is almost completely absent in the other primates.

Rejig on the right

In humans, the deeper groove lies in the right brain in the region that controls voice and face recognition and working out what other people are thinking – our so-called theory of mind. The shallower groove on the left is at the heart of the areas associated with language. The lack of symmetry could signify that tissue layers have been reorganised, says Leroy.

"Asymmetrical brain landmarks may be key features to understand what is so specific in our species," says Leroy, since left and right sides of the human brain tend to perform different tasks. "We think that [this asymmetry] is related to either speech or social cognition, which are both abilities for which humans outperform other primates."

Another avenue for research could be to look at which genes are active in forming this region in the developing embryos of primates, says Leroy.

Journal reference: PNAS, DOI: 10.1073/pnas.1412389112

http://www.medscape.com/viewarticle/837981

A First in Lung Cancer: Immunotherapy Improves Survival

Nivolumab shows survival advantage over chemotherapy in lung cancer

Zosia Chustecka

The immune checkpoint inhibitor nivolumab (Opvido, Bristol-Myers Squibb), which was recently approved for use in melanoma, has shown a survival advantage over chemotherapy in a pivotal trial in lung cancer. The trial (known as CheckMate 017) was stopped early due to benefit.

This is the first time that a survival advantage has been demonstrated in lung cancer with an immunomodulator drug, the company notes. It announced the top-line result of a superior overall survival in a press release, and says that clinical data will be presented at a forthcoming meeting.

The trial was conducted in 272 patients with advanced or metastatic squamous cell non-small cell lung cancer, and was open-label, randomizing patients to treatment with either nivolumab 3 mg/kg intravenously every 2 weeks or docetaxel 75 mg/m² intravenously every 3 weeks.

Pharmaceutical analysts reacting to the news speculate that the drug could be approved for use in lung cancer before the end of the year. The company has already filed for this indication in both the United States and Europe, and now says that it will "share" the new data with regulatory authorities.

Another check-point inhibitor is also making progress in lung cancer — pembrolizumab (Keytruda, Merck & Co). The company has announced that it is accelerating its development of the drug for use in lung cancer, and hopes to file for approval of this new indication by mid-year. Pembrolizumab is already marketed for use in melanoma. In fact, it beat nivolumab to the market to be the first program death inhibitor to become available in the United States, to the surprise of many analysts.

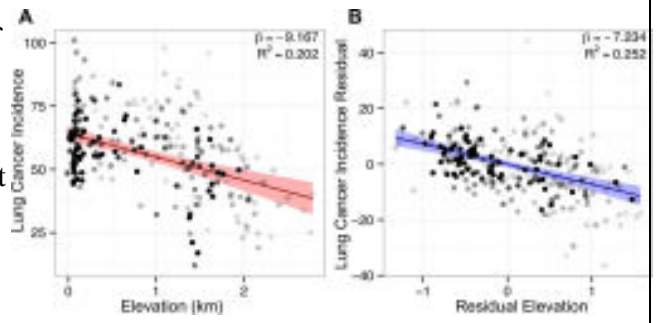
Early results with these immunomodulator drugs in lung cancer have been causing excitement at recent meetings, as previously reported by Medscape Medical News, leading one researcher to predict that "immunotherapy is heralding a new era of lung cancer treatment."

http://www.eurekalert.org/pub_releases/2015-01/p-cio010715.php

Can inhaled oxygen cause cancer?

Lung cancer rates fall dramatically with increasing elevation in the western US

The ancient physician/alchemist, Paracelsus, said: "The dose makes the poison." According to a new study published in PeerJ, even oxygen may fall prey to the above adage. While essential to human life, aspects of oxygen metabolism may promote cancer. Capitalizing on the inverse relationship of oxygen concentration with elevation, researchers found lower rates of lung cancer at higher elevations, a trend that did not extend to non-respiratory cancers, suggesting that carcinogen exposure occurs via inhalation.



In the left hand panel, lung cancer incidence is plotted against elevation for western US counties. Darker counties have higher populations and thus lower observational errors. The right hand panel shows the association when accounting for additional factors, such as smoking and education. **Simeonov and Himmelstein**

In the United States, lung cancer is responsible for 27% of all cancer deaths, claiming an estimated 160,000 lives per year [1]. While smoking is linked to as many as 90% of lung cancer cases, this new study suggests that atmospheric oxygen may play a role in lung carcinogenesis.

Oxygen is highly reactive and even when it is carefully and quickly consumed by our cells, it results in reactive oxygen species (ROS) which can lead to cellular damage and mutation. While oxygen composes 21% of the overall atmosphere, lower pressure at higher elevations results in less inhaled oxygen - an effect which notoriously frustrates athletes at high altitudes. For example, across United States counties, elevation differences account for a 34.9% decrease in oxygen from Imperial County, California (-11 m) to San Juan County, Colorado (3473 m).

To investigate whether inhaled oxygen could be a human carcinogen, two researchers compared cancer incidence rates across counties of the elevation-varying Western US. They found that as county elevation increased, lung cancer incidence decreased. The effect was dramatic with incidence decreasing by 7.23 cases per 100,000 individuals for every 1,000 meter (3,281 feet) rise in elevation, equating to approximately 13% of the mean lung cancer incidence of 56.8 cases per 100,000 individuals. A variety of statistical techniques attested that the association was not due to chance.

The observed association does not prove that oxygen causes lung cancer. The study looked at groups of people rather than individuals and many variables in addition to oxygen levels are correlated with elevation. Accordingly the researchers performed a thorough analysis to investigate confounding potentials. Their model accounted for important risk and demographic variables, such as smoking prevalence and education. The association was consistent across population subgroups, states, and models that included a range of additional factors.

The researchers also evaluated breast, colorectal, and prostate cancer: the remaining three most common cancers in the United States. Elevation's association with these non-respiratory cancers was either weak or absent, supporting the hypothesis of an inhaled risk factor. Furthermore, environmental correlates of elevation, such as sun exposure and fine particulate matter (a measure of pollution), produced vastly inferior predictions of lung cancer incidence compared to elevation itself.

Two past epidemiological reports, looking at elevation as a confounder, proposed that elevation-dependent oxygen variation was responsible for lower cancer mortality at high elevation [2, 3]. Unlike the two previous studies, the current study was specifically designed to assess the effect of elevation and benefited from a recent proliferation of high-quality county-level data. In total, the study relied on over 30 variables with sufficient coverage and precision to enable the inclusion of ~250 Western US counties. Using high resolution census data, the researchers calculated elevation values that reflected population dispersion within each county, thereby more accurately estimating the atmospheric exposure of each county's populace. All resources were public, underscoring the importance of open data for future scientific discovery.

The research was published today in the peer-reviewed open access journal PeerJ (http://peerj.com). Both authors are strong advocates for transparent science and open-access publishing and in addition to the full release of the dataset and analysis, the peer review history is also being made available by PeerJ---a nascent practice that is gaining popularity.

The authors hope additional researchers will focus their efforts on oxygen's role in human carcinogenesis. Analysis of diverse regions and individual-level datasets would contribute further epidemiological evidence. Ultimately, completely-controlled, experimental investigation using models of carcinogenesis will be critical to our understanding of the phenomenon.

If future analyses confirm oxygen-driven tumorigenesis, the medical implications could be large. For example, as the authors explain, "were the entire United States situated at the elevation of San Juan County, CO (3473 m), we estimate 65,496 fewer new lung cancer cases would arise per year." While the authors do not expect or recommend individuals to relocate based on this finding, identifying a universal and major risk factor could provide new insights into lung cancer etiology. From these insights, better treatments and preventative measures may arise.

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http://www.eurekalert.org/pub_releases/2015-01/f-ttt011315.php

Trust through the olfactory fragrance of lavender

Sellaro and her fellow researchers were the first to investigate whether the calming olfactory fragrance of lavender has a positive effect on mutual trust.

Aromatherapists already known that aromatic compounds can alter one's mood, cognitive, psychological or physical wellbeing. "Mutual trust is the social glue of society", says Sellaro. "Interpersonal trust is an essential element for social co-operation bargaining and negotiation."

Trust Game

To determine the effect of fragrances, the researchers exposed one group of test persons to the aroma of lavender, while a second group to the aroma of peppermint. Subsequently, the test persons played a trust game, a task that is often used to measure how much one test person trusts the other. A trustor was given 5 euros and was free to decide how much of that money he would give to a trustee in each round of the game. The trustor would then receive extra money, but only if the trustee gave him enough money in return. The money transferred to the trustee by the trustor served as an indicator of mutual trust.

Inexpensive way to increase trust

Test persons gave significantly more money to the other person when they were exposed to the aroma of lavender, compared to persons who had been exposed to the fragrance of peppermint.

Sellaro: "Our results might have various serious implications for a broad range of situations in which interpersonal trust is an essential element. Smelling the aroma of lavender may help a seller to establish more easily a trusting negotiation to sell a car, or in a grocery store it may induce consumers to spend more money buying products. The smell of lavender may also be helpful in sport psychology to enhance trust and build team spirit, for example in the case of team games such as soccer and volleyball."

1. Article title: A question of scent: lavender aroma promotes interpersonal trust
Journal: Frontiers in Psychology DOI: 10.3389/fpsyg.2014.01486
Authors: Roberta Sellaro, Wilco W. van Dijk, Claudia Rossi Paccani, Bernhard Hommel and Lorenza S. Colzato

http://www.eurekalert.org/pub_releases/2015-01/pp-dwo011315.php

Dinosaurs wiped out rapidly in Europe 66 million years ago

Dinosaurs flourished in Europe right up until the asteroid impact that wiped them out 66 million years ago, a new study shows.

The theory that an asteroid rapidly killed off the dinosaurs is widely recognized, but until recently dinosaur fossils from the latest Cretaceous--the final stanza of dinosaur evolution--were known almost exclusively from North America. This has raised questions about whether the sudden decline of dinosaurs in the American and Canadian west was merely a local story.

The new study synthesizes a flurry of research on European dinosaurs over the past two decades. Fossils of latest Cretaceous dinosaurs are now commonly discovered in Spain, France, Romania, and other countries.

By looking at the variety and ages of these fossils, a team of researchers led by Zoltán Csiki-Sava of the University of Bucharest's Faculty of Geology and Geophysics has determined that dinosaurs remained diverse in European ecosystems very late into the Cretaceous.

In the Pyrenees of Spain and France, the best area in Europe for finding latest Cretaceous dinosaurs, meat and plant-eating species are present and seemingly flourishing during the final few hundred thousand years before the asteroid hit.

Dr Csiki-Sava said "For a long time, Europe was overshadowed by other continents when the understanding of the nature, composition and evolution of latest Cretaceous continental ecosystems was concerned. The last 25 years witnessed a huge effort across all Europe to improve our knowledge, and now we are on the brink of fathoming the significance of these new discoveries, and of the strange and new story they tell about life at the end of the Dinosaur Era."

Dr Steve Brusatte of the University of Edinburgh's School of GeoSciences (UK), an author on the report, added: "Everyone knows that an asteroid hit 66 million years ago and dinosaurs disappeared, but this story is mostly based on fossils from one part of the world, North America. We now know that European dinosaurs were thriving up to the asteroid impact, just like in North America. This is strong evidence that the asteroid really did kill off dinosaurs in their prime, all over the world at once."

The new study is published in the open access journal ZooKeys. It reviews the fossil record of Late Cretaceous land-living vertebrates (including dinosaurs) from Europe and provides the most up-to-date survey of how these animals were changing in the run up to the asteroid impact.

Other authors on the paper include leading European paleontologists Eric Buffetaut from the Centre National de la Recherche Scientifique in Paris (France), Attila ?si from the MTA-ELTE Lendület Dinosaur Research Group in Budapest (Hungary), and Xabier Pereda-Suberbiola from the Universidad del País Vasco/Euskal Herriko Unibertsitatea in Bilbao (Spain).

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World's oldest butchering tools gave evolutionary edge to human communication

Scientists find Oldowan technology behind the genesis of language and teaching

Two and a half million years ago, our hominin ancestors in the African savanna crafted rocks into shards that could slice apart a dead gazelle, zebra or other game animal. Over the next 700,000 years, this butchering technology spread throughout the continent and, it turns out, came to be a major evolutionary force, according to new research from the University of California, Berkeley, the University of Liverpool and the University of St. Andrews, both in the UK.

Combining the tools of psychology, evolutionary biology and archaeology, scientists have found compelling evidence for the co-evolution of early Stone Age slaughtering tools and our ability to communicate and teach, shedding new light on the power of human culture to shape evolution.

To be reported Jan. 13 in the journal Nature Communications, the study is the largest to date to look at gene-culture co-evolution in the context of prehistoric Oldowan tools, the oldest-known cutting devices. It suggests communication among our earliest ancestors may be more complex than previously thought, with teaching and perhaps even a primitive proto-language occurring some 1.8 million years ago. "Our findings suggest that stone tools weren't just a product of human evolution, but actually drove it as well, creating the evolutionary advantage necessary for the development of modern human communication and teaching," said Thomas Morgan, lead author of the study and a postdoctoral researcher in psychology at UC Berkeley.

