http://www.eurekalert.org/pub_releases/2013-07/wsu-wrc062713.php

WSU researchers create superconductor from solvent

Research opens up new understanding of phenomenon

PULLMAN, Wash.—A study led by Washington State University researchers has turned a fairly common non-metallic solvent into a superconductor capable of transmitting electrical current with none of the resistance seen in conventional conductors.

"It is an important discovery that will attract a lot of attention from many scientific communities—physics, chemistry, and materials science," said Choong-Shik Yoo, a professor of chemistry and Institute for Shock Physics. The National Science Foundation-funded discovery, which grows out of research by Yoo doctoral student Ranga Dias, appears in the Proceedings of the National Academy of Sciences.

The field of superconductivity has a wide variety of potentially revolutionary applications, including powerful electromagnets, vehicle propulsion, power storage and vastly more efficient power transmission.

Three years ago, Yoo used super-high pressures similar to those found deep in the Earth to turn a white crystal into a "super battery," or what he called "the most condensed form of energy storage outside of nuclear energy." This time, Yoo saw how carbon disulfide subjected to high pressure and cold started to act like a metal, taking on properties like magnetism, a high energy density, and superhardness as its molecules reassembled in three-dimensional structures like those found in diamonds.

Typically, non-metallic molecules are too far apart from each other–three times farther apart than metal molecules—for electrical energy to move across them. But Yoo and his colleagues, including researchers at the Carnegie Institution of Washington, compressed the compound in the small, compact space of a diamond anvil cell to 50,000 atmospheres, a pressure equivalent to that found 600 miles into the Earth. They also chilled the compound to 6.5 degrees Kelvin, or nearly -447 F.

The pressure and temperature not only brought the carbon disulfide molecules together but rearranged them into a lattice structure in which the natural vibrations of the molecules can help electrons move so well the material becomes a resistance-free superconductor.

Yoo's research provides new insight into how superconductivity works in unconventional materials, an area that has intrigued scientists for several decades, he says. These unconventional materials are typically made of atoms with lower atomic weights that let them vibrate at higher frequencies, increasing their potential as superconductors at higher temperatures.

Yoo acknowledges that electronic materials are not about to be cooled to near absolute zero or subjected to extreme pressures. But he said this work could point the way to creating similar properties under more ordinary conditions, much as science paved the way to make synthetic diamonds at lower temperatures and pressures.

"This research will provide the vehicle for people to be clever in developing superconductors by understanding the fundamentals that guide them," said Yoo.

http://www.eurekalert.org/pub_releases/2013-07/ciot-pim062813.php

Psychology influences markets

When it comes to economics versus psychology, score one for psychology.

Written by Marcus Woo

Economists argue that markets usually reflect rational behavior—that is, the dominant players in a market, such as the hedge-fund managers who make billions of dollars' worth of trades, almost always make well-informed and objective decisions. Psychologists, on the other hand, say that markets are not immune from human irrationality, whether that irrationality is due to optimism, fear, greed, or other forces.

Now, a new analysis published the week of July 1 in the online issue of the Proceedings of the National Academy of Sciences (PNAS) supports the latter case, showing that markets are indeed susceptible to psychological phenomena. "There's this tug-of-war between economics and psychology, and in this round, psychology wins," says Colin Camerer, the Robert Kirby Professor of Behavioral Economics at the California Institute of Technology (Caltech) and the corresponding author of the paper.

Indeed, it is difficult to claim that markets are immune to apparent irrationality in human behavior. "The recent financial crisis really has shaken a lot of people's faith," Camerer says. Despite the faith of many that markets would organize allocations of capital in ways that are efficient, he notes, the government still had to bail out banks, and millions of people lost their homes.

In their analysis, the researchers studied an effect called partition dependence, in which breaking down—or partitioning—the possible outcomes of an event in great detail makes people think that those outcomes are more likely to happen. The reason, psychologists say, is that providing specific scenarios makes them more explicit in people's minds. "Whatever we're thinking about, seems more likely," Camerer explains.

For example, if you are asked to predict the next presidential election, you may say that a Democrat has a 50/50 chance of winning and a Republican has a 50/50 chance of winning. But if you are asked about the odds that a particular candidate from each party might win—for example, Hillary Clinton versus Chris Christie—you are likely to envision one of them in the White House, causing you to overestimate his or her odds.

The researchers looked for this bias in a variety of prediction markets, in which people bet on future events. In these markets, participants buy and sell claims on specific outcomes, and the prices of those claims—as set by the market—reflect people's beliefs about how likely it is that each of those outcomes will happen. Say, for example, that the price for a claim that the Miami Heat will win 16 games during the NBA playoffs is $6.50 for a $10 return. That means that, in the collective judgment of the traders, Miami has a 65 percent chance of winning 16 games.

The researchers created two prediction markets via laboratory experiments and studied two others in the real world. In one lab experiment, which took place in 2006, volunteers traded claims on how many games an NBA team would win during the 2006 playoffs and how many goals a team would score in the 2006 World Cup. The volunteers traded claims on 16 teams each for the NBA playoffs and the World Cup.

In the basketball case, one group of volunteers was asked to bet on whether the Miami Heat would win 4–7 playoff games, 8–11 games, or some other range. Another group was given a range of 4–11 games, which combined the two intervals offered to the first group. Then, the volunteers traded claims on each of the intervals within their respective groups. As with all prediction markets, the price of a traded claim reflected the traders' estimations of whether the total number of games won by the Heat would fall within a particular range.

Economic theory says that the first group's perceived probability of the Heat winning 4–7 games and its perceived probability of winning 8–11 games should add up to a total close to the second group's perceived probability of the team winning 4–11 games. But when they added the numbers up, the researchers found instead that the first group thought the likelihood of the team winning 4–7 or 8–11 games higher than did the second group, which was asked about the probability of them winning 4–11 games. All of this suggests that framing the possible outcomes in terms of more specific intervals caused people to think that those outcomes were more likely.

The researchers observed similar results in a second, similar lab experiment, and in two studies of natural markets—one involving a series of 153 prediction markets run by Deutsche Bank and Goldman Sachs, and another involving long-shot horses in horse races.

People tend to bet more money on a long-shot horse, because of its higher potential payoff, and they also tend to overestimate the chance that such a horse will win. Statistically, however, a horse's chance of winning a particular race is the same regardless of how many other horses it's racing against—a horse who habitually wins just five percent of the time will continue to do so whether it is racing against fields of 5 or of 11. But when the researchers looked at horse-race data from 1992 through 2001—a total of 6.3 million starts—they found that bettors were subject to the partition bias, believing that long-shot horses had higher odds of winning when they were racing against fewer horses.

While partition dependence has been looked at in the past in specific lab experiments, it hadn't been studied in prediction markets, Camerer says. What makes this particular analysis powerful is that the researchers observed evidence for this phenomenon in a wide range of studies—short, well-controlled laboratory experiments; markets involving intelligent, well-informed traders at major financial institutions; and nine years of horse-racing data.

The title of the PNAS paper is "How psychological framing affects economic market prices in the lab and field." In addition to Camerer, the other authors are Ulrich Sonnemann and Thomas Langer at the University of Münster, Germany, and Craig Fox at UCLA. Their research was supported by the German Research Foundation, the National Science Foundation, the Gordon and Betty Moore Foundation, and the Human Frontier Science Program.

http://www.eurekalert.org/pub_releases/2013-07/uoh-ntf070113.php

New treatment for schizophrenia discovered in Finland

With very large doses of famotidine, sufficient amounts can penetrate the blood-brain barrier to affect the histamine system in the brain

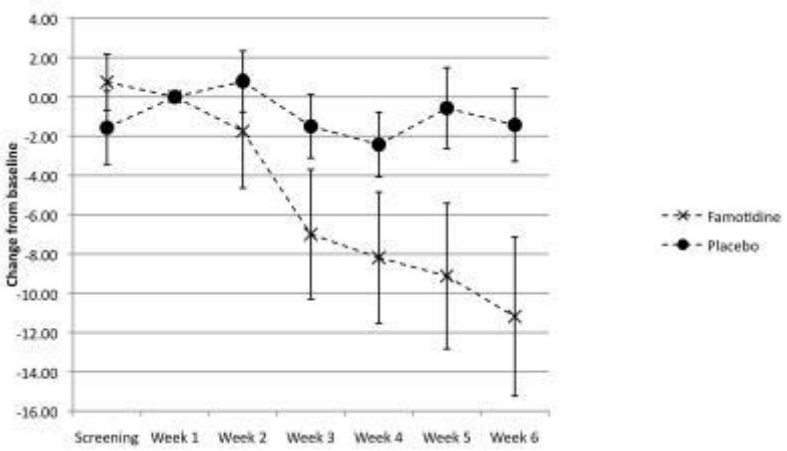
A research group led by professor Jesper Ekelund showed that by giving a very large dose of famotidine (200 mg daily), sufficient amounts of the drug are able to penetrate the so-called blood-brain barrier to affect the histamine system in the brain.

Famotidine has been used for the treatment of heartburn since the 1980s, but at regular dosing, famotidine almost does not enter the brain at all, since the brain is protected by the blood-brain barrier. By increasing the dosage five-fold the drug is able to enter the brain and affect the histamine system.

- Already after one week the symptoms of persons suffering from schizophrenia started to decrease and after four weeks of treatment the symptoms had decreased statistically significantly. The patients that participated in the study were also positively disposed towards the treatment, says Ekelund.

Thirty persons suffering from schizophrenia participated in the study. The patients had been on sickness pension for at least five years. They were randomly divided into two groups, one which received famotidine and one which received placebo. All of the patients who took famotidine responded positively to the treatment while the symptoms of those who were on a placebo did not change.

Schizophrenia is the most common and severe psychotic disorder, and is the cause of at least half of all psychiatric hospital treatment days. No randomized, controlled trials in humans that test the effect of H2 blockade in schizophrenia have been published so far.



This shows the change in symptoms (PANSS score) during the study. **J. Ekelund / University of Helsinki**

Innovation in psychiatric medication urgently needed

Since 1963, when the subsequent Nobel prize winner Arvid Carlsson showed that dopamine has a central role in psychosis, the so called dopamine-hypothesis has been central in psychosis. All presently available medications for psychosis are based around this principle. Since treatment response is all too often incomplete and side effects common, there is still a great, unmet medical need for medications with other mechanisms of action. Many other signaling substances have been the focus of attention, but so far, the brain histamine system has most widely been regarded as important only with regard to side effects of many psychosis medications.

- Famotidine shouldn't be used directly as treatment for schizophrenia until long-term use of a dose of this size has been proved safe. However, our study shows that the histamine system in the brain offers a novel approach to treating psychosis. This should lead to increased efforts by the pharmaceutical industry to develop medications based on this histamine-based mechanism, says Ekelund.

Famotidine works by blocking the histamine H2 receptor. There are important neurons in the brain that use histamine as their primary signaling substance. These neurons have an important role as regulators of other signaling substances. From animal research, it is known that by affecting the histamine system, one can also affect other signaling substances that are known to be involved in schizophrenia.

The project has already received international recognition. Katarina Meskanen, one of the members of Ekelunds research group, was awarded the Young Scientist Award of the SCNP (Scandinavian College of Neuropsychopharmacology) and the project has been awarded substantial funding (306,000 USD) from the Stanley foundation for follow-up studies.

The research group will replicate the finding through a larger, multinational study in collaboration with Karolinska Institutet in Sweden, where the study is coordinated by professor Jari Tiihonen.

http://www.eurekalert.org/pub_releases/2013-07/uons-cmo070113.php

Curious mix of precision and brawn in a pouched super-predator

A bizarre, pouched super-predator that terrorized South America millions of years ago had huge sabre-like teeth but its bite was weaker than that of a domestic cat, new research shows.

SYDNEY: Australian and American marsupials are among the closest living relatives of the extinct Thylacosmilus atrox, which had tooth roots extending rearwards almost into its small braincase.

"Thylacosmilus looked and behaved like nothing alive today," says University of New South Wales palaeontologist, Dr Stephen Wroe, leader of the research team.

"To achieve a kill the animal must have secured and immobilised large prey using its extremely powerful forearms, before inserting the sabre-teeth into the windpipe or major arteries of the neck – a mix of brute force and delicate precision." The iconic North American sabre-toothed 'tiger', Smilodon fatalis, is often regarded as the archetypal mammalian super-predator.

However, Smilodon - a true cat - was just the end point in one of at least five independent 'experiments' in sabre-tooth evolution through the Age of Mammals, which spanned some 65 million years.

Thylacosmilus atrox is the best preserved species of one of these evolutionary lines - pouched sabre-tooths that terrorised South America until around 3.5 million years ago.

For its size, its huge canine teeth were larger than those of any other known sabre-tooth.

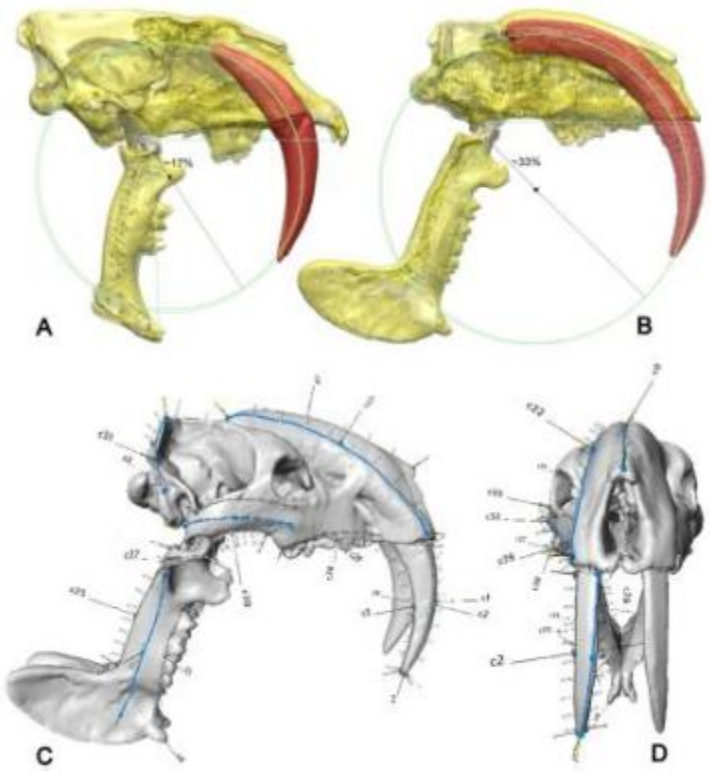
Smilodon's killing behaviour has long attracted controversy, but scientists now mostly agree that powerful neck muscles, as well as jaw muscles, played an important role in driving the sabre-teeth into the necks of large prey.

Little was known about the predatory behaviour in the pouched Thylacosmilus.

To shed light on this super-predator mystery, Dr Wroe's team of Australian and US scientists constructed and compared sophisticated computer models of Smilodon and Thylacosmilus, as well as a living conical-toothed cat, the leopard. These models were digitally 'crash-tested' in simulations of biting and killing behaviour. The results are published in the journal PLoS ONE.