"Our data show this process was ongoing two and a half million years ago, which allows us to consider a very drawn-out and gradual evolution of the modern human capacity for language and suggests simple 'proto-languages' might be older than we previously thought," Morgan added.

Morgan and University of Liverpool archaeologist Natalie Uomini arrived at their conclusions by conducting a series of experiments in teaching contemporary humans the art of "Oldowan stone-knapping," in which butchering "flakes" are created by hammering a hard rock against certain volcanic or glassy rocks, like basalt or flint.

Oldowan stone-knapping dates back to the Lower Paleolithic period in eastern Africa, and remained largely unchanged for 700,000 years until more sophisticated Acheulean hand-axes and cleavers, which marked the next generation of stone tool technology, came on the scene. It was practiced by some of our earliest ancestors, such as Homo habilis and the even older Australopithecus garhi, who walked on two legs, but whose facial features and brain size were closer to those of apes.

In testing five different ways to convey Oldowan stone-knapping skills to more than 180 college students, the researchers found that the demonstration that used spoken communication - versus imitation, non-verbal presentations or gestures - yielded the highest volume and quality of flakes in the least amount of time and with the least waste.

To measure the rate of transmission of the ancient butchery technology, and establish whether more complex communication such as language would get the best results, study volunteers were divided into five- or 10-member "learning chains." The head of the chain received a knapping demonstration, the raw materials and five minutes to try their hand at it. That person then showed it to the next person in the chain, who in turn showed the next person, and so on. Their competence picked up significantly with verbal instruction.

"If someone is trying to learn a skill that has lots of subtlety to it, it helps to engage with a teacher and have them correct you," Morgan said. "You learn so much faster when someone is telling you what to do."

As for what the results mean for the Oldowan hominins: "They were probably not talking," Morgan said. "These tools are the only tools they made for 700,000 years.

So if people had language, they would have learned faster and developed newer technologies more rapidly."

Without language, one can assume that a hominin version of, say, Steve Jobs would have been hard-pressed to pass on visionary ideas. Still, the seeds of language, teaching and learning were planted due to the demand for Oldowan tools, the study suggests, and at some point hominins got better at communicating, hence the advent of Acheulean hand-axes and cleavers some 1.7 million years ago.

"To sustain Acheulean technology, there must have been some kind of teaching, and maybe even a kind of language, going on, even just a simple proto-language using sounds or gestures for 'yes' or 'no,' or 'here' or 'there,'" Morgan said.

Indeed, the data suggest that when the Oldowan stone-tool industry started, it was most likely not being taught, but communication methods to teach it were developed later.

"At some point they reached a threshold level of communication that allowed Acheulean hand axes to start being taught and spread around successfully and that almost certainly involved some sort of teaching and proto-type language," Morgan said.

In addition to Morgan and Uomini, co-authors and researchers on the paper are Luke E. Rendell, Sally E. Street, Hannah M. Lewis, Catherine P. Cross, Cara Evans, Ronan Kearney, Andrew Whiten and Kevin N. Laland, all at the University of St. Andrews in Scotland, Ignacio de la Torre at University College London and Laura Chouinard-Thuly at McGill University in Canada.

http://bit.ly/1EaeiRo

Some Microbes Can Eat And Breathe Electricity

How many ways can life exist? Some recently discovered microbes can live on a cathode, apparently without the need for a carbon food-source

By Marissa Fessenden

In New York State, when the snow melts, Oneida Lake starts collecting manganese. Combined with oxygen from the air, it makes manganese oxide which sinks into the lake bed. But, as Corey S. Powell reports for Popular Science, scientists didn't find the compound at levels they'd expect, and the mystery of the missing manganese oxide set Kenneth Nealson, a microbiologist, searching for a microbe that seemed like it shouldn't exist.

It took him a few years, but he found it—Shewanella oneidensis, a bacterium that lives off of a poisonous heavy metal, manganese.

Powell writes exactly why Shewanella is so odd:

For most living, air-breathing creatures, Nealson says, "The glucose that we eat supplies the electrons, the oxygen we breathe receives the electrons, and that electron flow is what runs our bodies." That's basic metabolism. The challenge for every organism is finding both sources of electrons and places to discard them in order to complete the circuit. Shewanella consumes electrons from carbohydrates, but it sheds them in an unusual way: "It swims up to the metal oxide and respires it." Nealson says. "We call this 'breathing rocks.' "

The bacterium grows special wires out of its membrane that transport electrons from inside the cell and deposit them on the heavy metal. Maganese oxide works, but so do other heavy metals like lead. Other discoveries revealed bacteria that are doing the reverse—they scavenge electrons from metal and minerals. The electron exchange completes that circuit. The result is life that eats and breathes electricity.

Moh El-Naggar, another researcher at USC, has produced videos that show these bacteria in action, growing those wire-like probes.

In 1988, when Nealson published his findings on Shewanella, it defied long-held assumptions about biology, to paraphrase Rebecca Fairley Raney's profile of Nealson at AAAS.org. But now we know that Shewanella and other microbes are important drivers in the way Earth cycles metals.

Still, it gets weirder. One of Nealson's graduate students, Annette Rowe, has found six new bacterial strains dredged from the ocean floor that don't need a source of carbon at all, reports Powell. They can live off of electricity alone.

All studies of life at the extremes on Earth show scientists what life might look like on other planets. Powell writes:

Scrounging for electrons and sprouting nanowires are strategies for surviving when there is not enough food to do much growing and competing—just enough to help an organism hunker down and keep the flame of life lit. Such conditions are common in deep ocean sediments and far underground. If life exists on Mars and other worlds (Europa? Titan?), there's a good chance that it, too, is huddled in resource-constrained settings far beneath the surface.

Future missions to detect traces of life on other planets may take the electron-gobbling bacteria into account. Nealson points out that on Earth, there is a gradient of electrical potential in the ground that decreases with depth. As you reach deeper, only electrons are available for food, so bacteria that live there adapt to eat electricity — thus setting up the gradient. To see that sign of life, all future missions would need to do is stick probes in the ground and measure it.

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Can Pigs Empathize?

Empathy can be hard enough to measure in humans, let alone in other animals

By Felicity Muth | January 13, 2015 |

There are a handful of traits that scientists and philosophers would argue would make us human, including self-awareness and language. Another key part of being human is thought to be our ability to empathize (although I sometimes find myself doubting some humans' abilities to empathize). I also doubt that we are the

only animal that has empathy. However, this can be tricky to test. If we define empathy as Franz de Waal does as ‘‘the capacity to be affected by and share the emotional state of another, assess the reasons for the other’s state and identify with the other, adopting his or her perspective’’ how would we go about testing this in a non-human animal?

Take, for example, pigs. We know that pigs are ‘intelligent’ animals (whatever that word really means) and that they feel emotions such as stress. They are also social animals, and so presumably if other animals do empathise with one another, then a pig might be a likely candidate.

Well, scientists at Wageningen University in the Netherlands recently carried out an experiment to determine whether pigs might empathise with each other as part of a larger study looking at a number of aspects of pig empathy. This question is particularly pertinent to farming practices, as pigs are often kept in close quarters with fellow pigs, many of which are likely to be stressed.

Pigs are social animals with complex emotions - but do they empathize?

To look at this, the researchers housed pigs in 16 groups of six. They then took two of the pigs from each of these groups and either trained them to anticipate that something good would happen, or that something bad would happen. They did this by playing the pigs some music and then either giving them a good experience (food) or a stressful experience (social isolation and handling) in a pen next door. The idea of this stage was to train pigs that the music predicted food or stress.

The researches then took two of the pig’s penmates (‘naïve’ pigs) and put them with the pig that had either been trained to one of these two things. All the pigs were then played the music that held meaning to the trained pigs (which, incidentally, was Bach or a military march). A few of the trained pigs showed that they learned what the music predicted for them, showing either ‘happy’ behaviours (play behaviour, wagging their tail and barking) or stress (standing ‘alert’, put their ears back, urinated and defecated). However, on the whole the trained pigs did not seem to anticipate what was ahead.

Despite this, the naïve pigs still experienced their penmates going into a neighbouring pen to experience something good or bad, even though they had never experienced this themselves. The researchers wanted to see if the naïve pigs would show ‘emotional contagion’ (sharing the emotional response someone else is having), as it is one key aspect of the ability to empathize. They found that the pigs did indeed react to the behaviour of the other pig: when a naïve pig was near a trained pig that was acting stressed, the naïve pig also became more alert and also put their ears back. This happened to a much greater degree than when naïve pigs were paired with pigs that acted ‘happy’. The researchers could be sure that the naïve pigs were reacting to the behaviour of the other pigs and not just the sound of the music because when they just played naïve pigs music this had no effect on their behaviour at all.

Now this experiment might seem cruel, as it both involved stressing pigs and showed that the stress of pigs likely affects other pigs. However, practices much worse than those used in the current experiment are common in pig farming, and without experiments like this investigating pig ‘emotion’ current practices are unlikely to change.

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http://www.eurekalert.org/pub_releases/2015-01/uos-psa011415.php

Potassium salts aid bone health and limit osteoporosis risk, new research finds

Potassium bicarbonate and citrate play an important part in improving bone health

Latest research from the University of Surrey has found that the potassium salts (bicarbonate and citrate) plentiful in fruit and vegetables, play an important part in improving bone health. For the first time, the results also showed that these potassium salts reduce bone resorption, the process by which bone is broken down, therefore increasing their strength.

The study, published in the journal Osteoporosis International, also revealed that high intake of potassium salts significantly reduces the excretion of calcium and acid in urine.

"This means that excess acid is neutralised and bone mineral is preserved," said lead author Dr Helen Lambert from the University of Surrey.

"Excess acid in the body, produced as a result of a typical Western diet high in animal and cereal protein, causes bones to weaken and fracture. Our study shows that these salts could prevent osteoporosis, as our results showed a decrease in bone resorption."

Although bone resorption and bone formation is a natural process, allowing bones to grow, heal and adapt, in osteoporosis, the balance is shifted so that more bone is broken down than is built up, leading to fragility and fractures.

The debilitating disease affects almost three million people in the UK. One in two women and one in five men over the age of 50 will break a bone because of poor bone health. This study shows that eating more fruits and vegetables could be a way to improve the strength of our bones and prevent osteoporosis.

http://www.eurekalert.org/pub_releases/2015-01/pu-mmb011315.php

Meteorite material born in molten spray as embryo planets collided

Asteroids may be a byproduct of planet formation rather than planetary building blocks, according to a recent paper in Nature.

WEST LAFAYETTE, Ind. -- Research done at Purdue University suggests collisions of planetary embryos - the seeds to the planets in our solar system that existed 4 billion years ago - could be the origin of the material that formed asteroids.

When part of an asteroid falls onto the Earth it is called a meteorite. For more than a century scientists have studied the tiny bead-like grains of solidified melted rock called "chondrules" found in meteorites, but the origin of these grains remained a mystery, said Jay Melosh, a distinguished professor of earth, atmospheric and planetary sciences at Purdue who was involved in the research.

"Understanding the origin of chondrules is like looking through the keyhole of a door; while we can't see all that is happening behind the door, it gives us a clear view of one part of the room and a glimpse into the very beginnings of our solar system," said Melosh, who also is a professor of physics and aerospace engineering. "We've found that an impact model fits extremely well with what we know about this unique material and the early solar system, and this suggests that, contrary to the current opinion among meteorite experts, asteroids are not leftover planet-building material and clumps of chondrules are not prerequisite to a planet."

Some in the field may not warmly receive the study, said David Minton, an assistant professor of earth, atmospheric and planetary science at Purdue who also was involved in the research.

"Chondrule-bearing meteorites have long been thought to be similar to the building blocks of planets," said Minton, who studies planet formation and migration and the dynamics and structure of small bodies. "This study suggests that instead chondrules might actually be byproducts of impacts between objects of an earlier generation, and meteorites may not be representative of the material that made planets."

The impact model for chondrules also resolves striking similarities observed between chondrules and materials created by impacts on the Earth and the moon, Melosh said.

"Chondrules are identical in size, shape and texture to spherules on Earth and spherules found in the lunar soil," Melosh said. "The only difference among chondrules, impact spherules and lunar soil particles is in their chemical composition, which fits because they are made of different starting materials from impacts on different bodies."

Impact spherules are small droplets of solidified molten rock found embedded in rocks on Earth. It is widely accepted that impacts created the spherules, which formed from droplets of molten rock in the plume of debris ejected when large asteroids crashed into the Earth. The droplets condensed and solidified to form the spherules, which then fell back to the surface creating a distinct layer on the Earth, he said.

Melosh is an expert in impact cratering and has studied spherules and developed methods to infer the size and velocity of the responsible asteroid from characteristics of the spherules and the spherule layer.

The method of chondrule creation proposed by the team is slightly different and focuses on a small portion of debris ejected at the earliest moments of impact created by a process called "jetting." Jetting occurs at the beginning of impact as the surfaces of the two objects meet. The rock caught in the pinch between the two colliding objects is compressed to high pressure and intensely heated, which is responsible for the initial bright flash seen in laboratory impacts. The heat created by jetting is enough to melt rock and create droplets in the ejected debris that could become chondrules, Melosh said.

Impact origin theories proposed in the past had been dismissed because they could not explain the melted material found in chondrules, he said.

In the early solar system, collision speeds were much lower than they are now. The planetary embryos were no larger than the Earth's moon and their collisions were relatively gentle, occurring at a speed of a few kilometers per second. For the most part, impacts at this speed would blast rock into broken fragments, but not melt it, he said.

"Jetting allows a low-velocity impact to melt a small quantity of the target rock," Melosh said. "The melted material, but not the broken rock, is then ejected at high speed, such that the molten droplets can escape their parent bodies and depart into space, to later loosely bunch together. Millions of years of additional impacts and other compression mechanisms then created the asteroids and meteorites we know today."

The debris ejected at high speed escapes the gravitational pull of the planetary embryo, while the majority of the debris plume falls back to the surface. The dust and molten droplets quickly slow to relatively low velocities due to the nebular gas in the early solar system. The gas provides a "soft catch" for the chondrules that allows them to accumulate into smaller bodies that eventually become asteroids, he said.

Chondrules have long been a puzzling feature of meteorites and, if they weren't observable in meteorites, scientists would likely never have predicted their existence, Minton said.

"Chondrules are incredibly abundant and so they must be telling us something important about what conditions were like in the early solar system when the planets were forming," he said. "We think collisions were common in the early solar system and that planets are built out of the collisions between smaller bodies, so an impact theory for the origin of chondrules fits well with what we know of how planets formed."

The study was led by Brandon Johnson, a graduate student under Melosh when the research began, who is now a postdoctoral researcher at the Massachusetts Institute of Technology. Maria Zuber, the E.A. Griswold Professor of Geophysics and vice president for research at the Massachusetts Institute of Technology, also is a co-author of the paper.

The NASA-funded research focused on chondrules found in most stony meteorites. Chondrite is the term for meteorites that contain chondrules, and encompasses 92 percent of all meteorites, according to statistics produced by Washington University in St. Louis based on data from the Meteoritical Bulletin Database.

The idea of impact jetting producing chondrules is not entirely new, and a study of the creation of chondrules from jetting of the impacts of centimeter-scale particles was published in 1975. However, this model failed to produce chondrules that would cool at the expected rate or have the correct volatile abundance, Johnson said.

The idea of chondrule formation by jetting during large-scale impacts wasn't considered earlier because it was unknown if impacts could produce melt droplets that were millimeters in size and had cooling rates similar to the observed chondrules, he said. In addition, it was thought that because jetting only involves a small percentage of the mass of the impacting body it would not be able to produce the abundance of chondrules seen in meteorites.

"Chondrules are some of the earliest solar system solids and clearly contain important information about conditions in the nascent solar system," Johnson said. "It is no surprise that these enigmatic particles have intrigued countless scientists over more than a century. What had been thought of as the missing pieces of an impact theory fall into place in this model." The team's model builds on an earlier study of impact jetting by Johnson, Melosh and Timothy Bowling, a graduate student in earth, atmospheric and planetary sciences at Purdue.

Minton created a computer simulation based on accepted hypotheses of solar system development that follows the formation and growth of planets and estimates the location, timing, sizes and velocities of chondrule-forming impacts. He used the simulation to model the early stage of planetary formation through the accumulation of smaller bodies called planetesimals.

The team also calculated the cooling rates of chondrules produced by the impacts and found that they matched the slow cooling that has been determined from analysis of the textures of chondrules in meteorites, Melosh said.

A paper detailing their methods and results will be published in an upcoming issue of Nature and will be made available online Thursday (Jan. 15).

The next step in the research may be to explore how this chondrule formation mechanism fits into a new model for the early stages of planet formation called "pebble accretion," in which the effect of gas drag from the protoplanetary nebula is important, Minton said.

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Lack of exercise responsible for twice as many deaths as obesity

A brisk 20 minute walk each day could be enough to reduce an individual's risk of early death, according to new research published today.

The study of over 334,000 European men and women found that twice as many deaths may be attributable to lack of physical activity compared with the number of deaths attributable to obesity, but that just a modest increase in physical activity could have significant health benefits.

Physical inactivity has been consistently associated with an increased risk of early death, as well as being associated with a greater risk of diseases such as heart disease and cancer. Although it may also contribute to an increased body mass index (BMI) and obesity, the association with early death is independent of an individual's BMI.

To measure the link between physical inactivity and premature death, and its interaction with obesity, researchers analysed data from 334,161 men and women across Europe participating in the European Prospective Investigation into Cancer and Nutrition (EPIC) Study. Over an average of 12 years, the researchers measured height, weight and waist circumference, and used self-assessment to measure levels of physical activity. The results are published today in the American Journal of Clinical Nutrition.

The researchers found that the greatest reduction in risk of premature death occurred in the comparison between inactive and moderately inactive groups, judged by combining activity at work with recreational activity; just under a quarter (22.7%) of participants were categorised as inactive, reporting no recreational activity in combination with a sedentary occupation. The authors estimate that doing exercise equivalent to just a 20 minute brisk walk each day -

burning between 90 and 110 kcal ('calories') - would take an individual from the inactive to moderately inactive group and reduce their risk of premature death by between 16-30%. The impact was greatest amongst normal weight individuals, but even those with higher BMI saw a benefit.

Using the most recent available data on deaths in Europe the researchers estimate that 337,000 of the 9.2 million deaths amongst European men and women were attributable to obesity (classed as a BMI greater than 30): however, double this number of deaths (676,000) could be attributed to physical inactivity.

Professor Ulf Ekelund from the Medical Research Council (MRC) Epidemiology Unit at the University of Cambridge, who led the study, says: "This is a simple message: just a small amount of physical activity each day could have substantial health benefits for people who are physically inactive. Although we found that just 20 minutes would make a difference, we should really be looking to do more than this - physical activity has many proven health benefits and should be an important part of our daily life."

Professor Nick Wareham, Director of the MRC Unit, adds: "Helping people to lose weight can be a real challenge, and whilst we should continue to aim at reducing population levels of obesity, public health interventions that encourage people to make small but achievable changes in physical activity can have significant health benefits and may be easier to achieve and maintain."

http://www.eurekalert.org/pub_releases/2015-01/wuso-dbc011415.php

Depression, behavioral changes may precede memory loss in Alzheimer's

Evidence that the depression and behavior changes that often accompany Alzheimer's disease may arise before memory losses begin

Depression and behavioral changes may occur before memory declines in people who will go on to develop Alzheimer's disease, according to new research at Washington University School of Medicine in St. Louis.

Researchers have known that many people with Alzheimer's experience depression, irritability, apathy and appetite loss but had not recognized how early these symptoms appear. Pinpointing the origins of these symptoms could be important to fully understanding Alzheimer's effects on the brain and finding ways to counteract them.

"There has been conflicting evidence on the relationship between Alzheimer's and depression," said senior author Catherine M. Roe, PhD, assistant professor of neurology. "We still don't know whether some of these symptoms, such as irritability and sadness, are due to people realizing on some level that they are having problems with memory and thinking, or whether these symptoms are caused directly by Alzheimer's effects on the brain." The study appears Jan. 14 in Neurology.

Roe and her colleagues at the university's Charles F. and Joanne Knight Alzheimer's Disease Research Center analyzed data on 2,416 people ages 50 and older. Scientists regularly evaluated the participants for up to seven years, including how they performed in extensive tests of mental function and psychological health. All of the participants were cognitively normal at the start, but over the course of the study, 1,218 of them developed dementia.

Those who developed dementia during the study were more likely to have mood and behavioral changes first. For example, four years into the study, 30 percent of those who would go on to develop dementia had developed depression. In comparison, after the same period of time, only 15 percent of those who did not develop dementia during the study had become depressed. In addition, those who would go on to develop dementia were more than 12 times as likely to have delusions than those who did not develop dementia.

Alzheimer's researchers have been working to develop markers they can use to diagnose disease before the onset of dementia. The hope is to begin treating the condition before patients develop dementia.

However, Roe cautioned that the mood changes will not work well as markers in this regard until researchers better understand how these changes are connected to the disease.

The research was funded by the Longer Life Foundation; the National Institute on Aging of the National Institutes of Health (NIH), grants P50 AG005681, P01 AG003991, P01 AG026276, U01 AG016976; Fred Simmons and Olga Mohan; the Farrell Family Research Fund; and the Charles and Joanne Knight Alzheimer's Research Initiative of the Washington University Knight Alzheimer's Disease Research Center.

Masters MC, Morris JC, Roe CM. "Noncognitive" symptoms of early Alzheimer disease. Neurology. Jan. 14, 2015.

http://www.eurekalert.org/pub_releases/2015-01/oup-dsa011315.php

Does screening asymptomatic adults for disease save lives?

New paper published online today in the International Journal of Epidemiology says that randomized controlled trials (the gold standard method of evaluation) show that few currently available screening tests for major diseases where death is a common outcome have documented reductions in disease-specific mortality.

Screening for disease is a key component of modern healthcare. However, several popular screening tests have met with controversy, with breast cancer screening for women aged 40-49 and prostate cancer screening in healthy men losing their endorsement in the United States.

Researchers from the Stanford School of Medicine evaluated evidence on 39 screening tests for 19 major diseases from 48 randomized controlled trials (RCTs) and 9 meta-analyses identified via the Cochrane Database of Systematic Reviews, and PubMed - to find out whether screening asymptomatic adults for major disease led to a decrease in disease-specific and all-cause mortality.

Randomized trials were available only for 19 tests on 11 diseases (abdominal aortic aneurysm, breast cancer, cervical cancer, colorectal cancer, hepatocellular cancer, lung cancer, oral cancer, ovarian cancer, prostate cancer, type 2 diabetes, and cardiovascular disease). The authors' show that there is evidence of a reduction in mortality in only 30% of the disease-specific mortality estimates and 11% of the all-cause mortality estimates from the randomised controlled trials they evaluated. In the case of disease-specific mortality, findings from the individual randomised controlled trials are backed up by evidence from 4 meta-analyses, but none of the 6 meta-analyses that included estimates of all-cause mortality produced evidence of a reduction in mortality.

Professor John Ioannidis, senior author on the paper, says: "Our comprehensive overview shows that documented reductions in disease-specific mortality in randomized trials of screening for major diseases are uncommon. Reductions in all-cause mortality are even more uncommon. This overview offers researchers, policy-makers, and health care providers a synthesis of RCT evidence on the potential benefits of screening and we hope that it is timely in the wake of recent controversies."

The researchers argue that randomised evidence should be considered on a case-by-case basis, depending on the disease, adding that screening is likely to be effective and justifiable for a variety of other clinical outcomes besides mortality. "However," they conclude, "our overview suggests that expectations of major benefits in terms of reductions in mortality from screening need to be cautiously tempered".

The International Journal of Epidemiology also publishes three commentaries on this paper online today. Peter G&ostroke;tzsche of the Nordic Cochrane Center in Copenhagen argues that although screening is popular and has "great public and political appeal", we must "demand much stronger evidence" that it is effective. Paul Shekelle of UCLA, makes the point that too much screening has been allowed to get into routine practice without adequate evaluation. However, he also points out that mortality is not the only outcome and patients may value screening tests that decrease the risk of serious morbidity. Paul Taylor of UCL is more circumspect in his commentary, stating that "the cautious tempering of expectations advised by Saquib, Saquib, and Ioannidis is prudent but shouldn't be overdone".

http://www.eurekalert.org/pub_releases/2015-01/acs-dc011415.php

DNA 'glue' could someday be used to build tissues, organs

DNA strands can also act as a glue to hold together 3-D-printed materials

DNA molecules provide the "source code" for life in humans, plants, animals and some microbes. But now researchers report an initial study showing that the strands can also act as a glue to hold together 3-D-printed materials that could someday be used to grow tissues and organs in the lab. This first-of-its-kind demonstration of the inexpensive process is described in the brand-new journal ACS Biomaterials Science & Engineering.

Andrew Ellington and colleagues explain that although researchers have used nucleic acids such as DNA to assemble objects, most of these are nano-sized -- so tiny that humans can't see them with the naked eye. Making them into larger, visible objects is cost-prohibitive. Current methods also do not allow for much control or flexibility in the types of materials that are created. Overcoming these challenges could potentially have a big payoff -- the ability to make tissues to repair injuries or even to create organs for the thousands of patients in need of organ transplants. With this in mind, Ellington's group set out to create a larger, more affordable material held together with DNA.

The researchers developed DNA-coated nanoparticles made of either polystyrene or polyacrylamide. DNA binding adhered these inexpensive nanoparticles to each other, forming gel-like materials that they could extrude from a 3-D printer. The materials were easy to see and could be manipulated without a microscope. The DNA adhesive also allowed the researchers to control how these gels came together. They showed that human cells could grow in the gels, which is the first step toward the ultimate goal of using the materials as scaffolds for growing tissues.