"We found that both sabre-tooth species were similar in possessing weak jaw-muscle-driven bites compared to the leopard, but the mechanical performance of the sabre-tooths skulls showed that they were both well-adapted to resist forces generated by very powerful neck muscles," says Dr Wroe.

"But compared to the placental Smilodon, Thylacosmilus was even more extreme."



This shows cut away views through the skulls of (A) the sabre-toothed 'tiger' (Smilodon) and (B) the bizarre pouched sabre-tooth (Thylacosmilus). Note the incredibly wide gape and huge canine teeth with roots extending almost into the braincase of Thylacosmilus. **Credit: S. Wroe**

"Frankly, the jaw muscles of Thylacosmilus were embarrassing. With its jaws wide open this 80-100 kg 'super-predator' had a bite less powerful than a domestic cat. On the other hand - its skull easily outperformed that of the placental Smilodon in response to strong forces from hypothetical neck muscles."

"Bottom line is that the huge sabres of Thylacosmilus were driven home by the neck muscles alone and - because the sabre-teeth were actually quite fragile - this must have been achieved with surprising precision."

"For Thylacosmilus - and other sabre-tooths - it was all about a quick kill."

"Big prey are dangerous – even to super-predators – and the faster the kill the less likely it is that the predator will get hurt – or for that matter attract unwanted attention from other predators."

"It may not have been the smartest of mammalian super-predators – but in terms of specialisation – Thylacosmilus took the already extreme sabre-tooth lifestyle to a whole new level," says Dr Wroe.

http://www.eurekalert.org/pub_releases/2013-07/uob-rnc070113.php

Removing nerves connecting kidney to the brain shown to reduce high blood pressure

New technique is safe and effective in hard-to-treat cases

A new technique that involves removing the nerves connecting the kidney to the brain has shown to significantly reduce blood pressure and help lower the risk of stroke, heart and renal disease in patients. The procedure, which has very few side effects, has already shown promising results in hard-to-treat cases of high blood pressure.

The technique, published in the journal Hypertension, was performed by a team led by Professor Julian Paton at the University of Bristol who found that in an animal model of hypertension removing nerves connecting the kidney to the brain reduced blood pressure and improved its long-term stability.

Inspired by these results, cardiologists Dr Angus Nightingale and Dr Andreas Baumbach from the Bristol Heart Institute (BHI) adopted the technique called "renal denervation" to remove the nerves to the kidney in patients with high blood pressure.

The procedure, which has been successfully trialled on 19 patients at the BHI, is performed using a fine tube that is inserted in an artery in the patient's leg and positioned in the artery feeding blood to the patient's kidneys. The nerves to the kidney are around the artery and ablated by radio-frequency energy that is emitted from the tube.

The breakthrough is due to a new collaboration involving scientists at the University of Bristol and cardiologists at the BHI, who have joined forces to form the CardioNomics high blood pressure team. Together, they hope to tackle this major health problem by taking findings from the laboratory and translating them into

clinical practice. The CardioNomics team have just been awarded £100,000 grant from Medtronic to further improve the technique and expand patient trials.
Dr Nightingale, who runs the Specialist Hypertension Clinic at the BHI, said: "We have used renal denervation in patients who have hard-to-treat blood pressure. Similar to the results from the basic science experiments, we have also seen reductions in blood pressure which has been essential for reducing the risk of heart and renal disease, and stroke in our patients. This is an exciting new treatment for these patients who have struggled with high blood pressure which tablets are not controlling."
Dr Baumbach, an interventional cardiologist who performed the treatment, added: "The technique is very straight forward, performed as a day case and there are no side-effects. It is becoming a popular technique for patients with both resistance and poor tolerability to high blood pressure medication."
Professor Julian Paton, who led the research at the University's School of Physiology and Pharmacology, said: "The problem with high blood pressure is that patients develop resistance to their tablets or unpleasant side effects. Our new interventional approaches are based on studies where we have found causative mechanisms generating high blood pressure so we think that they will be most efficacious in patients. And, with luck, they will also mean less pill taking too."
This study is published in the journal Hypertension and is entitled 'Translational examination of changes in baroreceptor reflex function after bilateral renal denervation in hypertensive rats and humans'. The hypertension research team at the Bristol Heart Institute specialises in treating patients with hypertension and is trialling numerous drug-free interventional therapies.

http://www.eurekalert.org/pub_releases/2013-07/acs-nac070113.php

New American Chemical Society video focuses on ancient secrets of alchemy

Bytesize Science's new video presents alchemy and its quest for the "Philosopher's Stone"

The pursuit that obsessed some of the world's greatest geniuses for centuries - alchemy and its quest for the "Philosopher's Stone" that would transform lead and other base metals into gold - is the topic of a new episode in the American Chemical Society Bytesize Science video series. The video, from the world's largest scientific society, is at http://www.BytesizeScience.com.
It features Laurence Principe, Ph.D., a noted historian of science and expert on alchemy, which, far from being solely a misguided pseudoscience, helped set the stage for the emergence of modern science. Principe, who is with the Johns Hopkins University, shows viewers how to decipher cryptic alchemical symbols, images and texts. He explains how alchemists worked almost exclusively in symbols and codes to protect the powers of alchemy from falling into the wrong hands. Instead of recipes and chemical formulas, alchemists created woodcut prints and images of dragons, warriors and monsters — all symbolic representations of chemical ingredients.
Principe used these historical artifacts to recreate experiments once performed by alchemists. His lab features a collection of authentic alchemical tools and apparatuses, all used to perform alchemical experiments as accurately as possible.
For more entertaining, informative science videos and podcasts from the ACS Office of Public Affairs, view Prized Science, Spellbound, Science Elements and Global Challenges/Chemistry Solutions

http://www.eurekalert.org/pub_releases/2013-07/uoc--ua070113.php

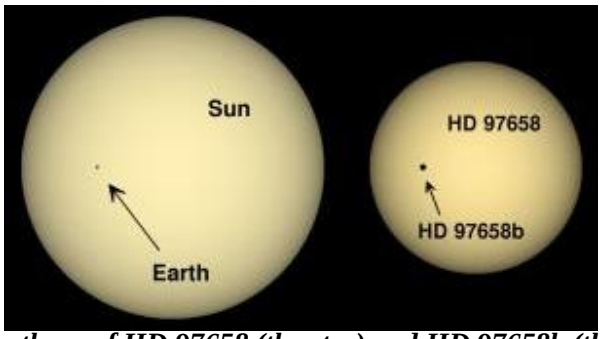
UCSB astronomer uncovers the hidden identity of an exoplanet

Hovering about 70 light-years from Earth - that's "next door" by astronomical standards - is a star astronomers call HD 97658, which is almost bright enough to see with the naked eye.

Santa Barbara, Calif. - But the real "star" is the planet HD 97658b, not much more than twice the Earth's diameter and a little less than eight times its mass. HD 97658b is a super-Earth, a class of planet for which there is no example in our home solar system.
While the discovery of this particular exoplanet is not new, determining its true size and mass is, thanks to Diana Dragomir, a postdoctoral astronomer with UC Santa Barbara's Las Cumbres Observatory Global Telescope (LCOGT). As part of her research, Dragomir looked for transits of this exoplanet with Canada's Microvariability & Oscillations of Stars (MOST) space telescope. The telescope was launched in 2003 to a pole-over-pole orbit about 510 miles high. Dragomir analyzed the data using code written by LCOGT postdoctoral fellow Jason Eastman. The results were published online today in the Astrophysical Journal Letters.
A super-Earth is an exoplanet with a mass and radius between those of the Earth and Neptune. Don't be fooled by the moniker though. Super-Earth refers to the planet's mass and does not imply similar temperature, composition, or environment to Earth. The brightness of HD 97658 means astronomers can study this star and planet in ways not possible for most of the exoplanet systems that have been discovered around fainter stars.

HD 97658b was discovered in 2011 by a team of astronomers using the Keck Observatory and a technique sometimes called Doppler wobble. But only a lower limit could be set on the planet's mass, and nothing was known about its size.

Transits, such as those observed by Dragomir, occur when a planet's orbit carries it in front of its parent star and reduces the amount of light we see from the star ever so slightly. Dips in brightness happen every orbit, if the orbit happens to be almost exactly aligned with our line of sight from Earth. For a planet not much bigger than our Earth around a star almost as big as our Sun, the dip in light is tiny but detectable by the ultraprecise MOST space telescope.



This image shows the relative size of the Earth and Sun next to those of HD 97658 (the star) and HD 97658b (the super-Earth exoplanet). **Jason Eastman and Diana Dragomir**

The first report of transits in the HD 97658 system in 2011 turned out to be a false alarm. That might have been the end of the story, but Dragomir knew that the ephemeris of the planet's orbit (a timetable to predict when the planet might pass in front of the star) was not exact. She convinced the MOST team to widen the search parameters, and during the last possible observing window for this star last year, the data showed tantalizing signs of a transit — tantalizing, but not certain beyond doubt. A year later, MOST revisited HD 97658 and found clear evidence of the planet's transits, allowing Dragomir and the MOST team to estimate the planet's true size and mass for the first time.

"Measuring an exoplanet's size and mass leads to a determination of its density, which in turn allows astronomers to say something about its composition," Dragomir said. "Measuring the properties of super-Earths in particular tells us whether they are mainly rocky, water-rich, mini gas giants, or something entirely different."

The average density of HD 97658b is about four grams per cubic centimeter, a third of the density of lead but denser than most rocks. Astronomers see great significance in that value - about 70 percent of the average density of Earth - since the surface gravity of HD 97658b could hold onto a thick atmosphere. But there's unlikely to be alien life breathing those gases. The planet orbits its sun every 9.5 days, at a distance a dozen times closer than we are from our Sun, which is too close to be in the Habitable Zone, nicknamed The Goldilocks Zone. The Goldilocks nickname is apropos: If a planet is too close to its star, it's too hot; if it's too far away, it's too cold, but if it's in the zone, it's "just right" for liquid water oceans, one condition that was necessary for life here on Earth.

Over the past few years, systems with massive planets at very small orbital radii have proved to be quite common despite being generally unexpected. The current number of confirmed exoplanets exceeds 600, with the vast majority having been discovered by radial velocity surveys. These are severely biased toward the detection of systems with massive planets (roughly the mass of Jupiter) in small orbits. Bucking that trend is HD 97658b, which orbits its star at a distance farther than many of the currently known exoplanets. HD 97658b is only the second super-Earth known to transit a very bright star.

"This discovery adds to the still small sample of transiting super-Earths around bright stars," said Dragomir. "In addition, it has a longer period than many known transiting exoplanets around bright stars, including 55 Cnc e, the only other super-Earth in this category. The longer period means it is cooler than many closer-in exoplanets, so studying HD 97658b's properties is part of the progression toward understanding what exoplanets in the habitable zone might be like."

http://www.sciencedaily.com/releases/2013/07/130701100602.htm

Discovery Sheds Light On Why Alzheimer's Drugs Rarely Help

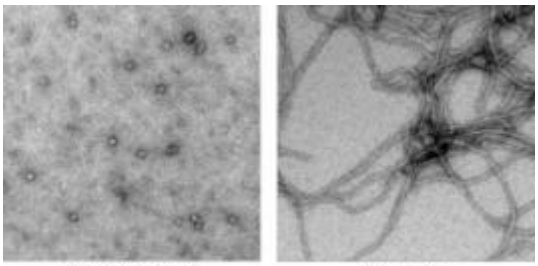
Current medications do not treat Alzheimer's or stop it from progressing

The Alzheimer's Association projects that the number of people living with Alzheimer's disease will soar from 5 million to 13.8 million by 2050 unless scientists develop new ways to stop the disease. Current medications do not treat Alzheimer's or stop it from progressing; they only temporarily lessen symptoms, such as memory loss and confusion.

Current Alzheimer's drugs aim to reduce the amyloid plaques -- sticky deposits that build up in the brain--that are a visual trademark of the disease. The plaques are made of long fibers of a protein called Amyloid β, or Aβ. Recent studies, however, suggest that the real culprit behind Alzheimer's may be small Aβ clumps called oligomers that appear in the brain years before plaques develop.

In unraveling oligomers' molecular structure, UCLA scientists discovered that Aβ has a vastly different organization in oligomers than in amyloid plaques. Their finding could shed light on why Alzheimer's drugs designed to seek out amyloid plaques produce zero effect on oligomers.

The UCLA study suggests that recent experimental Alzheimer's drugs failed in clinical trials because they zero in on plaques and do not work on oligomers. Future studies on oligomers will help speed the development of new drugs specifically aiming at Aβ oligomers.



Current Alzheimer's drugs target the amyloid fibers (on right), which have a vastly different molecular structure than amyloid oligomers (on left), the likely culprit behind the disease. The UCLA findings may shed light on why existing Alzheimer's drugs produce limited effect. **UCLA/Gao lab**

The study was published as Paper of the Week in the June 28 issue of the peer-reviewed Journal of Biological Chemistry.