The authors acknowledge funding from the National Institutes of Health, the Welch Foundation and the National Science Foundation.

http://bit.ly/1zp7Qah

A Prescription for Drug Companies on Social Media

***Drug companies are struggling to find ways to legally engage with consumers on social media, reports* Nature Biotechnology.**

By Emily Waltz

There are strict rules about how drug manufacturers can advertise their products, but when it comes to online patient forums and social media comments, things get murky.

For instance, if a patient leaves a comment on a pharmaceutical company's YouTube video complaining about a rash, does that count as an adverse event that the company must report to federal regulators? What happens when participants in

a clinical trial use online forums to share information about their drug's effectiveness—could that mess up the study?

Guidance from the U.S. Food and Drug Administration (FDA) has been variously described as non-existent, unclear, and overbearing, and the uncertainty has forced some drug companies to shy away completely from social media. In fact, half of the 50 largest pharma companies are not actively engaged on social media, according to a report by the IMS Institute of Healthcare Information, *Nature Biotechnology* reports.

Among the companies that have wandered into the ring, some have gotten themselves into trouble. Zarbee's Naturals, a dietary supplement manufacturer that sells products for congestion, cough and allergies, got rebuked by the FDA for some of its tweets. Seemingly innocuous messages such as, "Try @Zarbees #naturalremedies for cold and cough season" and "RT@MomCentral have you tried #ZarbeesCough for cold and cough relief?" did not sit well with the FDA. The tweets suggest that the supplements are drugs—a no-no according to federal regulations. The company also caught flak from the agency for how it handled a consumer's comments on Facebook. Someone posted: "Love Zarbee's, this is the only medicine we use for our 2 year old. Colds and congestion clear up in 2 days." Zarbee's "liked" the comment—also a no-no, according to the warning letter FDA sent to the company.

One of the trickiest areas is "pharmacovigilance": the rules requiring drug manufacturers to tell the FDA about adverse events—side effects—reported by doctors, patients, or sales reps. "With social media, anybody can publicly complain in just 140 characters," says *Nature Biotechnology*. "It's not yet clear under what circumstances companies are supposed to be monitoring these reports, so many of them are choosing the simplest option: ignore."

Another tricky area is in clinical trials. Many trials are supposed to be kept blind, meaning that the patients and/or their doctors don't know if they are getting the drug or the placebo—a practice that prevents bias in the experiment. A couple of years ago, during a phase-two trial for an experimental drug for amyotrophic lateral sclerosis (ALS), patients unmasked the experiment by talking about their experiences online. Roughly 27 percent of the patients in the trial were active on PatientsLikeMe, an online forum that allows people to share and track their symptoms. When some of them mentioned an unusual side effect called neutropenia, it became obvious which patients had received the active drug.

The FDA released preliminary guidance documents in the summer of 2014 with the aim of clearing things up, but many in the industry say the documents are overbearing and vague, *Nature Biotechnology* reports. "The guidelines suggest," says the article, "that products with 'complex indications or extensive serious risks' should not be discussed at all in platforms with space limitations, such as Twitter."

Ten days after the guidance came out, the FDA did a curious thing. One of the agency's Twitter accounts, @FDA_Drug_Info, tweeted "#FDA approves #Afreeza to treat diabetes" with a link to further information about the drug's risks. But according to the FDA's guidelines, it's own tweet would get a drug company in hot water.

The public comment period on FDA's guidance documents has ended, but the agency has not given a timeline for when the final versions will be published.

http://bit.ly/1xinI8J

First Contracting Human Muscle Grown in a Lab

For the first time, researcher have grown human skeletal muscle in the lab that contracts and responds to electrical pulses and medicine just like living tissue.

Jan 14, 2015 12:05 PM ET // by Tracy Staedter

The tissue, created by Duke University biomedical engineering Nenad Bursac and postdoctoral researcher Lauran Madden, represents a entirely new, more humanlike medium in which to study disease and use for drug testing.

"One of our goals is to use this method to provide personalized medicine to patients," Bursac said in a press release.

"We can take a biopsy from each patient, grow many new muscles to use as test samples and experiment to see which drugs would work best for each person."

After working with cells for years, making bioartifical muscles from animal cells, the team turned to human cells.

They started with a sample of cells that were in a stage beyond the stem cell level, but hadn't yet fully developed into muscle cells.

The team grew these cells on a three-dimensional, suspended in a nourishing gel to keep them viable.

It took years to find the right combination of cell and nourishment, but the scientists were finally able to grow the cells to muscle fibers.

Next, Bursac and Madden tested the artificial muscle to see how closely it resembled living muscle. In a research first, the team showed that the muscle contracted in response to an electrical stimuli.

They also showed that the muscles responded to certain drugs the way real muscle does.

For example, statins, which are used to lower cholesterol, caused fat accumulations, and clenbuterol, which is an athletic performance enhancer, increased contractions in the artificial muscle as it would in real tissue.

The research appears in this week's eLife. See the video of the contracting muscle here.

http://bit.ly/1xEH86B

How The Code Of Life Passed Through Primitive Kinds Of Cells

Life's origins are a mystery, but every year scientists get a little bit closer to understanding what made life possible on Earth, and possibly on other planets or moons.

By Elizabeth Howell - Jan 15, 2015

We only have one known case study of life so far, on our own planet, but microbial life is considered possible in many other areas around the Solar System, such as on Mars, Jupiter's icy Europa, and on Enceladus, a moon of Saturn that erupts water as geysers.

While some researchers examine the environmental conditions that lead to life, others are more interested in the evolution of simple cells into more complex ones. One large wish of scientists these days is to create artificial cells that closely mimic what biological ones do so that it would be easy to create laboratory conditions to test out how they evolve.

One recent line of research involves protocells, which are a very early form of the cells that are common on Earth today. They don't have a nucleus, or most other elements of the modern cell, but they do contain lipids, which are molecules such as vitamins and fats. In biology, one function of lipids is to help form membranes that hold a cell together.

Researchers would be happy to create an artificial protocell, but that's far from easy. Figuring out how inheritance work — how traits of a parent protocell are passed on to the next generation — is one of the largest problems facing scientists today.

A new line of research examined how to create "information polymers," the instructions that tell cells how to divide and underlie their metabolism. The paper called, "Structure and selection in an autocatalytic binary polymer model," was published in July in the journal Europhysics Letters.

Replication issues

Harold Fellermann, a co-author of the paper, was with the Center for Fundamental Living Technology at the University of Denmark when he began the research, and is now with Newcastle University as a senior research associate of computer science. He works closely with the biology department on advancing nanotechnology and synthetic biology. "I'm very interested in the creative potential of nature," he said. "Nature in general seems to be fertile with creativity that outperforms any human imagination. We find solutions to problems in nature that no engineer would envision."

One example, Fellermann said, has to do with the information encoding that passes from a cell to its descendants. Today, we are most familiar with DNA and another nucleic acid called RNA that pass molecular information though the generations.

Back when scientists first were studying these processes, they believed that information only flows from DNA to RNA into proteins. More examination, however, showed that the information can go in more than one direction. Sometimes RNAs can be written back into DNAs, for example. Or a DNA strand can be reoriented by a protein, thereby changing the genetic program on the fly.

The complexity of inheritance was part of the difficulty that Fellermann and his team, joined by fellow coauthor Shinpei Tanaka of Hiroshima University, faced as they attempted to simulate information polymers in a computer simulation.

Additionally, the researchers had two more problems to face down.

Information polymers are actually molecules, which themselves are broken apart in water, a fundamental part of life as we know it. How to keep that string together without it dissolving was one question the researchers faced.

Another issue was replication. Cells today create copies of themselves using enzymes, which are the proteins that underpin complex reactions. (Another example of a complex reaction would be food digestion.) Protocells, the researchers suggested, could have used a process called ligation, which connects shorter molecular strings into longer ones, along with matching longer strings.

The researchers brought in a hypothesis from three decades ago that assumed that any sequence of polymers (chain of small molecules) can encode information, and can be copied from one polymer strand to another using a process called template directed replication.

This type of ligation could have occurred without the help of any enzymes.

"We basically went back to what Stuart Kauffman and other scientists wrote about in the 1980s, but assuming we don't have random interactions among our molecules," Fellermann said of replication. "We have certain templates that can replicate themselves by taking two complementary subsequences and then use a chemical reaction to bond the replication product."

Molecular ecology

When simulating information strings in the computer simulation, the researchers came up with a surprising discovery. Replication occurred as expected, with information strings duplicating themselves, but the scientists were surprised to see shorter and longer strings being created in strikingly regular patterns.

Since the researchers had not put the pattern into the program themselves, they concluded that the strings had to be creating the pattern themselves through their interactions. In other words, the strings created a network of molecules (called an autocatalytic network) whereby each molecule assists other ones with chemical

reactions. It's considered an early form of metabolism, which is the chemical processes required for life to occur.

"What happens is you have almost a molecular ecology," Fellermann said. "Every species and strand, they service each other's reactants and products and catalysts."

Over time, the simulation showed the information strings were occurring in equal proportions of long and short lengths in predictable patterns. While the scientists can't say for sure that this was a step along the road to life, they said it bears further investigation as they work to create artificial protocells.

The researchers checked carefully to make sure their computer simulations weren't at fault, running up to 5,000 simulations a week and also double-checking their work with a completely different system and thorough mathematical analysis.

"We found exactly the same behavior," Fellermann concluded.

Secondary structures

These fundamental processes are not dependent on which environment the protocell was in, Fellermann said. In a larger sense, this means that the protocells could be transmitting information in the same way, whether they are embedded in an acidic environment, trying to survive in a hot spring underwater, or in any variety of environments. This means the same process could work in extraterrestrial environments.

The next stage for the researchers will be to look at higher-order activity, Fellermann said, focusing on activity associated with RNA, a single-stranded nucleic acid.

The researchers will look at secondary structures — fundamental biological structures of biopolymers, such as nucleic acids and proteins — to better understand how RNA's role works.

"Often the chemical activity of RNA is attributed to secondary structures not taken into account with our study," Fellermann said. "We can say that we should look for the catalytic activity of very simple sequences of RNA structure. The simple sequences are the ones that could emerge even without having to rely on the specific secondary structure."

Fellermann's research, in general, not only has promise for understanding life, but also for creating more intelligent computers. The team speculates that their work could eventually underlie technological advances, such as self-repairing computers.

These biological-type machines could be useful in space exploration, such as in robotic colonies on the Moon, or assisting scientists in a future Mars landing party. With the ability to do repairs without the extra materials required from Earth, long-term space exploration could be made cheaper — as long as the technology is there to support it.

http://bit.ly/1IQI4NI

Google expects public in driverless cars in two to five years

The head of self-driving cars for Google expects real people to be using them on public roads in two to five years.

Chris Urmson says the cars would still be test vehicles, and Google would collect data on how they interact with other vehicles and pedestrians.

Google is working on sensors to detect road signs and other vehicles, and software that analyzes all the data.

The small, bulbous cars without steering wheels or pedals are being tested at a Google facility in California.

Urmson wouldn't give a date for putting driverless cars on roads en masse, saying that the system has to be safe enough to work properly.

He told reporters Wednesday at the Automotive News World Congress in Detroit that Google doesn't know yet how it will make money on the cars.

Urmson wants to reach the point where his test team no longer has to pilot the cars.

"What we really need is to get to the point where we're learning about how people interact with it, how they are using it, and how can we best bring that to market as a product that people care for," he said.

Google may face state regulatory hurdles depending on where it chooses to test the cars in public.

Under legislation that Google persuaded California lawmakers to pass in 2012, self-driving cars must have a steering wheel and pedals.

Several other states have passed laws formally allowing autonomous cars on public roads without that restriction.

The company in December announced that it had a fully functioning prototype that's been driving on its test track.

It hoped to see the cars on the road in northern California this year, but they would have to have safety drivers and temporary manual controls.

Google also confirmed that it has hired Roush Enterprises Inc., a Detroit-area company that designs and builds prototypes for the auto industry, to build 150 prototype Google autonomous cars.

Urmson said Google is making laser and other sensors for the cars smaller and less costly.

He predicted that the cars would fail at some point on public roads, but said Google's cars have been driven more than 700,000 miles on public roads without causing a crash.

http://www.eurekalert.org/pub_releases/2015-01/luhs-ut8011415.php

Up to 8 percent of South Asians carry gene mutation that causes heart attacks

Genetic defect in MYBPC3 gene leads to cardiac dysfunction

MAYWOOD, Il. - Up to 8 percent of people from India, Pakistan, Bangladesh and other South Asian countries carry a mutated gene that causes heart failure and potentially fatal heart attacks. A new study demonstrates how this gene mutation impairs the heart's ability to pump blood. Results could point the way to eventual treatments and prevention strategies for an estimated 55 million people of South Asian descent worldwide, including 200,000 people in the United States, who carry the potentially fatal mutation. The study, led by Sakthivel Sadayappan, PhD, MBA, of Loyola University Chicago Stritch School of Medicine, is published in the prestigious Journal of Biological Chemistry, a publication of the American Society for Biochemistry and Molecular Biology.

The mutation causes hypertrophic cardiomyopathy, the most common form of inherited cardiac disease and the leading cause of sudden cardiac death in young people. Previous studies by Dr. Sadayappan and other researchers have found that between 5 percent and 8 percent of South Asians carry the mutation. Carriers have about a 80 percent chance of developing heart failure after age 45. Dr. Sadayappan first reported the mutation in 2001 at the World Congress of the International Society for Heart Research, and has been studying it ever since. He said that, based on a report from one of his collaborators, the mutation likely arose in a single person roughly 33,000 to 55,000 years ago. The mutation then spread throughout South Asia.

The mutated gene encodes for a protein, called cardiac myosin binding protein-C (cMyBP-C), that controls cardiac muscle contractions and is critical for the normal functioning of the heart. In the mutated gene, 25 base pairs (DNA letters) are missing. As a result, the tail end of the protein is altered.

In his new study, Dr. Sadayappan and colleagues introduced the mutated gene into adult rat cardiomyocytes (heart muscle cells) in a petri dish. These cells were compared with cardiomyocytes that received a normal gene.

In cells with the mutant gene, the cMyBP-C protein was not incorporated into sarcomeres, the basic units of heart muscle. So rather than helping the sarcomeres contract properly, the mutant protein floated around the cell's cytoplasm, producing a toxic effect. The study showed, for the first time, that expression of the mutant protein is sufficient to cause cardiac dysfunction.

The findings point the way toward future treatments that would remove the mutant protein from cells and introduce normal cMyBP-C protein. Researchers also hope to identify lifestyle and environmental risk factors that aggravate hypertrophic cardiomyopathy in people who carry the gene mutation.

Dr. Sadayappan and colleagues concluded that determining the disease mechanism will help in developing therapies, and is the "first priority to prevent the development of heart failure in millions of carriers worldwide."

Dr. Sadayappan is an associate professor in the Department of Cell and Molecular Physiology of Loyola University Chicago Stritch School of Medicine. Co-authors are Diederik W.D. Kuster (first author), Suresh Govindan and Jody Martin of Loyola University Chicago Stritch School of Medicine and Tzvia Springer and Natosha Finley of Miami University.

The study is titled "A hypertrophic cardiomyopathy-associated MYBPC3 mutation common in populations of South Asian descent causes contractile dysfunction." It is supported by grants from the National Institutes of Health and American Heart Association.

http://www.eurekalert.org/pub_releases/2015-01/bifa-whm011415.php

When heavy metals go off-kilter: Study in C. elegans shows excess iron promotes aging

Maintaining delicate balance of metals may be a key factor in healthy aging

It's been known for decades that some metals, including iron, accumulate in human tissues during aging and that toxic levels of iron have been linked to neurologic diseases, such as Parkinson's. Common belief has held that iron accumulation happens as a result of the aging process. But research in the nematode C. elegans in the Lithgow lab at the Buck Institute shows that iron accumulation itself may also be a significant contributor to the aging process, causing dysfunction and malfolding of proteins already implicated in the aging process. The research is online in Aging

Similar to what happens in humans and other mammals, researchers found that levels of calcium, copper, iron and manganese increased as the worms aged. But iron accumulated much more than the others, said Buck faculty Gordon Lithgow, PhD, senior scientist on the project. "We were drawn to iron because there is all this literature that links excess iron to Alzheimer's and Parkinson's."

Researchers began manipulating the nematode's diet. "We fed iron to four day-old worms, and within a couple of days they looked like 15 day-old worms," said Lithgow. "Excess iron accelerated the aging process." Lithgow says excess iron is known to generate oxidative stress and researchers expected to see changes in the worm based on that toxicity. "Instead, what we saw looked much more like normal aging," said Lithgow. "The iron was causing dysfunction and aggregation in proteins that have already been associated with the aging process. Now we're wondering if excess iron also drives aging. "

Researchers, led by graduate student Ida Klang, also treated normal nematodes with the FDA-approved metal chelator CaEDTA - a drug that's used in humans at risk for lead poisoning. The drug slowed age-related accumulation of iron and extended the healthspan and lifespan of the nematodes. Klang also gave the drug to worms genetically bred to develop specific protein aggregations implicated in human disease. The chelator was also protective in those animals.

Lithgow says the work has implications for the aging research field. "Maintaining the proper balance of metals is key to good health throughout the lifespan, and it's pretty obvious that this delicate balance can go off-kilter with age," he said. "This is a phenomena that has not been extensively studied by aging researchers and it's an area that has potential for positive exploitation." As far as the general public is concerned, Lithgow was quick to warn people away from taking CaEDTA and other available metal chelators as anti-aging medication. "CaEDTA has a very blunt mechanism of action and is associated with dangerous side effects in humans and the track record for other chelators is not well established," said Lithgow, who urged people to talk to their physicians about the use of iron supplementation, especially for postmenopausal women.

Lithgow said his lab wants to find new chelators that act more like drugs and then move those drugs into testing in mice.

Citation: Iron promotes protein insolubility and aging in C. Elegans

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Other contributors include: Birgit Schilling, Dylan J. Sorensen, Alexandria K. Sahu, Pankaj Kapahi, Julie K. Andersen, and Bradford W. Gibson, all from the Buck Institute; Peter Swoboda, Karolinska institute, Department of Biosciences and Nutrition, Huddinge, Sweden; and David W. Killilea, Nutrition and Metabolism Center, Children's Hospital Oakland Research Institute, Oakland, CA.

http://www.eurekalert.org/pub_releases/2015-01/afps-pcb011515.php

People can be convinced they committed a crime that never happened

Method of questioning may lead suspects to falsely believe in and confess to committing crimes they didn't actually commit

Evidence from some wrongful-conviction cases suggests that suspects can be questioned in ways that lead them to falsely believe in and confess to committing crimes they didn't actually commit. New research provides lab-based evidence for this phenomenon, showing that innocent adult participants can be convinced, over the course of a few hours, that they had perpetrated crimes as serious as assault with a weapon in their teenage years.

The research, published in Psychological Science, a journal of the Association for Psychological Science, indicates that the participants came to internalize the stories they were told, providing rich and detailed descriptions of events that never actually took place.

"Our findings show that false memories of committing crime with police contact can be surprisingly easy to generate, and can have all the same kinds of complex details as real memories," says psychological scientist and lead researcher Julia Shaw of the University of Bedfordshire in the UK.

"All participants need to generate a richly detailed false memory is 3 hours in a friendly interview environment, where the interviewer introduces a few wrong details and uses poor memory-retrieval techniques."

Shaw and co-author Stephen Porter of the University of British Columbia in Canada obtained permission to contact the primary caregivers of university students participating in the study. The caregivers were asked to fill out a questionnaire about specific events the students might have experienced from ages 11 to 14, providing as much detail as possible. The caregivers were instructed not to discuss the questions with the student.

The researchers identified a total of 60 students who had not been involved in any of the crimes designated as false memory targets in the study and who otherwise met the study criteria. These students were brought to the lab for three 40-minute interviews that took place about a week apart.

In the first interview, the researcher told the student about two events he or she had experienced as a teen, only one of which actually happened. For some, the false event related to a crime that resulted in contact with the police (assault, assault with a weapon, or theft). For others, the false event was emotional in nature, such as personal injury, attack by a dog, or loss of a huge sum of money. Importantly, the false event stories included some true details about that time in the student's life, taken from the caregiver questionnaire.

Participants were asked to explain what happened in each of the two events. When they had difficulty explaining the false event, the interviewer encouraged them to try anyway, explaining that if they used specific memory strategies they might be able to recall more details.

In the second and third interviews, the researchers again asked the students to recall as much as they could about both the true and false event. The students also described certain features of each memory, such as how vivid it was and how confident they were about it.

The results were truly surprising.

Of the 30 participants who were told they had committed a crime as a teenager, 21 (71%) were classified as having developed a false memory of the crime; of the 20

who were told about an assault of some kind (with or without a weapon), 11 reported elaborate false memory details of their exact dealings with the police.
A similar proportion of students (76.67%) formed false memories of the emotional event they were told about.
Intriguingly, the criminal false events seemed to be just as believable as the emotional ones. Students tended to provide the same number of details, and reported similar levels of confidence, vividness, and sensory detail for the two types of event.
Shaw and Porter speculate that incorporating true details, such as the name of an actual friend, into an account that was supposedly corroborated by the student's caregiver likely endowed the false event with just enough familiarity that it came to seem plausible.
"In such circumstances, inherently fallible and reconstructive memory processes can quite readily generate false recollections with astonishing realism," says Shaw. "In these sessions we had some participants recalling incredibly vivid details and re-enacting crimes they never committed."
There were, however, some differences between the students' memories for false events and their memories for true events. For example, they reported more details for true events and they reported more confidence in their descriptions of the true memories.
The fact that the students appeared to internalize the false events to the extent that they did highlights the fundamental malleability of memory:
"This research speaks to the distinct possibility that most of us are likely able to generate rich false memories of emotional and criminal events," says Shaw.
The findings have clear implications for criminal interrogation and other aspects of legal procedure, affecting suspects, witnesses, and those involved in both law enforcement and legal counsel. But they may also apply to interviews that take place in various other contexts, including therapeutic or even personal settings.
"Understanding that these complex false memories exist, and that 'normal' individuals can be led to generate them quite easily, is the first step in preventing them from happening," says Shaw. "By empirically demonstrating the harm 'bad' interview techniques - those which are known to cause false memories - can cause, we can more readily convince interviewers to avoid them and to use 'good' techniques instead."
Investigating the specific characteristics of interviewers and interview tactics that contribute to false memories can help improve interviewing procedure and minimize the risk of inducing false memories, the researchers conclude.

The researchers were supported by the University of British Columbia through the Lashley and Mary Haggman Memory Research Award and the Social Sciences and Humanities Research Council of Canada.
For more information about this study, please contact: Julia Shaw at julishaw@gmail.com .
The article abstract is available online:
http://pss.sagepub.com/content/early/2015/01/14/0956797614562862.abstract

http://phys.org/news/2015-01-trans-neptunian-planets-solar.html

Trans-Neptunian objects suggest that there are more planets in the solar system

At least two unknown planets could exist in our solar system beyond Pluto.

There could be at least two unknown planets hidden well beyond Pluto, whose gravitational influence determines the orbits and strange distribution of objects observed beyond Neptune. This has been revealed by numerical calculations made by researchers at the Complutense University of Madrid and the University of Cambridge. If confirmed, this hypothesis would revolutionise solar system models.
Astronomers have spent decades debating whether some dark trans-Plutonian planet remains to be discovered within the solar system. According to the calculations of scientists at the Complutense University of Madrid (UCM, Spain) and the University of Cambridge (United Kingdom) not only one, but at least two planets must exist to explain the orbital behaviour of extreme trans-Neptunian objects (ETNO).
The most accepted theory establishes that the orbits of these objects, which travel beyond Neptune, should be distributed randomly, and by an observational bias, their paths must fulfill a series of characteristics: have a semi-major axis with a value close to 150 AU (astronomical units or times the distance between the Earth and the Sun), an inclination of almost 0° and an argument or angle of perihelion (closest point of the orbit to our Sun) also close to 0° or 180°.
Yet what is observed in a dozen of these bodies is quite different: the values of the semi-major axis are very disperse (between 150 AU and 525 AU), the average inclination of their orbit is around 20° and argument of Perihelion -31°, without appearing in any case close to 180°.
"This excess of objects with unexpected orbital parameters makes us believe that some invisible forces are altering the distribution of the orbital elements of the ETNO and we consider that the most probable explanation is that other unknown planets exist beyond Neptune and Pluto," explains Carlos de la Fuente Marcos, scientist at the UCM and co-author of the study.
"The exact number is uncertain, given that the data that we have is limited, but our calculations suggest that there are at least two planets, and probably more, within the confines of our solar system," adds the astrophysicist.

To carry out the study, which is published as two articles in the journal 'Monthly Notices of the Royal Astronomical Society Letters', the researchers have analysed the effects of the so-called 'Kozai mechanism', related to the gravitational perturbation that a large body exerts on the orbit of another much smaller and further away object. As a reference they have considered how this mechanism works in the case of comet 96P/Machholz1 under the influence of Jupiter.

Two problems to solve

Despite their surprising results, the authors recognise that their data comes up against two problems. On the one hand, their proposal goes against the predictions of current models on the formation of the solar system, which state that there are no other planets moving in circular orbits beyond Neptune.

However, the recent discovery by the ALMA radio telescope of a planet-forming disk more than 100 astronomical units from the star HL Tauri, which is younger than the Sun and more massive, suggests that planets can form several hundred astronomical units away from the centre of the system.