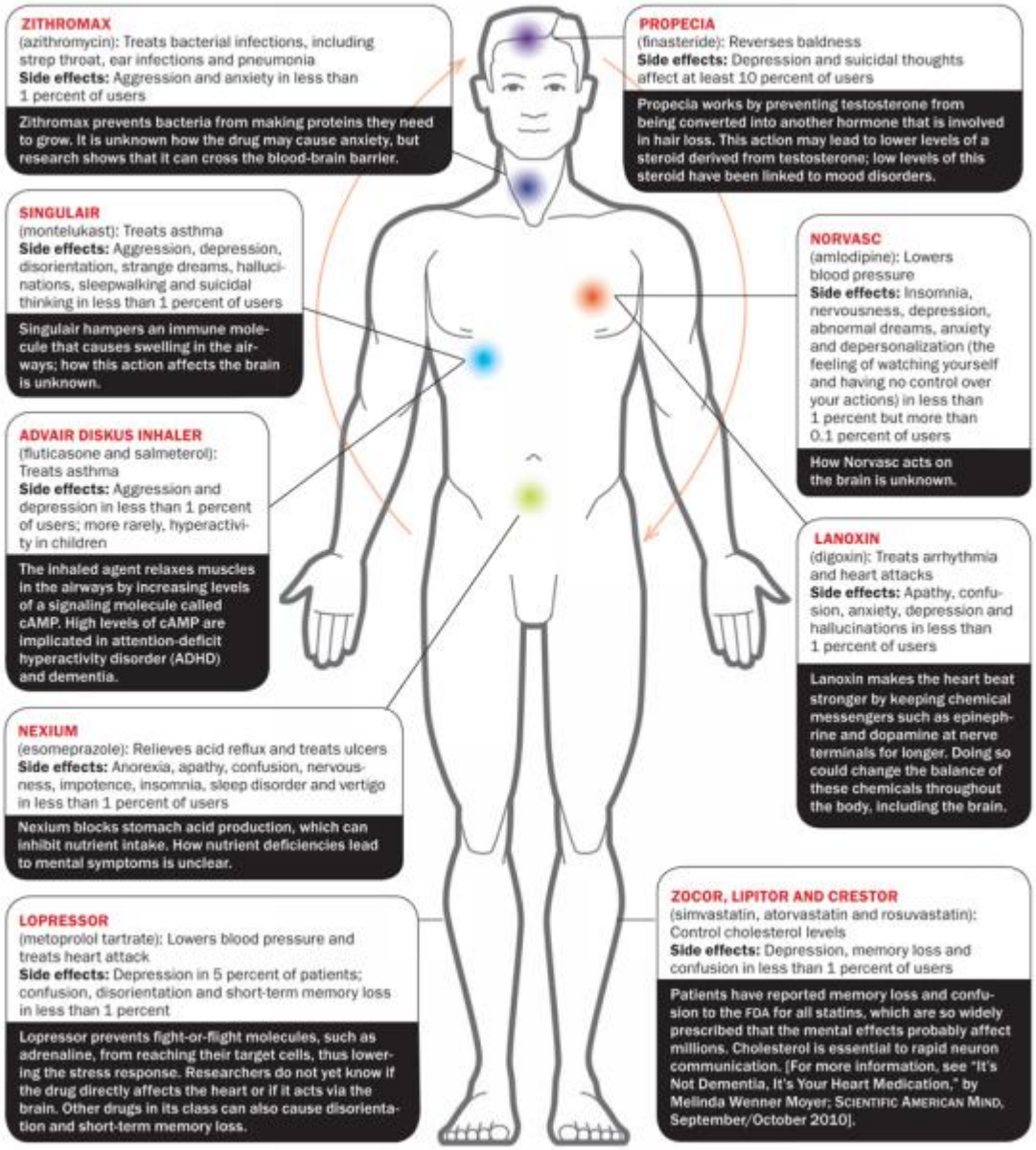
http://bit.ly/12yBKqF

These Body Drugs Can Affect the Mind

Bad mood? Sleep loss? Memory trouble? Check your prescriptions

By Luciana Gravotta | July 1, 2013 | 9

Many drugs that treat bodily ills can alter mood, memory and other mental functions. Often the trials required to approve new drugs miss these uncommon side effects, but when the medications go on the market and are doled out to millions, thousands of people can be at risk. The drugs listed below are some of the most commonly prescribed in America; each one (including its generic versions) likely causes at least 10,000 patients—some, more than 100,000—to experience mental side effects every year.



http://news.yale.edu/2013/07/01/yale-team-finds-nicotinic-receptor-essential-cognition-and-mental-health

Yale team finds nicotinic receptor essential for cognition — and mental health

Stimulation of the nicotinic alpha7 receptors allows the cells to communicate and thus generate higher cognition.

By Bill Hathaway

Nicotinic alpha7 receptors (indicated by red arrowheads) are next to a synapse between two brain cells in the prefrontal cortex. Stimulation of the nicotinic alpha7 receptors allows the cells to communicate and thus generate higher cognition. (Image from Dr. C. Paspalas, Yale University)

The ability to maintain mental representations of ourselves and the world — the fundamental building block of human cognition — arises from the firing of highly evolved neuronal circuits, a process that is weakened in schizophrenia. In a new study, researchers at Yale University School of Medicine pinpoint key molecular actions of proteins that allow the creation of mental representations necessary for higher cognition that are genetically altered in schizophrenia. The study was released July 1 in the Proceedings of the National Academy of Sciences,

Working memory, the mind's mental sketch pad, depends upon the proper functioning of a network of pyramid-shaped brain cells in the prefrontal cortex, the seat of higher order thinking in humans. To keep information in the conscious mind, these pyramidal cells must stimulate each other through a special group of receptors. The Yale team discovered this stimulation requires the neurotransmitter acetylcholine to activate a specific protein in the nicotinic family of receptors — the alpha7 nicotinic receptor.

Acetycholine is released when we are awake — but not in deep sleep. These receptors allow prefrontal circuits to come "online" when we awaken, allowing us to perform complex mental tasks. This process is enhanced by caffeine in coffee, which increases acetylcholine release. As their name suggests, nicotinic alpha-7 receptors are also activated by nicotine, which may may help to explain why smoking can focus attention and calm behavior, functions of the prefrontal cortex.

The results also intrigued researchers because alpha7 nicotinic receptors are genetically altered in schizophrenia, a disease marked by disorganized thinking. "Prefrontal networks allow us to form and hold coherent thoughts, a process that is impaired in schizophrenia," said Amy Arnsten, professor of neurobiology, investigator for Kavli Institute, and one of the senior authors of the paper. "A great majority of schizophrenics smoke, which makes sense because stimulation of the nicotinic alpha7 receptors would strengthen mental representations and lessen thought disorder."

Arnsten said that new medications that stimulate alpha-7 nicotinic receptors may hold promise for treating cognitive disorders.

Publication of the PNAS paper comes on the eve of the 10th anniversary of the death of Yale neurobiologist Patricia Goldman-Rakic, who was hit by a car in Hamden Ct. on July 31, 2003. Goldman-Rakic first identified the central role of prefrontal cortical circuits in working memory.

"Patricia's work has provided the neural foundation for current studies of molecular influences on cognition and their disruption in cognitive disorders," said Arnsten. "Our ability to apply a scientific approach to perplexing disorders such as schizophrenia is due to her groundbreaking research."

Yang Yang and Min Wang of Yale are lead author and co-senior authors, respectively. Constaninos D. Paspalas, Lu E Jin and Marina R. Picciotto are other Yale authors.

Yang Yang, Constantinos D. Paspalas, Lu E. Jin, Marina R. Picciotto, Amy F. T. Arnsten, and Min Wang. Nicotinic α7 receptors enhance NMDA cognitive circuits in dorsolateral prefrontal cortex. PNAS, 2013 DOI: 10.1073/pnas.1307849110

http://scitechdaily.com/glymphatic-system-may-hold-a-key-to-treating-alzheimers/

Glymphatic System May Hold a Key to Treating Alzheimer's

Alzheimers May Result From a Slowing Down of the Glymphatic System

Newly published research details how a better understanding of the glymphatic system and its process of slowing down as we age may result in new methods for treating Alzheimer's and other neurodegenerative diseases.

In a perspective piece appearing in the journal Science, researchers at University of Rochester Medical Center (URMC) point to a newly discovered system by which the brain removes waste as a potentially powerful new tool to treat neurological disorders like Alzheimer's disease. In fact, scientists believe that some of these conditions may arise when the system is not doing its job properly.

"Essentially all neurodegenerative diseases are associated with the accumulation of cellular waste products," said Maiken Nedergaard, M.D., D.M.Sc., co-director of the URMC Center for Translational Neuromedicine and author of the article. "Understanding and ultimately discovering how to modulate the brain's system for removing toxic waste could point to new ways to treat these diseases."

The body defends the brain like a fortress and rings it with a complex system of gateways that control which molecules can enter and exit. While this "blood-brain barrier" was first described in the late 1800s, scientists are only now just beginning to understand the dynamics of how these mechanisms function. In fact, the complex network of waste removal, which researchers have dubbed the glymphatic system, was only first disclosed by URMC scientists last August in the journal Science Translational Medicine.

The removal of waste is an essential biological function and the lymphatic system – a circulatory network of organs and vessels – performs this task in most of the body. However, the lymphatic system does not extend to the brain and, consequently, researchers have never fully understood what the brain does its own waste. Some scientists have even speculated that these byproducts of cellular function where somehow being "recycled" by the brain's cells.

One of the reasons why the glymphatic system had long eluded comprehension is that it cannot be detected in samples of brain tissue. The key to discovering and understanding the system was the advent of a new imaging technology called two-photon microscopy which enables scientists to peer deep within the living brain. Using this technology on mice, whose brains are remarkably similar to humans, Nedergaard and her colleagues were able to observe and document what amounts to an extensive, and heretofore unknown, plumbing system responsible for flushing waste from throughout the brain.

The brain is surrounded by a membrane called the arachnoid and bathed in cerebral spinal fluid (CSF). CSF flows into the interior of the brain through the same pathways as the arteries that carry blood. This parallel system is akin to a donut shaped pipe within a pipe, with the inner ring carrying blood and the outer ring carrying CSF. The CSF is draw into brain tissue via a system of conduits that are controlled by a type support cells in the brain known as glia, in this case astrocytes. The term glymphatic was coined by combining the words glia and lymphatic.

The CSF is flushed through the brain tissue at a high speed sweeping excess proteins and other waste along with it. The fluid and waste are exchanged with a similar system that parallels veins which carries the waste out of the brain and down the spine where it is eventually transferred to the lymphatic system and from there to the liver, where it is ultimately broken down.

While the discovery of the glymphatic system solved a mystery that had long baffled the scientific community, understanding how the brain removes waste – both effectively and what happens when this system breaks down – has significant implications for the treatment of neurological disorders.

One of the hallmarks of Alzheimer's disease is the accumulation in the brain of the protein beta amyloid. In fact, over time these proteins amass with such density that they can be observed as plaques on scans of the brain. Understanding what role the glymphatic system plays in the brain's inability to break down and remove beta amyloid could point the way to new treatments. Specifically, whether certain key 'players' in the glymphatic system, such as astrocytes, can be manipulated to ramp up the removal of waste.

"The idea that 'dirty brain' diseases like Alzheimer may result from a slowing down of the glymphatic system as we age is a completely new way to think about neurological disorders," said Nedergaard. "It also presents us with a new set of targets to potentially increase the efficiency of glymphatic clearance and, ultimately, change the course of these conditions."

Publication: Maiken Nedergaard, "Garbage Truck of the Brain," Science 28 June 2013: Vol. 340 no. 6140 pp. 1529-1530; DOI: 10.1126/science.1240514 Source: University of Rochester Medical Center

http://www.eurekalert.org/pub_releases/2013-07/yu-hcs070213.php

How cancer spreads: Metastatic tumor a hybrid of cancer cell and white blood cell

A human metastatic tumor can arise when a leukocyte and a cancer cell fuse to form a genetic hybrid

Yale Cancer Center scientists, together with colleagues at the Denver Police Crime Lab and the University of Colorado, have found evidence that a human metastatic tumor can arise when a leukocyte (white blood cell) and a cancer cell fuse to form a genetic hybrid. Their study, published in the journal PLOS ONE, may answer the question of how cancer cells travel from the primary tumor's site of origin to distant organs and tissues of the body — the deadly process of metastasis.

Such a theory was first proposed as an explanation for metastasis more than a century ago. But until now, the theory was unproven in human cancer because genomic differences between cells from the same patient cannot be distinguished. To get around this problem, the researchers analyzed genomic DNA in the secondary malignancies of a patient who had a melanoma brain metastasis and had received a bone marrow transplant from his brother.

They found signature genes from both the patient and donor together in the tumor cells, providing the first evidence that leukocytes (in this case from the donor) can fuse with cancer cells and initiate a tumor.

"Our results provide the first proof in humans of a theory, proposed in 1911 by a German pathologist, that metastasis can occur when a leukocyte and cancer cell fuse and form a genetic hybrid," said corresponding author John Pawelek, research faculty in the dermatology department of the Yale School of Medicine. "This could open the way to new therapy targets, but much work needs to be done to determine how fusion occurs, the frequency of such hybrids in human cancers, and the potential role of hybrids in metastasis," he added.
First authors are Rossitza Lazova of Yale and Greggory LaBerge of the University of Colorado and Denver Police Department Crime Lab; other authors are Vincent Klump, Mario Sznol, Dennis Cooper, and Joseph Chang of Yale; Eric Duvall of the Denver Police Crime Lab; and Nicole Spoelstra and Richard Spritz of the University of Colorado.
The study was supported by an unrestricted gift from the Amway Corporation and from the University of Colorado Cancer Center NCI Support Grant (P30CA046934).

http://boingboing.net/2013/07/01/former-seti-director-explains.html

Former SETI director explains what will happen when extraterrestrials contact us

Just over 30 years ago this month, E.T., The Extra-Terrestrial hit the big screen and made everyone feel warm and fuzzy about aliens with E.T.'s sweetly urgent message about wanting to "phone home."

Camille Sweeney and Josh Gosfield at 10:00 am Mon, Jul 1, 2013

This summer, Hollywood alien fare paints a far gloomier picture with a deadly alien monster in After Earth, a zombie invasion in World War Z, giant robots in Pacific Rim and more robot invaders in The World's End. But what do the experts really think?
We asked astronomer, Jill Tarter, the TED Prize–winning, former director of the world's most ambitious search for alien life at the Center for the Search for Extraterrestrial Intelligence (SETI) Research, who we interviewed on "How to Find Extraterrestrial Life" for our book on success, The Art of Doing. Tarter gave us SETI's 9-point plan should there be an extraterrestrial attempt of any kind to contact us:

Open the champagne (currently a bottle of $10 Freixenet sitting in the observatory fridge).
Verify our findings.
Get independent confirmation from a qualified facility to make sure it's not a hoax.
Call the directors of all SETI-related observatories.
Send out an official notice of discovery that goes to all the astronomical observatories of the world.
Inform our major donors.
Complete and immediately send for publication the scientific paper we've already prepared a template for.
Alert our interpreters, astronomers designated to explain our findings to regional and local news media.
Hold a press conference to announce the discovery to the world, because the signal isn't being sent to our observatory in California, it's being sent to planet Earth and planet Earth deserves to know about it.

"Carl Sagan envisioned such a moment as a circus springing up and surrounding the discovery site," Tarter told us. "Stephen Hawking believes that firing back something immediately could get the whole neighborhood destroyed and others believe that kind of attitude is rooted in paranoia. So our mandate is to wait for a calm and reasoned global consensus on what to say and how to say it. Then again, once a signal has been detected, anyone with a transmitter can get on the horn and shout back out whatever they want."
Something else to consider, Tarter noted, was summed up in the words of a SETI facility director: "Honestly, I wouldn't know whether to call for protection or port-a-potties."
Josh Gosfield and Camille Sweeney are authors of The Art of Doing: How Superachievers Do What They Do and How They Do It So Well.

http://www.medscape.com/viewarticle/807274?src=rss

Migraine Really Is a Brain Disorder

Positron emission tomography of patients experiencing the premonitory phase of migraine, prior to the headache setting in, shows activation in several areas of the brain, indicating that migraine is a brain disorder and not a response to pain stimuli.

Pauline Anderson

BOSTON, Massachusetts - The results are significant in terms of understanding the neurobiology of migraine and could have future implications for drug treatment, said study author Peter James Goadsby, MD, PhD, professor, neurology, and director, Headache Program, University of California at San Francisco, and president, International Headache Society.
"This is an important step in solidifying our ideas that migraine is fundamentally a disorder of the brain, not a disorder of structures outside the brain," said Dr. Goadsby. "We were able to address the question that people have wondered about for many, many years, that is, what is the degree to which pain is driving the initial symptomatology — and we got clear answers to that."
Dr. Goadsby and his colleagues won the Harold G. Wolff Lecture Award for this research during the 2013 International Headache Congress (IHC).