On the other hand, the team recognises that the analysis is based on a sample with few objects (specifically 13), but they point out that in the coming months more results are going to be published, making the sample larger. "If it is confirmed, our results may be truly revolutionary for astronomy," says de la Fuente Marcos.

Last year two researchers from the United States discovered a dwarf planet called 2012 VP113 in the Oort cloud, just beyond our solar system. The discoverers consider that its orbit is influenced by the possible presence of a dark and icy super-Earth, up to ten times larger than our planet.

More information: Carlos de la Fuente Marcos, Raúl de la Fuente Marcos, Sverre J. Aarseth. "Flipping minor bodies: what comet 96P/Machholz 1 can tell us about the orbital evolution of extreme trans-Neptunian objects and the production of near-Earth objects on retrograde orbits". Monthly Notices of the Royal Astronomical Society 446(2):1867-1873, 2015.

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http://www.eurekalert.org/pub_releases/2015-01/igp-npd010915.php

New planetary dashboard shows 'Great Acceleration' in human activity since 1950

Research supports proposal that Earth is now in a new geological epoch, the Anthropocene, with a start date for this epoch of around 1950.

Human activity, predominantly the global economic system, is now the prime driver of change in the Earth System (the sum of our planet's interacting physical, chemical, biological and human processes), according to a set of 24 global indicators, or "planetary dashboard", published in the journal Anthropocene Review (19 January 2015). The research charts the "Great Acceleration" in human activity from the start of the industrial revolution in 1750 to 2010, and the subsequent changes in the Earth System - greenhouse gas levels, ocean acidification, deforestation and biodiversity deterioration.

"It is difficult to overestimate the scale and speed of change. In a single lifetime humanity has become a planetary-scale geological force," says lead author Professor Will Steffen, who led the joint project between the International Geosphere-Biosphere Programme (IGBP) and the Stockholm Resilience Centre.

Twelve indicators depict human activity, for example, economic growth (GDP), population, foreign direct investment, energy consumption, telecommunications, transportation and water use. Twelve indicators show changes in major environmental components of the Earth System, for example, the carbon cycle, nitrogen cycle and biodiversity. This new "planetary dashboard" highlights how the trajectories of Earth and human development are now tightly bound. The findings will be presented at the World Economic Forum in Davos, Switzerland, 21-24 January.

"When we first aggregated these datasets, we expected to see major changes but what surprised us was the timing. Almost all graphs show the same pattern. The most dramatic shifts have occurred since 1950. We can say that around 1950 was the start of the Great Acceleration," said Professor Steffen, a researcher at the Australian National University and the Stockholm Resilience Centre.

"After 1950 you can see that major Earth System changes became directly linked to changes largely related to the global economic system. This is a new phenomenon and indicates that humanity has a new responsibility at a global level for the planet," he added.

Co-author IGBP Deputy Director, Dr Wendy Broadgate said, "The Great Acceleration indicators allow us to distinguish the signal from the noise. Earth is in a quantifiably different state than before. Several significant Earth System processes are now driven by human consumption and production."

Another co-author, Dr Lisa Deutsch, Senior Lecturer at the Stockholm Resilience Centre notes that: "Of all the socio-economic trends only construction of new large dams seems to show any sign of the bending of the curves - or a slowing of the Great Acceleration. Only one Earth System trend indicates a curve that may be the result of intentional human intervention - the success story of ozone depletion. The levelling off of marine fisheries capture since the 1980s is unfortunately not due to marine stewardship, but to overfishing."

The findings provide strong evidence that in recent decades key components of the Earth System have moved beyond the natural variability exhibited in the last 12,000 years, a period geologists call the Holocene. The Holocene, Latin for

"entirely recent", began at the end of the last ice age and provided the stability for agriculture to develop, leading eventually to townships and cities to flourish.

The Great Acceleration trends support the proposal that Earth has entered a new geological epoch, the Anthropocene, coined by researchers Paul Crutzen and Eugene Stoermer in 2000. Since then, the onset of the Anthropocene has been keenly contested by geologists, Earth System scientists and others, even though the term has not yet been formalised by the International Commission on Stratigraphy. Some say the dawn of agriculture 10,000 years ago - the Neolithic Age - is a likely candidate. Others say the industrial revolution, around the late 1700s.

The new paper argues that, "Of all the candidates for a start date for the Anthropocene, the beginning of the Great Acceleration is by far the most convincing from an Earth System science perspective. It is only beyond the mid-20th century that there is clear evidence for fundamental shifts in the state and functioning of the Earth System that are beyond the range of variability of the Holocene, and driven by human activities and not by natural variability."

Furthermore, choosing the beginning of the Great Acceleration leads to a possible specific start date: when the first atomic bomb was detonated in the New Mexico desert on Monday 16 July 1945.

"Radioactive isotopes from this detonation were emitted to the atmosphere and spread worldwide entering the sedimentary record to provide a unique signal of the start of the Great Acceleration, a signal that is unequivocally attributable to human activities," the paper reports. The research explores the underlying drivers of the Great Acceleration: predominantly globalisation.

The bulk of economic activity, and so too, for now, the lion's share of consumption, remain largely within the OECD countries, which in 2010 accounted for about 74% of global GDP but only 18% of the global population. This points to the profound scale of global inequality, which distorts the distribution of the benefits of the Great Acceleration and confounds international efforts, for example climate agreements, to deal with its impacts on the Earth System. However, the paper shows that recently, global production, traditionally based within OECD countries, has shifted towards BRICS nations -- Brazil, Russia, India, China and South Africa. Moreover, the mushrooming middle classes in BRICS nations are driving greater consumption here too.

About one half of the global population now lives in urban areas and about third of the global population has completed the transition from agrarian to industrial societies. This shift is evident in several indicators. Most of the post-2000 rise in fertilizer consumption, paper production and motor vehicles has occurred in the non-OECD world.

Coinciding with the publication of the Great Acceleration indicators, researchers also led by Professor Steffen have published a new assessment of the concept of "planetary boundaries" in the journal Science. The international team of 18 scientists identified two core planetary boundaries: climate change and "biosphere integrity". Altering either could "drive the Earth System into a new state." The planetary boundaries concept, first published in 2009, identifies nine global priorities relating to human-induced changes to the environment. The new research confirms many of the boundaries and provides updated analysis and quantification for several of them including phosphorus and nitrogen cycles, land use and biodiversity.

The original 24 indicators were published in the first IGBP synthesis in 2004, when Professor Steffen was IGBP Executive Director. The term 'Great Acceleration' was not used until 2005 at the Dahlem Conference on the history of the human-environment relationship, which brought together many IGBP scientists. This new research is part of IGBP's final synthesis, which will be completed in 2015.

The International Commission on Stratigraphy has set up a working group to analyse the validity of the Anthropocene claim. Professor Steffen is a member of this working group, which is due to report its conclusions in 2016.

The trajectory of the Anthropocene: The Great Acceleration (Anthropocene Review) 15 January 2015. http://anr.sagepub.com/content/early/recent

http://www.eurekalert.org/pub_releases/2015-01/uoc--cdr011515.php

Century-old drug reverses autism-like symptoms in fragile X mouse model

Drug used for almost a century to treat sleeping sickness, reversed environmental autism-like symptoms in mice

Autism spectrum disorders (ASD) affect 1 to 2 percent of children in the United States. Hundreds of genetic and environmental factors have been shown to increase the risk of ASD. Researchers at UC San Diego School of Medicine previously reported that a drug used for almost a century to treat trypanosomiasis, or sleeping sickness, reversed environmental autism-like symptoms in mice. Now, a new study published in this week's online issue of Molecular Autism, suggests that a genetic form of autism-like symptoms in mice are also corrected with the drug, even when treatment was started in young adult mice.

The underlying mechanism, according to Robert K. Naviaux, MD, PhD, the new study's principal investigator and professor of medicine at UC San Diego, is a phenomenon he calls the cellular danger response (CDR). When cells are exposed to danger in the form of a virus, infection, toxin, or even certain genetic mutations, they react defensively, shutting down ordinary activities and erecting barriers

against the perceived threat. One consequence is that communication between cells is reduced, which the scientists say may interfere with brain development and function, leading to ASD.

Researchers treated a Fragile X genetic mouse model, one of the most commonly studied mouse models of ASD, with suramin, a drug long used for sleeping sickness. The approach, called antipurinergic therapy or APT, blocked the CDR signal, allowing cells to restore normal communication and reversing ASD symptoms.

"Our data show that the efficacy of APT cuts across disease models in ASD. Both the environmental and genetic mouse models responded with a complete, or near complete, reversal of ASD symptoms," Naviaux said. "APT seems to be a common denominator in improving social behavior and brain synaptic abnormalities in these ASD models."

Weekly treatment with suramin in the Fragile X genetic mouse model was started at nine weeks of age, roughly equivalent to 18 years in humans. Metabolite analysis identified 20 biochemical pathways associated with symptom improvements, 17 of which have been reported in human ASD. The findings of the six-month study also support the hypothesis that disturbances in purinergic signaling - a regulator of cellular functions, and mitochondria (prime regulators of the CDR) - play a significant role in ASD.

Naviaux noted that suramin is not a drug that can be used for more than a few months without a risk of toxicity in humans. However, he said it is the first of its kind in a new class of drugs that may not need to be given chronically to produce beneficial effects. New antipurinergic medicines, he said, might be given once or intermittently to unblock metabolism, restore more normal neural network function, improve resilience and permit improved development in response to conventional, interdisciplinary therapies and natural play.

"Correcting abnormalities in a mouse is a long way from a cure in humans," cautioned Naviaux, who is also co-director of the Mitochondrial and Metabolic Disease Center at UC San Diego, "but our study adds momentum to discoveries at the crossroads of genetics, metabolism, innate immunity, and the environment for several childhood chronic disorders. These crossroads represent new leads in our efforts to understand the origins of autism and to develop treatments for children and adults with ASD."

Co-authors include Jane C. Naviaux, Lin Wang, Kefeng Li, A. Taylor Bright, William A. Alaynick, Kenneth R. Williams and Susan B. Powell, all at UC San Diego.

This study was supported, in part, by the Jane Botsford Johnson Foundation, the UC San Diego Christini Foundation, the UC San Diego Mitochondrial Research Fund, and the Wright Family Foundation.

http://www.eurekalert.org/pub_releases/2015-01/uot-poo011515.php

Planets outside our solar system more hospitable to life than thought

A study by astrophysicists at the University of Toronto suggests that exoplanets - planets outside our solar system - are more likely to have liquid water and be more habitable than we thought.

TORONTO, ON - "Planets with potential oceans could have a climate that is much more similar to Earth's than previously expected," said Jérémy Leconte, a postdoctoral fellow at the Canadian Institute for Theoretical Astrophysics (CITA) at the University of Toronto, and lead author of a study published today in Science Express.

Scientists have thought that exoplanets behave in a manner contrary to that of Earth - that is they always show their same side to their star. If so, exoplanets would rotate in sync with their star so that there is always one hemisphere facing it while the other hemisphere is in perpetual cold darkness.

Leconte's study suggests, however, that as exoplanets rotate around their stars, they spin at such a speed as to exhibit a day-night cycle similar to Earth.

"If we are correct, there is no permanent, cold night side on exoplanets causing water to remain trapped in a gigantic ice sheet. Whether this new understanding of exoplanets' climate increases the ability of these planets to develop life remains an open question."

Leconte and his team reached their conclusions via a three-dimensional climate model they developed to predict the effect of a given planet's atmosphere on the speed of its rotation, which results in changes to its climate," said Leconte.

"Atmosphere is a key factor affecting a planet's spin, the impact of which can be of enough significance to overcome synchronous rotation and put a planet in a day-night cycle."

Though astronomers are still awaiting observational evidence, theoretical arguments suggest that many exoplanets should be able to maintain an atmosphere as massive that of Earth. In Earth's case - with its relatively thin atmosphere - most of the light from the Sun reaches the surface of the planet, maximizing the effect of heating throughout the atmosphere and producing a more moderate climate across the planet. By creating temperature differences at the surface, between day and night and between equator and poles, the solar heating drives winds that redistribute the mass of the atmosphere.

The impact is so significant that it overcomes the effect of tidal friction exerted by a star on whatever satellite is orbiting it, much like Earth does on the Moon.

"The Moon always shows us the same side, because the tides raised by Earth create a friction that alters its spin," said Leconte. "The Moon is in synchronous rotation with Earth because the time it takes to spin once on its axis equals the time it takes for it to orbit around Earth. That is why there is a dark side of the moon. The tidal theory, however, neglects the effects of an atmosphere."

The researchers say that a large number of known terrestrial exoplanets should not be in a state of synchronous rotation, as initially believed. While their models show that they would have a day-night cycle making them much more similar to Earth, the duration of their days could last between a few weeks and few months.

The findings are reported in the paper "Asynchronous rotation of Earth-mass planets in the habitable zone of lower-mass stars" published today in Science Express. The work was supported by grants from the Natural Sciences and Engineering Research Council of Canada.

http://bit.ly/1xjuLOw

Fish Sperm Might Be the Secret to Recycling Rare Earth Elements

Japanese scientists have uncovered an unlikely source to aid in the extraction and recycling of rare earth metals

By Laura Clark smithsonian.com

File this under: Awesome things you didn't know fish semen was good for.