Subtle Symptoms

Premonitory symptoms of migraine can include yawning, neck discomfort, nausea, thirst, photophobia, phonophobia, craving sweet or savory foods, and mood swings. It's not clear what proportion of patients with migraine experience these early symptoms, which are often quite subtle, Dr. Goadsby said. Estimates vary widely, from about a third to 80%.

In the past, this symptomatology has not received much medical attention, said Dr. Goadsby. Physicians might not ask about premonitory symptoms because this information doesn't influence their diagnosis.

In years gone by, people used to think of migraine as a disorder of the blood vessels. In more recent times, the view has been that migraine is a reaction to pain stimuli. "I think our new research suggests that this is just not true," said Dr. Goadsby.

Using nitroglycerin, a well-documented trigger for migraine, researchers induced premonitory symptoms in patients who have migraine without aura. Instead of waiting for headache onset to begin scanning the patients' brains, as has been done in the past, researchers did the scanning during the premonitory phase. Eight patients had at least 1 premonitory scan without pain.

"Before this, all the imaging of migraine has been during the headache and the question has risen as to the degree to which what's happening in the brain is just a response to pain, or is something more fundamental, a part of the process of the migraine," said Dr. Goadsby. "By studying the premonitory symptoms, you get rid of that question because these patients don't have any pain."

Neuronal Activation

Researchers used H2 15O (radioactive water) to measure regional cerebral blood flow as a surrogate marker for neuronal activation.

They found that compared with baseline scans, there was activation in several key areas, including the hypothalamus, an area involved in low-level regulation of sleep, appetite, mood, and fluids. "It seems likely that the hypothalamus is pivotal in the onset of migraine," commented Dr. Goadsby.

Other structures that were activated included the midbrain, around the periaqueductal grey, which has been shown to be active during a migraine attack, and an area in the pons that past migraine imaging has also shown to be active.

"This shows you the areas of the brain that are involved at the earliest in the attack," said Dr. Goadsby.

Scans of the 8 patients plus another 2 patients experiencing photophobia symptoms, again before they felt any pain, showed activation in the visual cortex. "This suggests that the photophobia experience can be dissected away from the pain experience," said Dr. Goadsby.

Similarly, scans of patients experiencing nausea had activation of an area of the medulla that includes nausea and vomiting centers. "So it's entirely plausible that those areas are activated by the migraine process and that's why nausea and vomiting are so common in migraine; it's not simply a response to the pain," said Dr. Goadsby. "It was thought that nausea and pain were highly linked, but that doesn't seem to necessarily be the case," he added.

Dr. Goadsby hopes the research will "shift thinking" to consider migraine as a brain disorder, but he stressed that this should not lessen the importance of the pain that migraine patients suffer.

From a big picture treatment perspective, this says to me that we probably won't get away with developing drugs that don't get into the brain to have substantial effects on migraine prevention. Dr. Peter James Goadsby

The research could have ramifications for treatment in that the most obvious target would be the brain, but developing targeted therapies that don't have adverse effects could be challenging.

"From a big picture treatment perspective, this says to me that we probably won't get away with developing drugs that don't get into the brain to have substantial effects on migraine prevention," said Dr. Goadsby.

He noted that to date, the best proven migraine prevention therapies are anticonvulsant drugs, tricyclic antidepressants, and the β-blocker propranolol, all of which affect the brain. This, he said, is consistent with the theory that migraine is a disorder of the brain.

Relevant to Clinicians

Asked to comment on the study, Elizabeth E. Loder, MD, president, American Headache Society, associate professor, neurology, Harvard Medical School, and head, Division of Headache and Pain, Brigham and Women's Hospital, Boston, said it's nice to have a biological explanation for what patients experience and that the research might eventually lead to treatment.

"I was particularly heartened by the fact that this year's winner [of the Wolff Lecture Award] was able to say so many things that were relevant to clinicians," said Dr. Loder. "We all see patients who describe knowing through various signs and symptoms that they are likely to get a migraine attack and it's good to hear what the biological underpinnings for that recognition of an impending attack might be."

Dr. Loder said she and her colleagues wonder how this new information might be exploited to prevent attacks, not only with drugs but also behaviorally.
She doesn't think clinicians ignore the premonitory phase of migraine so much as lack the evidence to support making recommendations about what to do in these circumstances. "Most patients…already know what to do; for example, if they're hungry and feel an attack coming that eating may help or to putting sunglasses on in a bight sunny place."
Dr. Goadsby has received consulting fees/honoraria from Allergen, CoLucid, MSP, MSD, eNeura, ATI, Boston Sci, Eli Lilly, Medtronic, BMS, Pfizer, Nevro Corp, Impax, Zogenix, and Dr. Reddy's and research grants from MAP, MSD, Amgen, and Electrocore.

http://www.eurekalert.org/pub_releases/2013-07/aaon-dba062613.php

Does being a bookworm boost your brainpower in old age?

New research suggests that reading books, writing and participating in brain-stimulating activities at any age may preserve memory.

MINNEAPOLIS –The study is published in the July 3, 2013, online issue of Neurology®, the medical journal of the American Academy of Neurology.
"Our study suggests that exercising your brain by taking part in activities such as these across a person's lifetime, from childhood through old age, is important for brain health in old age," said study author Robert S. Wilson, PhD, with Rush University Medical Center in Chicago.
For the study, 294 people were given tests that measured memory and thinking every year for about six years before their deaths at an average age of 89. They also answered a questionnaire about whether they read books, wrote and participated in other mentally stimulating activities during childhood, adolescence, middle age and at their current age.
After they died, their brains were examined at autopsy for evidence of the physical signs of dementia, such as lesions, brain plaques and tangles.
The research found that people who participated in mentally stimulating activities both early and late in life had a slower rate of decline in memory compared to those who did not participate in such activities across their lifetime, after adjusting for differing levels of plaques and tangles in the brain. Mental activity accounted for nearly 15 percent of the difference in decline beyond what is explained by plaques and tangles in the brain.
"Based on this, we shouldn't underestimate the effects of everyday activities, such as reading and writing, on our children, ourselves and our parents or grandparents," said Wilson.
The study found that the rate of decline was reduced by 32 percent in people with frequent mental activity in late life, compared to people with average mental activity, while the rate of decline of those with infrequent activity was 48 percent faster than those with average activity.
The study was supported by the National Institute on Aging and the Illinois Department of Public Health.

http://phys.org/news/2013-07-chimp-pig-hybrid-humans.html

A chimp-pig hybrid origin for humans?

Impressive body of evidence suggesting that human origins can be best explained by hybridization between pigs and chimpanzees

Phys.org —These days, getting a Ph.D. is probably the last thing you want to do if you are out to revolutionize the world. If, however, what you propose is an idea, rather than a technology, it can still be a valuable asset to have. Dr. Eugene McCarthy is a Ph.D. geneticist who has made a career out of studying hybridization in animals. He now curates a biological information website called Macroevolution.net where he has amassed an impressive body of evidence suggesting that human origins can be best explained by hybridization between pigs and chimpanzees. Extraordinary theories require extraordinary evidence and McCarthy does not disappoint. Rather than relying on genetic sequence comparisons, he instead offers extensive anatomical comparisons, each of which may be individually assailable, but startling when taken together. Why weren't these conclusions arrived at much sooner? McCarthy suggests it is because of an over-dependence on genetic data among biologists. He argues that humans are probably the result of multiple generations of backcrossing to chimpanzees, which in nucleotide sequence data comparisons would effectively mask any contribution from pig.
Generally speaking, interspecies hybrids - like mules, ligers (lion-tiger hybrids), or zedonks (zebra-donkey hybrids) - are less fertile than the parents that produced them. However, as McCarthy has documented in his years of research into hybrids, many crosses produce hybrids that can produce offspring themselves. The mule, he notes, is an exceptionally sterile hybrid and not representative of hybrids as a whole. When it comes time to play the old nuclear musical chairs and produce gametes, some types of hybrids do a much better job. Liger females, for example, can produce offspring in backcrosses with both lions and tigers. McCarthy also points out that fertility can be increased through successive backcrossing with one of the parents, a common technique

used by breeders. In the case of chimp - pig hybridization, the "direction of the cross" would likely have been a male boar or pig (Sus scrofa) with a female chimp (Pan troglodytes), and the offspring would have been nurtured by a chimp mother among chimpanzees (shades of Tarzan!). The physical evidence for this is convincing, as you can discover for yourself with a trip over to macroevolution.net.

When I asked McCarthy if he could give a date estimate for the hybridization event, he said that there are a couple broad possibilities: (1) It might be that hybridization between pigs and apes produced the earliest hominids millions of years ago and that subsequent mating within this hybrid swarm eventually led to the various hominid types and to modern humans; (2) separate crosses between pigs and apes could have produced separate hominids (and there's even a creepy possibility that hybridization might even still be occurring in regions where Sus and Pan still seem to come into contact, like Southern Sudan).

This latter possibility may not sound so far-fetched after you read the riveting details suggesting that the origin of the gorilla may be best explained by hybridization with the equally massive forest hog. This hog is found within the same habitat as the gorilla, and shares many uncommon physical features and habits. Furthermore, well-known hybridization effects can explain many of the fertility issues and other peculiarities of gorilla physiology.

It is not yet clear if or when genetic data might support, or refute, our hybrid origins. The list of anatomical specializations we may have gained from porcine philandering is too long to detail here. Suffice it to say, similarities in the face, skin and organ microstructure alone is hard to explain away. A short list of differential features, for example, would include, multipyramidal kidney structure, presence of dermal melanocytes, melanoma, absence of a primate baculum (penis bone), surface lipid and carbohydrate composition of cell membranes, vocal cord structure, laryngeal sacs, diverticuli of the fetal stomach, intestinal "valves of Kerkring," heart chamber symmetry, skin and cranial vasculature and method of cooling, and tooth structure. Other features occasionally seen in humans, like bicornuate uteruses and supernumerary nipples, would also be difficult to incorporate into a purely primate tree.

McCarthy has done extensive research into the broader issues, and shortcomings, of our currently incomplete theory of evolution. As the increasing apparent, magnificant, speed with which morphological change can occur continues to present itself for us to comprehend, the standard theory of random mutation followed by slow environmental selection, seems to stall. In my own opinion, female choice undoubtedly provides much of the functional "speed-up" we observe, but other mechanisms of mutation, or pathways for acquired characteristics to be fed back to the gonads (through retroviral transfer?), now need to be considered anew. The role of hybridization in driving morphological change, as McCarthy has observed time and time again, particularly in his studies of avian species (Oxford University Press, 2006), may be the most powerful mechanism of all.

http://arstechnica.com/science/2013/07/why-good-deeds-dont-go-unpunished/

Why good deeds don't go unpunished

Being overly generous can get you punished as a nonconformist.

by Kate Shaw Yoshida - July 4 2013, 12:35am TST

Nonconformists may eventually find themselves worn down by their peers.

From an early age, we are taught that cooperation, generosity, and altruism are generally things we should strive for. But altruistic acts aren't always lauded, and researchers have found that generous individuals are sometimes punished for their behavior. Studies suggest that people often react negatively to large contributions, are suspicious of those who offer help, and want to expel particularly charitable individuals from cooperative endeavors. These seemingly counterintuitive behaviors are called "antisocial punishment" and are more common than you might think. But why would people want to punish anyone who is particularly charitable? The answer to that question would explain a puzzling human behavior, and it could have important ramifications for public policy. Tackling many of the major problems we currently face—from climate change to political stalemates—requires cooperation and collaboration. Understanding why people are sometimes willing to undermine joint efforts out of what appears to be nothing more than spite could go a long way to improve cooperation and discourse in many areas.

Sociologists Kyle Irwin and Christine Horne suggest that our inclination to punish do-gooders may stem from our adherence to social norms. Using a clever experimental design that allowed them to manipulate the level of conformity among group members, the researchers investigated the relationship between antisocial punishment and social norms.

The setup

During the study, 310 undergraduates were asked to take part in a game based on points; the more points a participant ended up with, the better chance they had of winning one of three $100 Amazon gift cards.

The premise was relatively simple. Each participant was given 100 points and randomly assigned to a group of six players. In each round of the game, individuals would be asked to contribute however many points they like to a "group fund" that would be doubled by the experimenters and divided equally among the participants. In this scenario, everyone in the group would end up with twice what they started with if all participants donate all their points, but free-riders that donated fewer points—or even none at all—could still benefit from others' contributions.

The participants made their choices in a predetermined order and could see each contribution as it was made, but they interacted with other group members through a computer rather than face-to-face.

But there was a pretty significant twist: since the researchers wanted to control some variables while manipulating others, much of what happened in the study was decided in advance (which, of course, was unbeknownst to the participants). There was only one actual study participant in each group; the other five "group members" were computer programs playing out predetermined roles. The human participant was always "randomly" chosen to be the fifth player to donate, and the four contributions that he or she observed before contributing always averaged 50 points, or half the total possible contribution.

By preprogramming these values, the researchers could manipulate the "social norm," or the way most group members behaved. In the "strong" social norm condition, the contributions varied only slightly, ranging between 45 and 55 points; this represented a situation in which social conformity was high. In the "weak" social norm condition where conformity was lower, the first four predetermined contributions varied between 30 and 70 points.

Lastly, the contribution of the sixth and final group member was also set by the researchers and was either overly generous (donating 90 of the 100 possible points), or overly stingy (donating only 10 points).

The fallout

The researchers weren't particularly concerned with the size of the participants' donations; instead, they wanted to know whether or not they would choose to punish this final nonconforming group member, which they called the "deviant."

After all the contributions were made, the participant was given the opportunity to punish any of the other group members if desired. He or she could deduct points from any other player, but this came at a cost: for every three points subtracted from another group member, the punisher also lost a point.

Participants weren't reluctant to punish other players despite the fact that this action took away from their own earnings; 77 percent of the participants deducted at least one point from another group member, and the average cost the punisher incurred was nearly 7 points. Not surprisingly, most people (nearly 70 percent) chose to punish the stingy deviants that contributed much less than the average. After all, these players were benefiting from others' donations to the group fund without making large contributions of their own.

But here's the amazing part: 51 percent of the participants also chose to punish the overly generous deviant. In other words, a majority of the people in this study were willing to reduce their own chance to win $100 just to punish a particularly cooperative group member. Furthermore, many participants actually wanted this individual to be kicked out of the group. When asked to rate how much they would like each player to remain in the group on a scale of 1 (not at all) to 9 (very much), the average rating for the overly generous player was less than a 3.

But why?

Examining the interaction between the strength of the social norm (as set by the range of donations) and the size of the punishment meted out suggests a basis for this puzzling behavior. Irwin and Horne found that strong social norms encouraged punishment of the cooperative player: the more similar the first four pre-programmed donations were, the higher the punishments tended to be for the overly generous deviant. When there is a clear "right way" to behave, the researchers suggest, people respond more strongly to behaviors that don't fit the norm.

However, the strength of social norms didn't affect the punishments of the stingy deviant. Players tended to punish this individual equally under both conditions. The researchers suggest that no matter how high or low conformity is among group members, people always see stinginess as a punishable offense.

So it appears that nonconformity is a bit of a double-standard, at least under these specific circumstances. We always dislike free-riders, but we will also punish cooperators when their behavior is particularly atypical. As of now, we can only speculate about the rationale for this behavior; the presence of strong social norms may foster a feeling that the generous contributor is trying to make him or herself look rich or powerful, or that they are trying to make everyone else look bad.

When it comes to self-interest, this behavior is completely counter-intuitive; it seems absurd to punish these super-cooperators and want to expel them from the group. After all, their generosity increases other players'

chances, generally at their own expense. But humans' adherence to conformity is strong, and when the stakes aren't high, social norms may win out over self-interest.
The researchers acknowledge that under different circumstances—for example, if rewards are large or the type of punishment varies—the outcome might be different. This study had a very homogeneous subject pool and was tightly managed in order to control for multiple variables, so its external validity and applicability to real world problems are limited at this point. However, there's no doubt that in certain situations, "big givers" are subject to punishment, even when this isn't in anyone's best interest.
Social Science Research, 2013. DOI: 10.1016/j.ssresearch.2012.10.004 (About DOIs).

http://www.eurekalert.org/pub_releases/2013-07/dumc-bph070113.php

Biomarker predicts heart attack risk based on response to aspirin therapy

Aspirin has been widely used for more than 50 years as a common, inexpensive blood thinner for patients with heart disease and stroke, but doctors have little understanding of how it works and why some people benefit and others don't.

DURHAM, N.C. - Now researchers at Duke Medicine have solved some of the mysteries related to the use of this century-old drug, and developed a blood-based test of gene activity that has been shown to accurately identify who will respond to the therapy.
The new gene expression profile not only measures the effectiveness of aspirin, but also serves as a strong predictor of patients who are at risk for heart attack, according to a study appearing July 3, 2013, in the online edition of the Journal of the American College of Cardiology.
"We recognized the concept of aspirin resistance among a population of patients who have cardiac events or stroke," said senior author Geoffrey S. Ginsburg, M.D., PhD, director of genomic medicine at Duke's Institute for Genome Sciences & Policy and executive director of the Center for Personalized Medicine. "We give the same dose to all patients, but maybe some patients need a larger dose of aspirin, or maybe they need to try a different therapy entirely. We need better tools to monitor patients and adjust their care accordingly, and the findings from our study move us in that direction."
The Duke researchers enlisted three groups of participants – two of healthy volunteers and one comprised of patients with heart disease seen in outpatient cardiology practices.
The healthy volunteers were given a dosage of 325 mg of aspirin daily for up to a month; the heart disease patients had been prescribed a low dose of aspirin as part of their treatment. Blood was then analyzed for the impact of aspirin on RNA expression and the function of platelets, which are the blood cells involved in clotting.
The RNA microarray profiling after aspirin administration revealed a set of 60 co-expressed genes that the researchers call the "aspirin response signature," which consistently correlated with an insufficient platelet response to aspirin therapy among the healthy subjects as well as the heart disease patients.
The researchers also examined the aspirin response signature in another group of patients who had undergone cardiac catheterizations. They found the signature was also effective in identifying those patients who eventually suffered a heart attack or died.
"The aspirin response signature can determine who is at risk for heart attack and death," said Deepak Voora, M.D., assistant professor of medicine at Duke and lead author of the study. "There is something about the biology of platelets that determines how well we respond to aspirin and we can now capture that with a genomic signature in blood."
Ginsburg said the research is progressing to recreate the findings in other populations, and to develop a standardized testing system that could one day move the analysis into daily practice.
"Nearly 60 million people take aspirin regularly to reduce their chances of heart attack and death, but it doesn't work for everyone," said Rochelle Long, Ph.D., of the National Institutes of Health's National Institute of General Medical Sciences, which partly supported the study. "By monitoring gene activity patterns these investigators uncovered a 'signature' linked to inadequate responsiveness. This work may eventually lead to a simple blood test to identify those who do not benefit from aspirin, enabling them to seek other therapeutic options."
In addition to Ginsburg and Voora, study authors include Derek Cyr; Joseph Lucas; Jen-Tsan Chi; Jennifer Dungan; Timothy A. McCaffrey; Richard Katz; L. Kristin Newby; William E. Kraus; Richard C. Becker; and Thomas L. Ortel.
The study received funding from the Duke Institute for Genome Sciences & Policy; the National Institutes of Health (T32HL007101 to DV); the National Center for Research Resources (UL1RR024128); the National Institutes of General Medical Sciences (RC1GM091083); the Centers for Disease Control and Prevention (5U01DD000014); and the David H. Murdock Research Institute.

http://www.eurekalert.org/pub_releases/2013-07/uoo-cp070313.php

Cockatoos 'pick' puzzle box locks

A species of Indonesian parrot can solve complex mechanical problems that involve undoing a series of locks one after another, revealing new depths to physical intelligence in birds.

A team of scientists from Oxford University, the University of Vienna, and the Max Planck Institute, report in PLOS ONE a study in which ten untrained Goffin's cockatoos [Cacatua goffini] faced a puzzle box showing food (a nut) behind a transparent door secured by a series of five different interlocking devices, each one jamming the next along in the series.

To retrieve the nut the birds had to first remove a pin, then a screw, then a bolt, then turn a wheel 90 degrees, and then shift a latch sideways. One bird, called 'Pipin', cracked the problem unassisted in less than two hours, and several others did it after being helped either by being presented with the series of locks incrementally or being allowed to watch a skilled partner doing it. The scientists were interested in the birds' progress towards the solution, and on what they knew once they had solved the full task.

Watch a video of cockatoos solving the puzzle box: http://www.zoo.ox.ac.uk/group/kacelnik/lb_movie_s1.mov

The team found that the birds worked determinedly to sort one obstacle after another even though they were only rewarded with the nut once they had solved all five devices. The scientists suggest that the birds seemed to progress as if they employed a 'cognitive ratchet' process: once they discovered how to solve one lock they rarely had any difficulties with the same device again. This, the scientists argue, is consistent with the birds having a representation of the goal they were after.

After the cockatoos mastered the entire sequence the scientists investigated whether the birds had learnt how to repeat a sequence of actions or instead responded to the effect of each lock.

Dr Alice Auersperg, who led the study at the Goffin Laboratory at Vienna University, said: 'After they had solved the initial problem, we confronted six subjects with so-called 'Transfer tasks' in which some locks were re-ordered, removed, or made non-functional. Statistical analysis showed that they reacted to the changes with immediate sensitivity to the novel situation.'

Professor Alex Kacelnik of Oxford University's Department of Zoology, a co-author of the study, said: 'We cannot prove that the birds understand the physical structure of the problem as an adult human would, but we can infer from their behaviour that they are sensitive to how objects act on each other, and that they can learn to progress towards a distant goal without being rewarded step-by-step.'

Dr Auguste von Bayern, another co-author from Oxford University said: 'The birds' sudden and often errorless improvement and response to changes indicates pronounced behavioural plasticity and practical memory. We believe that they are aided by species characteristics such as intense curiosity, tactile exploration techniques and persistence: cockatoos explore surrounding objects with their bill, tongue and feet. A purely visual explorer may have never detected that they could move the locks.'

Professor Kacelnik said: 'It would be too easy to say that the cockatoos understand the problem, but this claim will only be justified when we can reproduce the details of the animals' response to a large battery of novel physical problems.'

http://www.eurekalert.org/pub_releases/2013-07/snu-pds070313.php

People's diets show a sugar-fat seesaw

Research published today shows why people find it hard to follow Government guidelines to cut their fat and sugars intake at the same time - a phenomenon known as the sugar-fat seesaw.

The review, published in the journal Critical Reviews in Food Science and Nutrition, looked at 53 scientific papers and found a strong and consistent inverse association in the percentage of energy coming from fats and sugars. People with diets low in sugars were likely to be high in fat, and vice-versa. Nutritionists have labelled this the 'sugar-fat seesaw'.

Dr Michele Sadler, who led the research team, said: "A key reason that we see this sugar-fat seesaw is likely to be because sources of sugars such as fruit, breakfast cereals and juices are low in fat, while sources of fat such as oils and meat products are low in sugar."

In the UK dietary guidelines are set and described as a percentage of daily energy intakes. Therefore, the researchers suggest that people may find it difficult to follow advice to reduce the sugars and fats contribution to energy intakes at the same time, something recommended by the Government.

Dr Sadler added: "This study highlights the need to focus dietary messages on eating a healthy balanced diet and not categorising individual nutrients as good or bad, which could result in unbalanced dietary habits."

Sadler MJ, McNulty H & Gibson S (2013) Sugar-fat seesaw: A systematic review of the evidence. Critical Reviews in Food Science and Nutrition, DOI: 10.1080/10408398.2011.654013

Dr Michele Sadler and Ms Sigrid Gibson are both freelance Registered Public Health Nutritionists. Prof Helene McNulty is a registered dietitian and Professor of Nutritional Sciences at the University of Ulster.
This study was supported by an unrestricted-research grant from Sugar Nutrition UK (formerly The Sugar Bureau). The funding source had no involvement in any of the research process or in production of the published manuscript, as stated in the papers acknowledgments.

http://www.eurekalert.org/pub_releases/2013-07/m-gfm070313.php

Gateway for metastases

Activated blood platelets enable cancer cells to penetrate blood vessels

Malignant tumours often spread to remote areas of the body. In the majority of cases, metastases formation develops via the blood vascular system. The blood platelets thereby provide invaluable help to the tumour cells in penetrating new organs.

Scientists from the Max Planck Institute for Heart and Lung Research in Bad Nauheim have identified the P2Y2 receptor molecule on the cells of the blood platelet wall as the gateway that allows the cancer cells to enter the organs. They now aim to prevent the formation of metastases through the targeted blocking of this key molecule.

Blood platelets play a crucial role in haemostasis. When a blood vessel is injured, the platelets ensure the rapid initial closure of the wound. To do this, they quickly adhere to the wall of the injured blood vessel, thereby attracting more platelets which aggregate and form a plug that blocks the opening in the blood vessel wall.

To enable the optimal functioning of this "rapid reaction force" in the event of injury to blood vessel walls, the blood platelets release a veritable shower of signal molecules. The cells communicate with each other in this manner. Moreover, the platelets, which normally circulate in the blood stream in an inactive state, are activated in a matter of seconds and fundamentally alter their characteristics.

Malignant tumours, which often spread to previously unaffected organs through the blood stream, use the blood platelets to penetrate the hermetically-sealed blood vessel wall. "It has long been known that metastasising tumour cells are capable of establishing close contact with blood platelets and activating them.

Animal experiments have shown that tumour cells form far fewer metastases in the absence of blood platelets," says Stefan Offermanns, Director of the Department of Pharmacology at the Bad Nauheim-based Max Planck Institute.

In addition, clinical studies have shown that patients who receive long-term treatment with platelet inhibitors like acetylsalicylic acid present a lower risk of developing metastasising tumours.

Offermanns' Research Group has succeeded in explaining exactly how this process unfolds. Activated blood cells release a large amount of molecules including adenosine triphosphate (ATP). The scientists observed in cell cultures that blocking ATP release from blood platelets resulted in a significant reduction in the number of tumour cells migrating through the endothelial cells in the blood vessel wall.

"We succeeded in demonstrating the same phenomenon in experiments on mice, in which the release of ATP from blood platelets was blocked. In this case too, far fewer tumour cells slipped through the endothelial barrier and fewer metastases formed," says Dagmar Schuhmacher, one of the study's first authors.

However, what exactly happens in the blood vessel wall that enables the tumour cells to penetrate it? The Max Planck researchers were able to demonstrate that ATP from the blood platelets binds with a particular receptor called P2Y2. This docking site is located on the surface of the endothelial cells.

"When ATP binds to these receptors, small openings form between the individual endothelial cells. The tumour cells exit the blood vessel through these openings and migrate into the organ," explains Boris Strilic, also a first author of the study.

With the identification of this hitherto unknown role of blood platelets in metastases formation, the researchers hope to have found possible starting points for a new therapeutic approach. "We will now test whether specific blockers for the P2Y2 receptor or substances that inhibit the release of ATP from blood platelets can suppress tumour cell metastasis in different animal models," says Offermanns.

The specific challenge the scientists must overcome here is to avoid suppressing the actual job of the platelets, namely haemostasis, in the process. If they manage to do this, a better treatment for malignant tumours may become available in the future.

Original publication: *Dagmar Schumacher, Boris Strilic, Kishor Kumar Sivaraj, Nina Wettschureck, Stefan Offermanns: Platelet-derived nucleotides promote tumor-cell transendothelial migration and metastasis via P2Y2-receptor. Cancer Cell (2013), http://dx.doi.org/10.1016/j.ccr.2013.05.008*

http://www.medscape.com/viewarticle/807334?src=rss

New Headache Classification System Published

The *International Classification of Headache Disorders, Third Edition* (ICHD-III beta version) is now complete and ready for field testing.

Pauline Anderson

BOSTON — The *International Classification of Headache Disorders, Third Edition* (ICHD-III beta version) is now complete and ready for field testing.

"It's out, it's published, you should start using it immediately because it's much better than the second edition," Jes Olesen, MD, PhD, professor of neurology, University of Copenhagen, Glostrup Hospital, Denmark, told delegates to the 2013 International Headache Congress (IHC).

Dr. Olesen, who chaired the working group on migraine, encouraged delegates to start citing this new classification system and to participate in field testing, which will take place during the next few years, before publication of the final version.

If physicians note any mistakes or have comments, they should contact the chairperson of the relevant chapter, said Dr. Olesen, who anticipates that only minor modifications will be necessary.

The ICHD-III beta version is available at the International Headache Society Web site.

Chronic Migraine

One of the biggest changes in the current edition, which has been in the works for 3 years, is the addition of chronic migraines that occur on at least 15 days of the month for more than 3 months.

In the past, patients with these headaches were all diagnosed with migraine, whether they had 1 attack a year, 1 a month, 1 a week, or 1 a day, but there has been growing interest in considering the most severe end of the migraine spectrum as a separate entity, said Dr. Olesen.

Separating out chronic migraine is "parallel" to how tension type headache is treated in the classification system, he said. "Even in the first and second editions we had chronic tension type headache, which are tension type headaches on 15 days a month or more."

In fact, many patients have tension headaches on a daily basis and are debilitated by it, he said. "So it's important to single out that severe end of the spectrum; and for some reason we didn't do it for migraine, but we're doing it now."

In addition to the frequency of attacks, there are a number of other criteria that have to be met before a diagnosis of chronic migraine should be given.

Other migraine classifications include the following: migraine with aura, migraine without aura, complications of migraine, probable migraine, and episodic syndromes that may be associated with migraine.

Migraine with aura is subdivided into migraine with typical aura; typical aura with headache; typical aura without headache; migraine with brainstem aura; hemiplegic migraine; several types of familial hemiplegic migraine; sporadic hemiplegic migraine, and retinal migraine.