The DNA within salmon milt (or semen) has been found capable of aiding in the extraction and recycling of the rare earth metals commonly used in technologies from smart phones to wind turbines.

A team of scientists in Japan made this discovery while seeking out better ways to extract rare earth elements like neodymium from the crude ore in which they are found. Current methods use large amounts of environmentally damaging chemicals, including mercury and arsenic, and are severely compromising water sources in mining regions like parts of China.

As Newsweek reports:

The scientists, led by Yoshio Takahashi of Hiroshima University, found that several rare earth elements bound strongly to phosphate-containing molecules on the surface of bacterial cells, according to* Chemistry World*, a publication of the Royal Society of Chemistry. So they turned to salmon sperm, since it is largely made up of DNA, which contains a lot of phosphate. (And it's also insoluble in water, unlike pure DNA, making it easier to work with.)

When applied to neodymium, the team found that the salmon milt DNA made a strong bond with the metal, allowing its subsequent extraction following an acid bath and a spin through a centrifuge.

Salmon semen has the benefit of being both cheap and green. Even better, experts say the discovery could be applied to recycling rare earth metals used in smart phones, computers and electronic circuits—metals that otherwise would end up in a landfill.

This isn't the only research performed on the wondrous powers of fish semen. Previous studies have found that the same DNA that binds to metals like neodymium also lends itself to fireproof coating. As for fish semen in its natural form: it is considered a delicacy in Japan.

http://bit.ly/1BNXqAP

Study: Islamic fundamentalism is not a marginal phenomenon in Europe

Study shows hostility towards other out-groups is not an isolated phenomenon among Muslims living in Europe; but nor is it a synonym of violence

Last week's attacks in Paris, committed in the name of a god, reopen a badly-healed scar in Europe. The world once again turns towards religious fundamentalism. A new study shows that hostility towards other out-groups is not an isolated phenomenon among Muslims living in Europe; but nor is it a synonym of violence. According to the author of the study, Ruud Koopmans, director of the WZB Berlín Social Science Centre (Germany), "Islam is not the problem".

The attack on the French satirical magazine Charlie Hebdo -which sold five million copies of its latest issue around the world on Wednesday 14 January- was not merely an act of aggression against freedom of expression and against human life; it was also an attack on the religious values of a large majority of Muslims living in the European Union, whose ideals are peaceful and even flexible among the youngest members of the community.

For Ruud Koopmans, sole author of a study published in early January in the Journal of Ethnic and Migration Studies and director of the WZB Berlin Social Science Centre (Germany), religious fundamentalism is defined in three ways: that believers should return to the eternal and unchangeable rules laid down in the past; that these rules only allow one interpretation and are binding for all believers; and that religious rules should have priority over secular laws.

The sociologist insists that religious fundamentalism -also interpreted as strict religiosity- is an ideology, that is a set of ideas that refer to attitudes towards the way of viewing life.

"Fundamentalism does not necessarily include or justify violence, as this is a form of behaviour and not an ideology," explains Koopmans in a phone call from Berlin (Germany). The specialist compares this fundamentalism with fascism and communism, other ideologies that are not synonymous with violence.

Nevertheless, "religious fundamentalism may encourage radicalisation. In general, it should not imply violence, although out-group hostility may be evident," continues the expert.

But religious fundamentalism is not unique to Islam: the term originated with a Protestant movement in the early 20th century in the USA, which propagated a return to the 'fundaments' of the Christian faith and to a literal interpretation of the rules of the Bible.

Extended ideologies but not universal

Koopmans' study, based on a survey in 2008 of 9000 Europeans, compares the religious fundamentalism of immigrants and the children and grandchildren of Turkish and Moroccan Muslim immigrants (Sunni Muslims and to a lesser extent Alevites) of Turkish and Moroccan origin and native European Christians (Catholics, Protestants, Seventh Day Adventists, Jehova's Witnesses and Pentecost believers) in Germany, France, the Netherlands, Belgium, Austria and Sweden, countries with a long generational history of immigration.

"Broadly speaking, between 40% and 45% of European Muslims have fundamentalist religious ideas, that is they agree with the three definitions of the term. Austria is the country with the highest percentage, 55%, while Germany has the lowest, 30%", explains Koopmans.

According to the scientist, fundamentalism is not a marginal phenomenon among Muslims in Western Europe. "Although a majority of Muslims have more liberal views of the religion, this minority of fundamentalist Muslims is significant", underlines the researcher who adds that although these attitudes are widespread "they are not universal among European Muslims".

The results show that if first and second generations are considered and if each definition is taken independently, almost 60% would return to the roots of Islam, 75% think there is only one interpretation of the Koran possible to which every Muslim should stick, and 65% say that religious rules are more important to them than the rules of the country in which they live. "However in second generation Muslims the levels are slightly lower (between 50% and 70%)," states the expert.

According to the study, Islamic fundamentalism, also known as Islam, prevails in Europe if compared to Christian fundamentalism, in which only 4% of Christians shared the ideas of the three statements of the definition. Among Protestants, fundamentalism reached 12%. "All fundamentalists are strictly religious but this does not mean that all strictly religious individuals are fundamentalists. Strict religiosity is more frequently associated to Islamic fundamentalists than to Christians," claims the author.

In addition, Christian and Islamic fundamentalism decrease when the social and economic status is higher, "and this is even more so among the Muslim community", indicates the sociologist. Nevertheless, "although in Europe religious fundamentalism is more widespread in Islam, in the USA it is Christian fundamentalism, especially among Protestants, which has the greatest support," observes Koopmans who points out that the data from the study cannot be extrapolated to the rest of the world.

In Spain, with a more recent history of immigration, and for this reason not included in the study, followers of religious fundamentalism, in particular Islam, reach similar figures. A study conducted by the American PEW Research Centre revealed that Islamic fundamentalists make up more than 30% of the followers. "In fact, there is not much variation in the European countries," declares the Researcher.

Hostility towards out-groups

The reactions generated as a result of the latest attacks in the French capital have merely served to fortify a growing Islamophobia and rejection of Muslims. "But Islam is not the problem. Nor is it true that a majority of Muslims have fundamentalist ideals," says the expert.

Religious fundamentalism is not new. Since the nineties, these attitudes are found among Christians and in Islam, remaining stable in the case of the latter.

"What is relatively recent is the growth of violence, linked to the situation in Syria and Iraq, and which has served to aggravate the problem", maintains Koopmans. Other studies claim that between 10% and 15% of EU Muslims are prepared to use violence to defend their faith.

Although violence does not necessarily form part of this ideology, hostility towards other out-groups including homosexuals, Jews, and Westerners (in the case of Muslims) or Muslims (in the case of Christians) is evident. As a whole, Muslims are shown to be more hostile towards the three out-groups mentioned above, with between 25% and 30% rejecting these groups. Christian hostility is not as much as 5%.

However, independently, Christian fundamentalists show greater hostility towards Muslims (more than 50%) and towards Jews (between 30 and 35% of Christian fundamentalists were revealed to be hostile). In the case of Islamic fundamentalists, more than 70% of followers feel hostility towards homosexuals, Jews and Westerners.

Religious fundamentalism is closely linked to hostility towards other out-groups," says Koopmans. But social and economic levels also have a bearing. Individuals with a high social and economic status are more tolerant and less xenophobic.

More information: Koopmans, Ruud. "Religious Fundamentalism and Hostility against Out-groups: A Comparison of Muslims and Christians in Western Europe" Journal of Ethnic and Migration Studies 41(1): 33-57 DOI: 10.1080/1369183X.2014.935307, 2 January 2015

http://1.usa.gov/15qgKHw

NASA, NOAA Find 2014 Warmest Year in Modern Record

The year 2014 now ranks as the warmest on record since 1880, according to an analysis by NASA scientists.

The year 2014 ranks as Earth's warmest since 1880, according to two separate analyses by NASA and National Oceanic and Atmospheric Administration (NOAA) scientists. The 10 warmest years in the instrumental record, with the exception of 1998, have now occurred since 2000. This trend continues a long-term warming of the planet, according to an analysis of surface temperature measurements by scientists at NASA's Goddard Institute of Space Studies (GISS) in New York. In an independent analysis of the raw data, also released Friday, NOAA scientists also found 2014 to be the warmest on record.

"NASA is at the forefront of the scientific investigation of the dynamics of the Earth's climate on a global scale," said John Grunsfeld, associate administrator for the Science Mission Directorate at NASA Headquarters in Washington. "The observed long-term warming trend and the ranking of 2014 as the warmest year on record reinforces the importance for NASA to study Earth as a complete system, and particularly to understand the role and impacts of human activity."

Since 1880, Earth's average surface temperature has warmed by about 1.4 degrees Fahrenheit (0.8 degrees Celsius), a trend that is largely driven by the increase in carbon dioxide and other human emissions into the planet's atmosphere. The majority of that warming has occurred in the past three decades.

"This is the latest in a series of warm years, in a series of warm decades. While the ranking of individual years can be affected by chaotic weather patterns, the long-term trends are attributable to drivers of climate change that right now are dominated by human emissions of greenhouse gases," said GISS Director Gavin Schmidt.

While 2014 temperatures continue the planet's long-term warming trend, scientists still expect to see year-to-year fluctuations in average global temperature caused by phenomena such as El Niño or La Niña. These phenomena warm or cool the tropical Pacific and are thought to have played a role in the flattening of the long-term warming trend over the past 15 years. However, 2014's record warmth occurred during an El Niño-neutral year.

"NOAA provides decision makers with timely and trusted science-based information about our changing world," said Richard Spinrad, NOAA chief scientist. "As we monitor changes in our climate, demand for the environmental intelligence NOAA provides is only growing. It's critical that we continue to work with our partners, like NASA, to observe these changes and to provide the information communities need to build resiliency."

Regional differences in temperature are more strongly affected by weather dynamics than the global mean. For example, in the U.S. in 2014, parts of the Midwest and East Coast were unusually cool, while Alaska and three western states – California, Arizona and Nevada – experienced their warmest year on record, according to NOAA.

The GISS analysis incorporates surface temperature measurements from 6,300 weather stations, ship- and buoy-based observations of sea surface temperatures, and temperature measurements from Antarctic research stations. This raw data is analyzed using an algorithm that takes into account the varied spacing of temperature stations around the globe and urban heating effects that could skew the calculation. The result is an estimate of the global average temperature difference from a baseline period of 1951 to 1980. NOAA scientists used much of the same raw temperature data, but a different baseline period. They also employ their own methods to estimate global temperatures.

GISS is a NASA laboratory managed by the Earth Sciences Division of the agency's Goddard Space Flight Center, in Greenbelt, Maryland. The laboratory is affiliated with Columbia University's Earth Institute and School of Engineering and Applied Science in New York.

NASA monitors Earth's vital signs from land, air and space with a fleet of satellites, as well as airborne and ground-based observation campaigns. NASA develops new ways to observe and study Earth's interconnected natural systems with long-term data records and computer analysis tools to better see how our planet is changing. The agency shares this unique knowledge with the global community and works with institutions in the United States and around the world that contribute to understanding and protecting our home planet.

The data set of 2014 surface temperature measurements is available at:
http://data.giss.nasa.gov/gistemp/
The methodology used to make the temperature calculation is available at:
http://data.giss.nasa.gov/gistemp/sources_v3/

http://bit.ly/1yBV9rq

A Significant Step Towards Explaining the Cosmic Origins of the Seeds of Galaxies

3D Simulation Shows Small Protostellar-Like Core Can Grow into a Supermassive Black Hole

Simulation of the collapse of gas in the very early universe into a small black hole, the first step in producing a more massive black hole that will become the seed for the future development of a galaxy. (The scale of the image is 20 au; one au – astronomical unit – is the average distance of the Earth from the Sun.

In a new study, astronomers from Harvard-Smithsonian Center for Astrophysics found that a small protostellar-like core of only 0.1 solar-masses can develop in only a few years from a suitable environment and then can grow into a supermassive black hole in only millions of years.

Supermassive black holes with millions or billions of solar-masses of material are found at the nuclei of most galaxies. During the embryonic stages of these galaxies they are thought to play an important role, acting as seeds around which material collected. During the later lifetime of galaxies they can power dramatic outflowing jets of material (among other phenomena) as infalling dust and gas accretes onto the disks that typically surround them. These active, later phases of supermassive black holes can result in turning galaxies into an extremely bright objects like quasars, whose luminosities allow them to be seen at cosmic distances. In fact, quasars have recently been detected from eras less than a billion years after the big bang.

But where do all these black holes come from – especially the ones present in the early universe!? The explosive death of massive stars, one nominal route, can take many hundreds of millions of years while the star itself coalesces from ambient gas and then evolves, after which material must be added to the black hole seed to grow it into a supermassive monster. It is not clear that there is enough time in the early universe for this to happen. A second method has been proposed for these cosmic seeds, the direct collapse of primordial gas into seedlings that are much more massive – about ten thousand solar-masses – than are those present in stellar ashes.