For a diagnosis of migraine with aura, the following criteria must be met:

- ***One or more visual; sensory; speech; motor; brainstem; or retinal symptoms;***
- ***At least 2 of these 4 criteria: (1) at least 1 aura symptom spreading gradually over 5 or more minutes*** and/or 2 or more symptoms occurring in succession; (2) each aura symptom lasts 5 to 60 minutes; (3) at least 1 aura symptom is unilateral; (4) the aura is accompanied or followed shortly by headache.

Although in the main body of the text, it is specified that a patient needs 2 of 4 criteria for migraine with aura, in the Appendix, they need to have 3 of 6 criteria; field testing will reveal which approach is better, said Dr. Olesen.

As in earlier editions, the new classification system distinguishes primary headaches, which are diseases in their own right, from secondary headaches, which are caused by something else.

Other Primary Headaches

For primary headaches other than migraine, some diagnostic entities have been rearranged and renamed. There are 4 subgroups:

(1) physical exertion (primary cough headache; primary exercise headache; primary headache associated with sexual activity; primary thunderclap headache;

(2) headaches associated with direct physical stimuli (cold-stimulus headache; external pressure headache);

(3) epicranial headaches (primary stabbing headache; nummular headache; epicrania fugax (in the Appendix); and

(4) other (hypnic headache; new daily persistent headache).

Some changes in the primary headache section include the following:

- ***Under headaches associated with sexual activity, the subtypes of preorgasmic and orgasmic headache have been eliminated.***
- ***For thunderclap headaches, the headache must last at least 5 minutes, but the criterion of not recurring regularly during subsequent weeks or months has been discarded.***
- ***Hypnic headaches no longer have to first occur after age 50 years.***
- ***A number of pain characteristics under the new daily persistent headaches section have been eliminated.***

New daily persistent headache is the only headache category in which onset should be "distinct and clearly remembered," noted Shuu Jiun Wang, MD, professor and chairman, Faculty of Medicine, National Yang-Ming University School of Medicine, and deputy head, the Neurological Institute, Taipei Veterans General Hospital, Taiwan, who chaired the working group on other primary headaches.

As for Epicrania fugax, now included in the Appendix, this could be a possible new headache entity, said Dr. Wang. It consists of brief stabbing head pain that stems from a particular area of the head and rapidly radiates forward or backward in a wide linear or zigzag movement.

Secondary Headaches

The criteria in the secondary headache section have been presented in a new format. One change here is that it is not required that the causative agent be removed before a diagnosis. There are also no longer "probable secondary" headaches.

The main categories of secondary headache include the following: posttraumatic headache; headaches due to vascular disorders; headaches due to nonvascular disorders (such as tumors); headaches due to medications, toxins and other substances; medication overuse headaches; headaches due to infections; headaches due to metabolic (homeostatic) disturbances; headaches due to cranial, cervical, EENT, and dental disorders; and headaches due to psychiatric disease.

The Appendix lists headaches associated with various psychiatric disorders, including depressive disorder, separation anxiety, panic disorder, and social anxiety disorder. Also in the Appendix is the novel headache attributed to travel in space as well as headache due to airplane travel during landing.

Another addition in the Appendix is vestibular migraine. Among the criteria for this diagnosis are having vestibular symptoms of moderate or severe intensity lasting between 5 minutes and 72 hours, photophobia, and visual aura.

Dr. Olesen said he was "sceptical" about including vestibular migraine in the new classification system, but he supports having it in the Appendix. "The way it's defined, it sort of overlaps with other entities, in particular, migraine with brainstem aura, but we will see how it works out. At least it can get more rigorous studies."

The diagnostic criteria in the expanded Appendix can be field tested and used for research, but they are not meant for clinical use, added Dr. Olesen.

Classification Rule

An important "rule" with the new classification system is still "to put a diagnosis on every single distinct kind of headache the patient has," said Dr. Olesen. "So some people need 2 headache diagnoses, and even 3 headache diagnoses."

For example, a patient can have a diagnosis of both cluster headache and tension type headache. A patient with chronic migraine and medication overuse headache will also have 2 diagnoses.

Asked by a delegate why menstruation-related migraine is still in the Appendix and not in the main body, Dr. Olesen said that this type of migraine "is very important but not suitable" for the main classification body, partly because it does not apply to men and partly because subdividing migraine could create "a mess."

"People have suggested dividing migraine into whether it's refractory or nonrefractory; people have suggested subdividing it on whether its associated with sensitization and not associated with sensitization; people have suggested various other ways of subdividing migraine, but it becomes too confusing.

The first edition of the *International Classification of Headache Disorders* was published in 1988, and the second in 2004.

Information on field testing is available on the International Headache Society Web site or the World Health Organization (WHO) Web site. WHO is field testing the *International Classification of Diseases, 11th Edition* (ICD-11), and for its headache section, it will also test the ICHD-III. The 2 are identical except for the degree of detail, said Dr. Olesen. Field testing should continue for 3 years, with the final version of the updated edition ready by 2016, said Dr. Olesen.

2013 International Headache Congress (IHC). Special HIS Session. Presented June 27, 2013.

http://www.scientificamerican.com/article.cfm?id=pill-of-goods

Pill of Goods: International Counterfeit Drug Ring Hit in Massive Sting

Court documents review process that led the FDA to shut down more than 1,600 illegal pharmacy Web sites

By Dina Fine Maron | Wednesday, July 3, 2013 | 5

It may be the largest organized crime network that you have never heard of, and it deals in counterfeit drugs. So says the U.S. Food and Drug Administration, which seized and shut down 1,677 illegal pharmacy Web sites last month as part of the largest Internet-based counterfeit drug sting yet.

The shuttered Web sites all claimed to be "Canadian pharmacies" but the FDA says that not a single drug shipment actually came from the U.S.'s northern neighbor. And testing on the multiple undercover purchases of drugs made by FDA offices in Colorado, New Hampshire and western Pennsylvania—described in official court documents reviewed by Scientific American—found that the drugs were actually not cheap, generic versions of the drugs; they were all counterfeits.

The bust is expected to be a major blow to a complex web of online drug distribution that "appears to be highly nimble," according to the agency. The FDA agent leading this operation believes that the Web sites are part of a major online drug distribution affiliate network that calls itself EvaPharmacy. That network processes roughly 30,000 orders and grosses around $2.7 million—monthly, according to earlier research (pdf) from of the University of California, San Diego. All the Web sites shut down by the FDA were displaying fake licenses and certifications to convince potential U.S. customers that the "FDA approved" and "brand name" drugs were legitimate.

The agency found "a clear linkage and presence of a large, organized online drug distribution network," according to the affidavit of Daniel Burke, special agent in the FDA's Office of Criminal Investigations. The crime network identified by the agency included 6,263 Web sites that all used one of at least eight site templates. Researchers believe the large international crime network is based in Russia and the Middle East, and that the seized Web sites were marketing directly to the U.S.

Most of the sites were slight adaptations of templates the network created, Burke said in his affidavit. (The agency declined to comment for this article.) They were carefully constructed to appear to be from real pharmacies like CVS, Walmart or Walgreens, according to the affidavit. In reality the shipments of counterfeit drugs came from India or Singapore instead of pharmacies in Canada. Federal agency warning banners displayed across Web sites like "www.walgreens-store.com" and "http://www.c-v-s-pharmacy.com/" now indicate that they are fraudulent and illegal. The U.S. government says it seized the domain names of the sites to prevent third parties from acquiring the Web site URLs and using them to commit additional crimes.

The FDA's sting, which was carried out in conjunction with international partners, built on the work of academic researchers who have been carefully identifying these sites for the past several years. It took a coalition of computer scientists several years to identify the pages, as they worked through tracking which were legitimate Canadian pharmacies and which were illegal and did not ask for prescriptions. The only sure-fire test was to order drugs (pdf) and see how the Web site performed. "Making the call" about whether a site was from a real Canadian pharmacy or was a fake "requires a little internet detective work," says Chris Kanich, professor of computer science at the University of Illinois at Chicago, who led some of the research in this area.

Creating a complex computer algorithm that could capture all these sites is impossible, he says, because it remains too challenging to distinguish legitimate online pharmacies from fraudulent sites without making some online purchases. The FDA provides consumers with advice on how to find an online pharmacy through BeSafeRx: Know Your Online Pharmacy.

For this crime investigation there were no meetings in back alleys or surreptitious hand offs—just online purchases akin to what a consumer might do sitting at home. In one instance an FDA special agent purchased $105.45 of the diabetes drug Actos and arthritis medication Celebrex, and had them shipped to a U.S. address. As a free "bonus" the site offered to throw in four free pills of Viagra, according to official records. At no point during the purchase was the agent asked to provide a prescription from a licensed medical practitioner, complete a medical questionnaire or consult with a health professional.

Two weeks later, an agent received the purported drugs with a package postmarked from India. They were not the branded drugs as advertised; they were drugs that are illegal to sell in the U.S., and that purportedly contained the same active ingredient as the advertised drug. Some of the drugs came in a package simply labeled "sample-hermless [sic] medicine for personal use—'Not for sale.'" Moreover, no directions for use or package inserts were included with the shipment.

Shutting down this slice of EvaPharmacy's business amounts to a significant blow to the faux firm's infrastructure, Kanich says. "They would need a really resilient business to recover from this."

http://www.eurekalert.org/pub_releases/2013-07/wcmc-ubt070313.php

Urine biomarker test can diagnose as well as predict rejection of transplanted kidneys

National clinical trial demonstrates the 3-gene signature test, developed at Weill Cornell Medical College, will improve care of kidney transplant patients

NEW YORK - A breakthrough non-invasive test can detect whether transplanted kidneys are in the process of being rejected, as well as identify patients at risk for rejection weeks to months before they show symptoms, according to a study published in The New England Journal of Medicine (NEJM).

By measuring just three genetic molecules in a urine sample, the test accurately diagnoses acute rejection of kidney transplants, the most frequent and serious complication of kidney transplants, says the study's lead author, Dr. Manikkam Suthanthiran, the Stanton Griffis Distinguished Professor of Medicine at Weill Cornell Medical College and chief of transplantation medicine, nephrology and hypertension at NewYork-Presbyterian Hospital/Weill Cornell Medical Center.

"It looks to us that we can actually anticipate rejection of a kidney several weeks before rejection begins to damage the transplant," Dr. Suthanthiran says.

The test may also help physicians fine-tune the amount of powerful immunosuppressive drugs that organ transplant patients must take for the rest of their lives, says Dr. Suthanthiran, whose laboratory developed what he calls the "three-gene signature" of the health of transplanted kidney organs.

"We have, for the first time, the opportunity to manage transplant patients in a more precise, individualized fashion. This is good news since it moves us from the current one-size-fits-all treatment model to a much more personalized plan," he says, noting that too little immunosuppression leads to organ rejection and too much can lead to infection or even cancer.

Given the promise of the test first developed in the Suthanthiran laboratory at Weill Cornell and previously reported in NEJM, the National Institutes of Health (NIH) sponsored a multicenter clinical trial of nearly 500 kidney transplant patients at five medical centers, including NewYork-Presbyterian/Weill Cornell Medical Center and NewYork-Presbyterian/Columbia University Medical Center. The successful results of that trial are detailed in the July 4 issue of NEJM.

Such a test is sorely needed to help improve the longevity of kidney transplants and the lives of patients who receive these organs, says study co-author Dr. Darshana Dadhania, associate professor of medicine and medicine in surgery at Weill Cornell Medical College and associate attending physician at NewYork-Presbyterian Hospital.

Dr. Dadhania says that the primary blood test now used to help identify rejection -- creatinine, which measures kidney function -- is much less specific than the three-gene signature.

"Creatinine can go up for many reasons, including simple dehydration in a patient, and when this happens we then need to do a highly invasive needle-stick biopsy to look at the kidney and determine the cause. Our goal is to provide the most effective care possible for our transplant patients, and that means individualizing their post transplant care," she says. "Using an innovative biomarker test like this will eliminate unnecessary biopsies and provide a yardstick to measure adequate immunosuppression to keep organs -- and our patients -- healthy."

Although a number of researchers have tried to develop blood or urine-based tests to measure genes or proteins that signify kidney organ rejection, Dr. Suthanthiran and his research team were the first to create a gene expression profile urine test -- an advance that was reported in NEJM in 2001 and, with an update also in NEJM, in 2005.

The research team measured the levels of messenger RNA (mRNA) molecules produced as genes are being expressed, or activated, to make proteins. To do this, they developed a number of sophisticated tools to measure this genetic material. "We were told we would never be able to isolate good quality mRNA from urine," he says. "Never say never."

He and his colleagues found that increased expression of three mRNAs can determine if an organ will be, or is being, rejected. The mRNAs (18S ribosomal (rRNA)–normalized CD3ε mRNA, 18S rRNA–normalized interferon-inducible protein 10 (IP-10) mRNA, and 18S rRNA) indicate that killer T immune cells are being recruited to the kidney in order to destroy what the body has come to recognize as alien tissue.

The signature test consists of adding levels of the three mRNAs in urine into a composite score. Tracked over time, a rising score can indicate heightened immune system activity against a transplanted kidney, Dr. Suthanthiran says. A score that stays the same suggests that the patient is not at risk for rejection.

"We were always looking for the most parsimonious model for an organ rejection biomarker test," Dr. Suthanthiran says. "Minimizing the number of genes that we test for is just more practical and helps to give us a clearer path towards diagnosis and use in the clinic."

Physicians can tailor a patient's use of multiple immunosuppressive drugs by lowering the doses steadily, and monitoring the patient's composite score over time. Any increase would suggest a somewhat higher dose of therapy is needed to keep the organ safe.
"This is akin to monitoring blood glucose in a patient with diabetes," Dr. Suthanthiran says. "Because different people have different sensitivity to the two-to-four immunosuppressive drugs they have to take, this test offers us a very personalized approach to managing transplantations."

Predicting rejection weeks before it happens

The clinical trial began in 2006 with participation from five medical centers -- NewYork-Presbyterian/Columbia University Medical Center, the University of Pennsylvania's Perelman School of Medicine, the Northwestern University Feinberg School of Medicine, the University of Wisconsin School of Medicine and Public Health and NewYork-Presbyterian/Weill Cornell Medical Center, which contributed 122 of the total 485 kidney transplant patients.
The gene-expression studies were led by Dr. Suthanthiran with his laboratory serving as the Gene Expression Monitoring (GEM) core and the clinical trial was led by Dr. Abraham Shaked, director of the PENN Transplant Institute at the Perelman School, on behalf of the Clinical Trials in Organ Transplants 04 (CTOT-04) Study Investigators. The GEM core was blinded to the clinical status of the patients including their biopsy results and the data collection and analysis were performed by an independent statistical center sponsored by NIH.
Researchers collected 4,300 urine specimens during the first year of transplantation, starting at day three post-transplantation. The urine samples were shipped to the GEM core at Weill Cornell Medical College, where analysis of the urine revealed that the three gene-based biomarkers signature could distinguish kidney recipients with biopsy confirmed rejection from those whose biopsies did not show signs of rejection or who did not undergo a biopsy because there was no clinical sign of rejection.
The researchers used the signature to derive a composite score and identify a threshold value indicative of rejection. This score accurately detected transplant rejection with a low occurrence of false-positive and false-negative results. "It is about 85 percent accurate, which is much higher than the creatinine test used today," Dr. Suthanthiran says. Investigators then validated the diagnostic signature by obtaining similar results when they tested a set of urine samples collected in a separate CTOT clinical trial.
Dr. Suthanthiran anticipates conducting another NIH-funded clinical trial to test whether the signature test can be used to personalize individual immunosuppressive therapy. He says that NIH is also interested in submitting the test to the federal Food and Drug Administration for approval.

These studies have provided enough information that many medical centers can test their own kidney transplant patients for rejection using the publicly-available formula for the biomarker test. Dr. Suthanthiran also is working to develop a way for patients to submit samples via mail for biomarker testing, and avoid an office visit. The study was supported by NIH grants UO1AI63589 and R37AI051652, the Qatar National Research Foundation (NPRP 08-503-3-111) and by a Clinical and Translational Science Center Award (UL1TR000457, to Weill Cornell Medical College).
Additional co-authors include Dr. Ruchuang Ding, Dr. Vijay K. Sharma, Christina S. Chang and Christine Hoang, of Weill Cornell Medical College; Dr. Thangamani Muthukumar and Dr. Phyllis August of Weill Cornell Medical College and NewYork-Presbyterian Hospital/Weill Cornell Medical Center; Dr. Benjamin Samstein, from Columbia University College of Physicians and Surgeons, New York, N.Y.; Dr. Peter S. Heeger, from Mount Sinai School of Medicine, New York, N.Y.; Dr. Joseph E. Schwartz, from Stony Brook University, Stony Brook, N.Y.; Dr. Michael Abecassis and Dr. John Friedewald, from Northwestern University Feinberg School of Medicine, Chicago, Ill.; Dr. Yolanda T. Becker, from the University of Chicago, Chicago, Ill.; Dr. Stuart J. Knechtle, from Emory University, Atlanta, Ga.; Nikki M. Williams and Dr. Nancy Bridges, from the National Institute of Allergy and Infectious Diseases, Bethesda, Md.; Karen S. Keslar and Dr. Robert L. Fairchild, from the Cleveland Clinic, Cleveland, Ohio; Dr. Donald E. Hricik, from Case Medical Center, Cleveland, Ohio; Dr. Leiya Han and Dr. Jun Liu, from Pharmaceutical Product Development, Wilmington, N.C.; and Dr. Michael Riggs and Dr. David N. Ikle, from Rho Federal Systems, Chapel Hill, N.C.

http://bit.ly/1ba0EQU

Mindscapes: First man to hear people before they speak

Name: PH

Condition: Badly dubbed sight and sound

10:49 04 July 2013 by Helen Thomson

Mindscapes is our new column on brain science with a difference: we meet people who live with the world's most mysterious neurological conditions

"I told my daughter her living room TV was out of sync. Then I noticed the kitchen telly was also dubbed badly. Suddenly I noticed that her voice was out of sync too. It wasn't the TV, it was me."
Ever watched an old movie, only for the sound to go out of sync with the action? Now imagine every voice you hear sounds similarly off-kilter – even your own. That's the world PH lives in. Soon after surgery for a heart problem, he began to notice that something wasn't quite right.

"I was staying with my daughter and they like to have the television on in their house. I turned to my daughter and said 'you ought to get a decent telly, one where the sound and programme are synchronised'. I gave a little chuckle. But they said 'there's nothing wrong with the TV'."
Puzzled, he went to the kitchen to make a cup of tea. "They've got another telly up on the wall and it was the same. I went into the lounge and I said to her 'hey you've got two TVs that need sorting!'."
That was when he started to notice that his daughter's speech was out of time with her lip movements too. "It wasn't the TV, it was me. It was happening in real life."
PH is the first confirmed case of someone who hears people speak before registering the movement of their lips. His situation is giving unique insights into how our brains unify what we hear and see.
It's unclear why PH's problem started when it did – but it may have had something to do with having acute pericarditis, inflammation of the sac around the heart, or the surgery he had to treat it.
Brain scans after the timing problems appeared showed two lesions in areas thought to play a role in hearing, timing and movement. "Where these came from is anyone's guess," says PH. "They may have been there all my life or as a result of being in intensive care."

Disconcerting delay

Several weeks later, PH realised that it wasn't just other people who were out of sync: when he spoke, he registered his words before he felt his jaw make the movement. "It felt like a significant delay, it sort of snuck up on me. It was very disconcerting. At the time I didn't know whether the delay was going to get bigger, but it seems to have stuck at about a quarter of a second."
Light and sound travel at different speeds, so when someone speaks, visual and auditory inputs arrive at our eyes and ears at different times. The signals are then processed at different rates in the brain.
Despite this, we normally perceive the events as happening simultaneously – but how the brain achieves this is unclear.
To investigate PH's situation, Elliot Freeman at City University London and colleagues performed a temporal order judgement test. PH was shown clips of people talking and was asked whether the voice came before or after the lip movements. Sure enough, he said it came before, and to perceive them as synchronous the team had to play the voice about 200 milliseconds later than the lip movements.
The team then carried out a second, more objective test based on the McGurk illusion. This involves listening to one syllable while watching someone mouth another; the combination makes you perceive a third syllable.
Since PH hears people speaking before he sees their lips move, the team expected the illusion to work when they delayed the voice.
So they were surprised to get the opposite result: presenting the voice 200 ms earlier than the lip movements triggered the illusion, suggesting that his brain was processing the sight before the sound in this particular task.
And it wasn't only PH who gave these results. When 37 others were tested on both tasks, many showed a similar pattern, though none of the mismatches were noticeable in everyday life.

Many clocks

Freeman says this implies that the same event in the outside world is perceived by different parts of your brain as happening at different times. This suggests that, rather than one unified "now", there are many clocks in the brain – two of which showed up in the tasks – and that all the clocks measure their individual "nows" relative to their average.
In PH's case, one or more of these clocks has been significantly slowed – shifting his average – possibly as a result of the lesions. Freeman thinks PH's timing discrepancies may be too large and have happened too suddenly for him to ignore or adapt to, resulting in him being aware of the asynchrony in everyday life.
He may perceive just one of his clocks because it is the only one he has conscious access to, says Freeman.
PH says that in general he has learned to live with the sensory mismatch but admits he has trouble in noisy places or at large meetings.
Since he hears himself speak before he feels his mouth move, does he ever feel like he's not in control of his own voice? "No, I'm definitely sure it's me that's speaking," he says, "it's just a strange sensation."
Help may be at hand: Freeman is looking for a way to slow down PH's hearing so it matches what he is seeing.
PH says he would be happy to trial a treatment, but he's actually not that anxious to fix the problem.
"It's not life-threatening," he says. "You learn to live with these things as you get older. I don't expect my body to work perfectly." *Journal reference: Cortex, doi.org/m3k*

http://www.eurekalert.org/pub_releases/2013-07/aaft-ns062813.php

No single origin for agriculture in the Fertile Crescent

Transition from foraging to farming occurred over the entire Fertile Crescent

A rich assemblage of fossils and artifacts in the foothills of the Zagros Mountains in Iran has revealed that the early inhabitants of the region began cultivating cereal grains for agriculture between 12,000 and 9,800 years ago. The discovery implies that the transition from foraging to farming took place at roughly the same time across the entire Fertile Crescent, not in a single core area of the "cradle of civilization," as previously thought. Until recently, political pressures had limited excavations of archaeological sites in the eastern Fertile Crescent, or modern-day Iran, while findings to the west—at sites in Cyprus, Syria, Turkey and Iraq, for example—provided detailed clues to the origins of agriculture.

Now, Simone Riehl from the University of Tübingen in Germany, along with colleagues from the Tübingen Senckenberg Center for Human Evolution and Paleoecology, have analyzed plant remains at the aceramic (pre-pottery) Neolithic site of Chogha Golan in Iran, and their results show that people were growing and grinding cereal grains like wheat and barley at the same time as their counterparts to the west.

Their findings appear in the 5 July issue of the journal Science.

"During the last few decades, numerous archaeological excavations were conducted in the Near East that led researchers to consider the possibility that multiple regions in the Fertile Crescent began cultivating cereal grains roughly at the same time, rather than just a single core area," Riehl explained.

The plant remains found at the Chogha Golan site document more than 2,000 years of the region's land use and represent the earliest record of long-term plant management in Iran, according to the researchers. The site's excavation, which was conducted by archaeologists from the University of Tübingen and the Iranian Center for Archaeological Research between 2009 and 2010, shows that Chogha Golan's early inhabitants cultivated wild barley, wheat, lentil and grass peas—and eventually domesticated emmer wheat—during their occupation, which began about 12,000 years ago.

"Plentiful findings of chaff remains of the cereals indicate that people processed their harvest within the sites they were living in," Riehl said. "Mortars and grinding stones may have been used for turning the grain into some kind of bulgur or flour, which may have been further processed either by cooking or roasting." (The author also notes, however, that chemical studies of the grinding tools showed that they were multi-purpose—not just for processing plant materials.)

Taken together, these new insights suggest that the eastern region of the Fertile Crescent likewise made significant contributions to the development of Neolithic culture. The findings by Riehl et al. indicate that essentially simultaneous processes led to the management of wild plants and the domestication of cereal grains across most of the Fertile Crescent.

But, how such strategies were disseminated over the entire Fertile Crescent—whether by the communication of ideas, the spread of crops or the migration of people—remains to be seen, according to the researchers.

"For some time, the emergence of agriculture in Iran was considered as part of a cultural transfer from the west," Riehl said. "This opinion was, however, mostly based on the lack of information from Iranian sites."

"We meanwhile assume that key areas for emerging domestication existed over the whole Fertile Crescent, and that there were several locations where domesticated species evolved as a result of cultivation by local human groups," the author concluded. "This does not, of course, exclude the possibility of some kind of transfer of ideas and materials between the different groups populating the Fertile Crescent."

The report by Riehl et al. was supported by the Eberhard-Karls-Universität Tübingen, the Heidelberg Academy of Sciences, the Tübingen Senckenberg Center for Human Evolution and Palaeoecology and the German Research Foundation.

http://www.eurekalert.org/pub_releases/2013-07/rhuo-sra070313.php

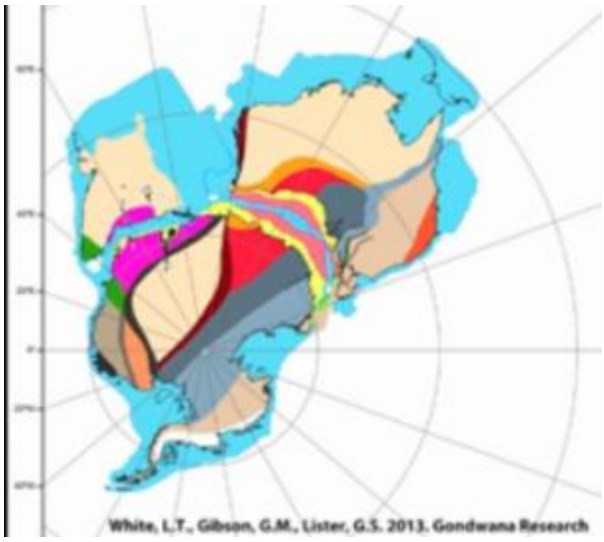
Study reveals ancient jigsaw puzzle of past supercontinent

A new study published today in the journal Gondwana Research, has revealed the past position of the Australian, Antarctic and Indian tectonic plates, demonstrating how they formed the supercontinent Gondwana 165 million years ago.

Researchers from Royal Holloway University, The Australian National University and Geoscience Australia, have helped clear up previous uncertainties on how the plates evolved and where they should be positioned when drawing up a picture of the past.

Dr Lloyd White from the Department of Earth Sciences at Royal Holloway University said: "The Earth's tectonic plates move around through time. As these movements occur over many millions of years, it has previously been difficult to produce accurate maps of where the continents were in the past.

"We used a computer program to move geological maps of Australia, India and Antarctica back through time and built a 'jigsaw puzzle' of the supercontinent Gondwana. During the process, we found that many existing studies had positioned the plates in the wrong place because the geological units did not align on each plate."



The researchers adopted an old technique used by people who discovered the theories of continental drift and plate tectonics, but which had largely been ignored by many modern scientists.

"It was a simple technique, matching the geological boundaries on each plate. The geological units formed before the continents broke apart, so we used their position to put this ancient jigsaw puzzle back together again," Dr White added.

"It is important that we know where the plates existed many millions of years ago, and how they broke apart, as the regions where plates break are often where we find major oil and gas deposits, such as those that are found along Australia's southern margin."

A video demonstrating the ancient jigsaw puzzle can be viewed here: https://vimeo.com/68311221

http://www.eurekalert.org/pub_releases/2013-07/uoea-fmt070413.php

From manga to movies: Study offers new insights into Japan's biggest media industries

Japanese films have retaken the box office in their home market in a major shift not seen since the 1960s, according to new research by the University of East Anglia (UEA).

A boom in production numbers has taken place since 2000 - in 2012 Japan produced 554 films, the first time it had broken the 500-film barrier since 1961. This is in contrast to the period from the 1950s to the end of the 1990s, when Japanese production steadily declined from about 500 movies a year to only around 250.

However, despite their popularity at home this success has yet to translate into the same kind of popular global success generated for manga (comic books) and anime, with Japan's film industry remaining locally rather than globally focused.

The findings are from the Manga Movies Project, which has been examining contemporary Japanese manga, anime and films – three of the country's biggest media industries. Dr Rayna Denison and Dr Woojeong Joo, from the School of Film, Television and Media Studies at UEA, explored the current industries, aiming to offer new insights into their markets and franchising, their success at home and beyond, and how they are responding to a fast-changing global media landscape.

Focusing on the period since 2004, the study also considered the impact of the Tohoku disaster of March 2011 on media production, distribution and consumption. The huge earthquake off the east coast of Japan and resulting tsunami left almost 16,000 people dead and almost one million buildings damaged or destroyed, including more than 100 cinemas.

The study findings are published in two new reports and Dr Denison said one of the clearest trends in contemporary Japanese film production is that many films form just a part of much larger media franchises, many of which begin with manga.

"It is well known that Japan's film industry is mature and highly diverse in terms of its genres and audiences," said Dr Denison. "What is less well known is that Japanese films have quietly retaken a dominant share of their home market since 2006 and compete head-to-head with Hollywood's biggest global blockbusters. The rise in film numbers has happened extremely fast in comparison to the previous decline, suggesting a boom cycle of production that some commentators claim is reaching its limits."

The researchers found that differences in the budgets for Japanese cinema, plus the huge amounts of capital resting behind the country's biggest films, suggest a highly competitive marketplace, but also one in which independent cinema is increasingly squeezed.