Computer simulations have struggled for years to predict what happens in direct collapse, with mixed successes. CfA astronomers Fernando Becerra, Thomas Greif, and Lars Hernquist, and a colleague, have just published the most detailed 3-D simulation of the process in the early universe with an amazingly fine spatial scale precision — as small as the solar-system — and spanning a factor of over ten trillion in size and twenty orders of magnitude (a factor of one hundred million trillion) in gas density. They find that a small protostellar-like core of only 0.1 solar-masses can develop in only a few years from a suitable environment and then can grow into a supermassive black hole in only millions of years. In particular, they find that fragmentation, which had been predicted to disrupt the growth of these seedlings, is not a serious problem.

Their result is a significant step towards explaining the cosmic origins of the seeds of galaxies.

Publication: Fernando Becerra, et al., "Formation of massive protostars in atomic cooling haloes," MNRAS (January 21, 2015) 446 (3): 2380-2393; doi: 10.1093/mnras/stu2284

PDF Copy of the Study: Formation of massive protostars in atomic cooling haloes

http://bit.ly/1zgZbUJ

This Smart Stethoscope Attachment Could Lead to More Accurate Diagnoses

Eko Core clips on to existing stethoscopes and lets physicians share heart sounds through their smartphones and the Web

By Matt Safford

Sometimes, the best way to make new technology appealing is to integrate it into existing devices.

That's the idea behind the Eko Core, a tool that brings the modern stethoscope into the age of the smartphone and cloud computing.

The Core, developed by Berkeley, California-based startup Eko Devices, pairs with a smartphone or tablet over Bluetooth, and records heart sounds. The audio can instantly be shared with a cardiologist anywhere for an expert opinion, or compared to heart sounds in a cloud-based database, to help discern the likelihood of a heart murmur or other serious issue.

Rather than replacing the traditional stethoscope, which many physicians see as an emblem of their profession, the Eko Core attaches to it, between the ear and chest pieces, allowing the analogue features of the stethoscope to remain intact.

Eko_Core.jpg (Eko Devices)

According to Jason Bellet, co-founder and COO of the company, the initial idea came out of a class on healthcare innovations that he and his business partners took at UC Berkeley in 2012.

"During a visit to a Bay Area hospital, it became very apparent that the stethoscope, the physician's lead tool for cardiac monitoring, is a 200-year-old outdated technology," says Bellet. "An icon of medicine is really at fault for a tremendous amount of healthcare waste and overscreening."

One might think, given the prevalence of the stethoscope, that every general practitioner and ER resident has an expert ear for heart sounds. But correctly reading these sounds is a tricky skill that can take years to develop, especially if a doctor isn't a cardiologist.

This reality leads to expensive and often unnecessary tests and in-person consultations with specialists.

While hard statistics for the cost of unnecessary cardiologists are hard to come by, an eConsult program at UC San Francisco that lets primary care physicians communicate with specialists virtually has reportedly cut wait times by 52 percent, while reducing the number of new patient visits to specialists, and reducing referral costs from $232 and up for one in-person consultation to just $57 for an eConsult.

The Eko Core aims to make virtual consultation even simpler and, in doing so, cut costs dramatically, while more efficiently and accurately diagnosing serious heart issues. With it, a physician can send heart sounds directly to a cardiologist anywhere in the world, as long as the consulting doctor also has a stethoscope fitted with an Eko Core. If not, the specialist on the receiving end can listen to the sounds on his or her computer, smartphone or tablet using headphones.

A few stethoscopes already on the market have the ability to record. 3M's Littmann 3200, for instance, can record and store up to 12 heart readings. But it pairs with a proprietary USB dongle, so is meant to be used with a desktop or laptop computer, not mobile devices, and Apple products are not supported. Bellet says this model doesn't jibe with the transient nature of clinical medicine, which involves physicians constantly traveling from room to room.

"Efficiency is the biggest thing in modern healthcare," says Bellet. "A connected device needs to be connected to the tools that physicians rely on." Eko Devices has developed software that streams stethoscope sounds to Apple or Android phones and tablets, then uploads them to the cloud where they can be listened to, securely, from virtually any Web-connected device.

With recorded heart sounds that can be played back from a cloud-based database, the device could be used for teaching as well. Similar web-based tools for doctors already exist, such as Johns Hopkins University's Murmurlab, a Web database of recorded heart sounds designed to teach physicians how to make better diagnoses by listening to thousands of examples. But while Murmurlab is designed to be used with a computer, the Eko Core would let medical students and physicians listen to heart sounds virtually anywhere.

The company will sell the Core for approximately $200, which is about a third the cost of current digital stethoscopes. It also features active noise cancelling and amplification, which will no-doubt benefit doctors trying to get heart readings in crowded emergency rooms or in other noisy situations.

Don't expect to see the Eko Core around the neck of your primary care physician at your next checkup though, unless your doctor's office is located in the San Francisco Bay Area. Pilot programs using the Eko Core could begin at hospitals there as early as February, according to Bellet. While the company says the institutional review board process is underway, the device still has to be approved by the FDA before interested physicians across the country can add the Core to their own stethoscopes.

"We're really focused on commercializing [the Eko Core], and the impact it can have on cardiac monitoring - particularly long-term patient management," says Bellet. "That said, we're always looking at other uses for this particular technology."

http://www.bbc.com/news/health-30836057

Popular medical students 'should get flu jab first'

Prioritising medical students with lots of friends for flu jabs could help increase the number of healthcare workers protected against the virus, say Lancaster University researchers.

In a study in The Lancet, they calculated that vaccination rates would rise if people with large social networks influenced their peers.

The government wants 75% of healthcare workers to be vaccinated.

At present, only about half of them are vaccinated.

More than 200 medical students at Lancaster University - who are soon to become healthcare workers - gave researchers information on how friendly they were with other students and how much time they spent with them.

'Limit the spread'

The Lancaster research team then ran a computer simulation of an influenza outbreak 1,500 times to find out what effect vaccinating some well-connected individuals had on the spread of the flu.

"It is clear that some individuals have a disproportional effect on disease dynamics," researcher Rhiannon Edge said.

"This study suggests that vaccination strategies that target highly connected individuals within a network might limit the spread of infectious disease."

They said this was because people who are connected within a social network can influence each other's behaviour, even when not connected directly.

And sometimes this can work both ways.

"If an individual's vaccination decision is affected by their immediate social circle, clusters of unvaccinated individuals can develop - and these clusters may then facilitate outbreaks of infection."

Vaccine uptake

PHE encourages healthcare workers and carers to get vaccinated because they could pass the infection on to vulnerable people with whom they come into contact.

Latest flu vaccine uptake figures from Public Health England show that more than 70% of people aged 65 and over have been vaccinated.

However, fewer than 50% of those aged under 65 with a health condition have been vaccinated, and only 43% of pregnant women.

In addition, 37% of all two-year-olds, 40% of all three-year-olds, and 32% of all four-year-olds have been vaccinated with the nasal spray vaccine as part of the childhood flu immunisation programme.

http://apne.ws/15jECx0

Questions and answers about Sri Lanka mystery kidney disease

A mystery kidney disease is killing Sri Lankan farmers

By MARGIE MASON

KONKETIYAWA, Sri Lanka (AP) -- The first cases surfaced some two decades ago in the country's North Central province, the main rice-producing area. Since then, the disease has killed up to an estimated 20,000 people on the Indian Ocean island nation. As researchers work to unravel the cause, and doctors continue to diagnose new patients, here are a few questions and answers about the illness.

Q: What's the cause of the disease?

A: A World Health Organization study pointed to cadmium, pesticides and other factors, such as arsenic, as possible causes, but there was no clear link to any specific source. Water came back clean, though it has not been ruled out, and many suspect it is connected. Tobacco and certain vegetables, such as lotus root, were found to contain elevated levels of cadmium and lead.

Q: Who's sick and how does the disease progress?

A: An estimated 70,000 to 400,000 people are believed to be affected. Kidney disease is typically caused by diabetes or hypertension, but not in Sri Lanka, where people in their 30s and 40s are stricken by the mystery version. The so-called chronic kidney disease of unknown etiology, or CKDu, acts like a toxin, destroying the tissue and causing the kidneys to shrink. Once the disease reaches the end stage, the only way to survive is by undergoing regular dialysis or getting a transplant. Often, several members of one family fall ill, and men are more severely sickened than women.

Q: Do agrochemicals play a role?

A: Sri Lanka is among the world's top fertilizer-using countries, and some question whether heavy metals could be leaching into the soil and groundwater, though the government says regularly tested samples are within permitted limits. Last year, one scientist hypothesized that the popular weed killer glyphosate may be to blame. He suggested that the chemical, first introduced in Monsanto's Roundup, forms a bond with heavy metals that persists in food and drinking water until reaching the kidneys, slowly destroying them. This has not been proven, and Monsanto denies the allegations, but Sri Lanka has officially banned the herbicide - though it's still being sold.

Q: How is Sri Lanka coping with the problem?

A: The onslaught of patients has left Sri Lanka struggling to care for them. There are only 183 dialysis machines nationwide, forcing many to get treatment twice a week - or less - instead of the recommended three times. There's also a shortage of trained specialists, with only six transplant surgeons and 10 nephrologists at public hospitals in the country. There is no national transplant program that uses cadaver kidneys, leaving desperate patients to rely on relatives or altruistic donors. Since many die at home, their deaths are often not recorded as a result of kidney disease, masking the scope of the problem.

http://www.eurekalert.org/pub_releases/2015-01/uom-hdt011615.php

How does the brain adapt to the restoration of eyesight?

Surgery cannot completely undo the brain rewiring caused by long term blindness

Recent scientific advances have meant that eyesight can be partially restored to those who previously would have been blind for life. However, scientists at the University of Montreal and the University of Trento have discovered that the rewiring of the senses that occurs in the brains of the long-term blind means that visual restoration may never be complete. "We had the opportunity to study the rare case of a woman with very low vision since birth and whose vision was suddenly restored in adulthood following the implantation of a Boston Keratoprosthesis in her right eye," explained Giulia Dormal, who led the study. "On one hand, our findings reveal that the visual cortex maintains a certain degree of plasticity - that is the capacity to change as a function of experience - in an adult person with low vision since early life. On the other, we discovered that several months after the surgery, the visual cortex had not regained full normal functioning." The visual cortex is the part of the brain that processes information from our eyes.

Scientists know that in cases of untreatable blindness, the occipital cortex - that is the posterior part of the brain that is normally devoted to vision - becomes responsive to sound and touch in order to compensate for the loss of vision. "This important brain reorganization represents a challenge for people encountering eye surgery to recover vision, because the deprived and reorganized occipital cortex may not be capable of seeing anymore after having spent years in the dark," Dormal said.

In order to ascertain how much of a challenge this may be, the researchers worked with the patient, a 50 year old Quebec woman. They conducted behavioral and neurophysiological measurements before and after surgery to track changes in her sight and brain anatomy, and in the way her brain responded to sights and sounds. This involved taking MRI images as she completed various visual and auditory tasks and comparing her scans with scans that had been taken from people with normal eyesight and people with untreatable blindness who had performed the same tasks. "We show that structural and functional reorganization of occipital regions were present in this patient before surgery as a result of longstanding visual impairment, and that some reorganizations can be partially reversed by

visual restoration in adulthood," said Oliver Collignon, who supervised the research. "Because of important advances in visual restoration techniques, such findings have important clinical implications for the predictive outcome of blind individuals who are candidate to such interventions."

The study suggests that eye surgery can lead to a positive outcome even when performed in adulthood after a life-time of profound blindness. There is however an important caveat. "The recovery observed in the visual cortex, that is highlighted by a decrease in auditory-driven responses and by an increase in both visually-driven responses and grey matter density with time, is not total," Dormal explained. "Indeed, auditory-driven responses were still evidenced in certain regions of the visual cortex even 7 months after surgery, and these responses overlapped with visually-driven responses. This overlap may be the reason some aspects of vision, despite having improved with time, still remained below normal range 7 months after surgery."

The clinical implications of the research are two-fold. "Our findings open the door to the use of functional magnetic resonance imaging before surgery as a prognostic tool for visual outcome and pave the way for the development of adapted rehabilitation programs following visual restoration," Collignon said.

Giulia Dormal, Olivier Collignon and their colleagues published "Tracking the evolution of crossmodal plasticity and visual functions before and after sight-restoration" in the Journal of Neurophysiology on December 17, 2014. The research received funding from the Canada Research Chair Program, the Canadian Institutes of Health Research, the Saint-Justine Foundation, the European Research Council (starting grant MADVIS, ERC-StG 337573, the Veronneau Troutman Foundation, the Fonds de recherche en ophtalmologie de l'Université de Montréal, PAI/UIAP grant PAI/33, and the Belgian National Fund for Scientific Research. The University of Montreal is officially known as Université de Montréal.