The "explosion" in films is seen to be the result of changes in production practices, particularly television companies moving into filmmaking, but also the growth in cinemas and screens. Since the late 1990s the numbers and types of screens have changed dramatically. From a largely segregated cinema system in the 1990s, where cinemas were fairly evenly divided between local, imported and mixed films, the situation has now drastically swung in favour of combined showings of domestic Japanese films and foreign imports.

In 1990 there were 600 screens devoted to Japanese cinema, 735 to overseas cinema, and 501 to mixed, whereas in 2012 there were only 91 screens solely devoted to Japanese films, and only 80 to overseas imports.

The shift is the result of the creation of multiplexes, which have led the way in increasing screen numbers from 1734 in 1990 to 3229 as of 2012.
Screen numbers were seriously affected in 2011 following the tsunami, when at least 100 cinemas in North Eastern Honshu were destroyed, and many others lacked power and other facilities that would enable regular screening schedules. By the end of that year, there were reportedly still 30 theatres in the affected areas that had been unable to reopen.
"The expansion in screen numbers has created greater space for Japanese cinema within its own market and multiplexes have created a space where all kinds of Japanese cinema are being release alongside American and other overseas releases," said Dr Denison. "The success of Japanese films at home over the last decade is strongly linked to this increase in screens and new multiplex cinema construction, which in turn has created new film-going cultures in Japan."
The study found that the movement of TV producers into films has also brought certain audience groups back to cinemas, in particular Japanese women. This shift in audiences and production strategies has resulted in producers increasing the number of movies aimed at women in their 20s and 30s, while it has also been suggested that the country's aging population is becoming an expanding target for media such as films.
Dr Denison said that when the global picture for Japanese live action cinema is examined, it is clear that older films still drive the market – particularly those from directors like Akira Kurosawa and Yasujiro Ozu - while J-horror continues to play a significant role. But unlike manga, and anime, which can be translated or over-dubbed without obvious differences between the visuals of the texts and the sounds heard, Japanese cinema is more resistant to change.
"If language remains a major boundary for Japanese media, then it is likely the country's media markets will remain limited," said Dr Denison. "However, there is a strong sense that Japanese media producers are themselves becoming more ready for the global media landscape. Japanese companies are becoming much more open to the online, global world around them. Increasing numbers of companies are shifting to dual Japanese and English language, and sometimes Chinese, versions of their websites. This has the benefit of making these industries more open to international exchanges and trade."
The project Manga Movies: Contemporary Japanese Cinema, Media Franchising and Adaptation, was funded by the Arts and Humanities Research Council. Further information and the reports are available at http://www.mangamoviesproject.com/

http://www.eurekalert.org/pub_releases/2013-07/cchm-nsr070113.php

New study reveals important role of insulin in making breast milk

Why do so many mothers have difficulty making enough milk to breastfeed? A new study by scientists at Cincinnati Children's Hospital Medical Center and the University of California Davis adds to their previous research implicating insulin's role in lactation success.

The study is the first to describe how the human mammary gland becomes highly sensitive to insulin during lactation. It is also the first study to get an accurate picture of how specific genes are switched on in the human mammary gland during lactation.
The researchers used next generation sequencing technology, RNA sequencing, to reveal "in exquisite detail" the blueprint for making milk in the human mammary gland, according to Laurie Nommsen-Rivers, PhD, a scientist at Cincinnati Children's and corresponding author of the study, published online in PLOS ONE, a journal of the Public Library of Science.
Nommsen-Rivers' previous research had shown that for mothers with markers of sub-optimal glucose metabolism, such as being overweight, being at an advanced maternal age, or having a large birth-weight baby, it takes longer for their milk to come in, suggesting a role for insulin in the mammary gland. The new research shows how the mammary gland becomes sensitive to insulin during lactation.
For a long time, insulin was not thought to play a direct role in regulating the milk-making cells of the human breast, because insulin is not needed for these cells to take in sugars, such as glucose. Scientists now, however, appreciate that insulin does more than facilitate uptake of sugars.
"This new study shows a dramatic switching on of the insulin receptor and its downstream signals during the breast's transition to a biofactory that manufactures massive amounts of proteins, fats and carbohydrates for nourishing the newborn baby," says Dr. Nommsen-Rivers. "Considering that 20 percent of women between 20 and 44 are prediabetic, it's conceivable that up to 20 percent of new mothers in the United States are at risk for low milk supply due to insulin dysregulation."
Dr. Nommsen-Rivers and her colleagues were able to use a non–invasive method to capture mammary gland RNA – a chain of molecules that are blueprints for making specified proteins – in samples of human breast milk. They then created the first publicly accessible library of genes expressed in the mammary gland based on RNA-sequencing technology.

This approach revealed a highly sensitive portrait of the genes being expressed in human milk-making cells. They discovered an orchestrated switching on and off of various genes as the mammary gland transitions from secreting small amounts of immunity-boosting colostrum in the first days after giving birth to the copious production of milk in mature lactation.
In particular, the PTPRF gene, which is known to suppress intracellular signals that are usually triggered by insulin binding to its receptor on the cell surface, may serve as a biomarker linking insulin resistance with insufficient milk supply. These results lay the foundation for future research focused on the physiological contributors to mothers' milk supply difficulties.
Now that they've demonstrated the significance of insulin signaling in the human mammary gland, they are planning a phase I/II clinical trial with a drug used to control blood sugar in type 2 diabetes to determine whether it improves insulin action in the mammary gland, thus improving milk supply. While a drug is not an ideal way to solve the problem of sub-optimal glucose metabolism impairing breastfeeding, according to Dr. Nommsen-Rivers, it is excellent for establishing proof-of-concept through the use of a placebo controlled randomized clinical trial.
"The ideal approach is a preventive one," she says. "Modifications in diet and exercise are more powerful than any drug. After this clinical trial, we hope to study those interventions."
Dr. Nommsen-Rivers began her quest to understand why so many U.S. mothers today struggle with low milk supply when she was a doctoral student at the University of California Davis.
The lead author of the study is Danielle Lemay, PhD, of the University of California Davis Research Center.

http://www.eurekalert.org/pub_releases/2013-07/bgsu-isl070513.php

In subglacial lake, surprising life goes on

Rogers team identifies species in most inhospitable realm

BOWLING GREEN, O.-Lake Vostok, buried under a glacier in Antarctica, is so dark, deep and cold that scientists had considered it a possible model for other planets, a place where nothing could live.
However, work by Dr. Scott Rogers, a Bowling Green State University professor of biological sciences, and his colleagues has revealed a surprising variety of life forms living and reproducing in this most extreme of environments. A paper published June 26 in PLOS ONE (Public Library of Science - http://dx.plos.org/10.1371/journal.pone.0067221) details the thousands of species they identified through DNA and RNA sequencing.
"The bounds on what is habitable and what is not are changing," Rogers said.
This is the fourth article the group has published about its Lake Vostok investigations. The team included Dr. Paul Morris, biology, who with Scott and doctoral student Yury Shtarkman conducted most of the genetic analyses; former doctoral students Zeynep Koçer, now with the Department of Infectious Diseases, Division of Virology, at St. Jude's Research Hospital in Memphis, performed most of the laboratory work; Ram Veerapaneni, now at BGSU Firelands, Tom D'Elia, now at Indian River State College in Florida, and undergraduate student Robyn Edgar, computer science.
Their work was supported by several grants, including two from the National Science Foundation, one from U.S. Department of Agriculture and one from the BGSU Faculty Research Committee. Together, the amount dedicated to the project was more than $250,000.
When thinking about Lake Vostok, you have to think big. The fourth-deepest lake on Earth, it is also the largest of the 400-some subglacial lakes known in Antarctica. The ice that has covered it for the past 15 million years is now more than two miles deep, creating tremendous pressure in the lake. Few nutrients are available. The lake lies far below sea level in a depression that formed 60 million years ago when the continental plates shifted and cracked. The weather there is so harsh and unpredictable that scientists visiting must have special gear and take survival training.
Not only had most scientists believed Lake Vostok completely inhospitable to life, some thought it might even be sterile.
Far from it, Rogers found. Working with core sections removed from the deep layer of ice that accreted from lake water that froze onto the bottom of the glacier where it meets the lake, Rogers examined ice as clear as diamonds that formed in the great pressure and relatively warm temperatures found at that depth. The team sampled cores from two areas of the lake, the southern main basin and near an embayment on the southwestern end of the lake.
"We found much more complexity than anyone thought," Rogers said. "It really shows the tenacity of life, and how organisms can survive in places where a couple dozen years ago we thought nothing could survive."
By sequencing the DNA and RNA from the accretion ice samples, the team identified thousands of bacteria, including some that are commonly found in the digestive systems of fish, crustaceans and annelid worms, in

addition to fungi and two species of archaea, or single-celled organisms that tend to live in extreme environments. Other species they identified are associated with habitats of lake or ocean sediments. Psychrophiles, or organisms that live in extreme cold, were found, along with heat-loving thermophiles, which suggests the presence of hydrothermal vents deep in the lake. Rogers said the presence of marine and freshwater species supports the hypothesis that the lake once was connected to the ocean, and that the freshwater was deposited in the lake by the overriding glacier.

The largest number of species overall was found in the area near the embayment, including many that are common to freshwater environments, as well as marine species, psychrophiles and thermophiles. Numerous others were found that remain unidentified. The embayment appears to contain much of the biological activity in the lake.

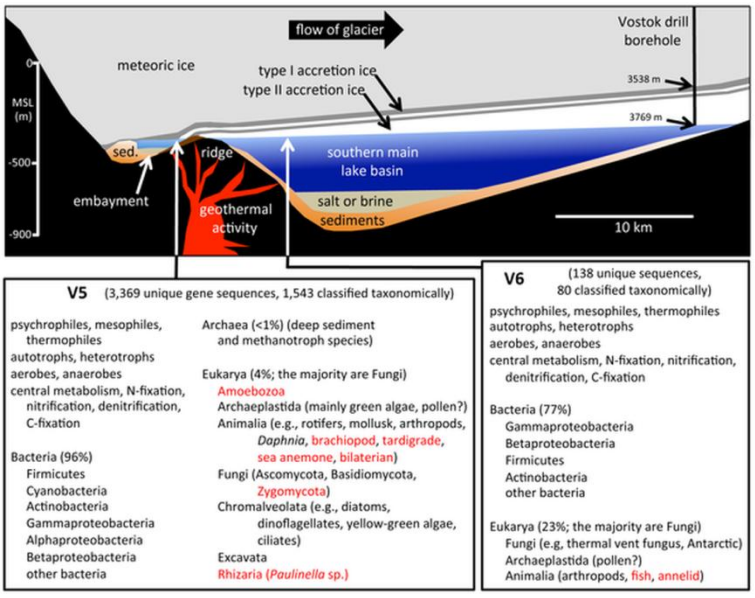
"Many of the species we sequenced are what we would expect to find in a lake," Rogers said. "Most of the organisms appear to be aquatic (freshwater), and many are species that usually live in ocean or lake sediments."

For Shtarkman, who came to BGSU from St. Petersburg, Russia, the project has proven so engrossing that he foresees a possible lifetime of study around it. "It's a very challenging project and the more you study, the more you want to know," he said. "Every day you are discovering something new and that leads to more questions to be answered. In studying the environmental DNA and RNA, we ask how similar are these sequences to those of sequences from organisms already identified in national databases. We are tracing the evolution and the ecology of the lake itself.

Before 35 million years ago, Antarctica had a temperate climate and was inhabited by a diverse assemblage of plants and animals. About 34 million years ago, Rogers said, a "huge drop in temperature occurred" and ice covered the lake, when it was probably still connected to the Southern Ocean. This lowered sea level by about 300 feet, which could have cut off Lake Vostok from the ocean. The ice cover was intermittent until a second big plunge in temperature took place 14 million years ago, and sea level dropped even farther.

As the ice crept across the lake, it plunged the lake into total darkness and isolated it from the atmosphere, and led to increasing pressure in the lake from the weight of the glacier. While many species probably disappeared from the lake, many seem to have survived, as indicated by Rogers' results.

Rogers's group had worked for several years on identifying and studying organisms in the Vostok accretion ice using a procedure involving culturing colonies of bacteria and fungi, but the process was slow, especially for graduate students who needed results for their theses.



Schematic cross-section of Lake Vostok (above), drawn to scale (based on a radar study of Lake Vostok along the glacial flow line to the ice core drill site [2]) and metagenomic/metatranscriptomic summary (below). The overlying glacier (meteoric ice – light gray) is 3538 m thick at the Vostok drill site (right). At that depth, the ice is estimated to be approximately 1 to 2 million years old [53]. Organisms and biological molecules entrapped in the meteoric ice are deposited in the lake due to breakage and melting of the ice as it flows into the lake (left) [2], [8]. The transit time for the glacier to move across the lake is approximately 15,000 to 20,000 years [2], [8], [12]. As the glacier moves over the lake, water at its surface freezes (accretes) onto the bottom of the glacier. The uppermost regions of the accretion ice represent lake water from the vicinity of the embayment followed by ice accreting near a ridge (or peninsula), and then ice accreting over the southern main lake basin. Accretion ice closest to the bottom of the meteoric ice (3538–3539 m at the drill site) is approximately 10,000 years old, while ice closest to the lake surface (3769 m at the drill site) has accreted recently. The microbes in this study originated from core sections that represent water from the vicinity of the embayment (V5, approximate location indicated by arrow) and a section of the southern main lake basin (V6, approximate location indicated by arrow). Locations of the possible hydrothermal source (red), sediment depths (orange), and extent of saltwater layers (tan) are hypothetical. Type I ice is indicated in dark gray, while type II ice is white. Lower portions of the figure summarize the types of organisms and metabolic functions indicated by sequences found in each of the samples, based on the metagenomic/metatranscriptomic analyses (complete data set used). Red font indicates organisms whose sequence identities were <97% and/or were deduced from sequence identification of organisms normally associated with those organisms.

"We started thinking of doing it a different way," Rogers said.
Instead of culturing living organisms, they concentrated on sequencing DNA and RNA in the ice. These methods, called metagenomics and metatranscriptomics, produced thousands of sequences at a time that were then analyzed using computers — procedures referred to collectively as "Big Data" methods. In contrast, it usually took years to generate enough cultured organisms for a few dozen sequences.
The problem changed from having too few sequences to having too many sequences to analyze, Rogers said.
After two years of computer analysis, the final results showed that Lake Vostok contains a diverse set of microbes, as well as some multicellular organisms.
Long before he began using metagenomics and metatranscriptomics to study the ice, Rogers and his team had developed a method to ensure purity. Sections of core ice were immersed in a sodium hypochlorite (bleach) solution, then rinsed three times with sterile water, removing an outer layer. Under strict sterile conditions, the remaining core ice was then melted, filtered and refrozen.
"Using this method, we can assure its reliability almost to 100 percent," Rogers said.
Eventually, the process rendered pellets of nucleic acids containing both DNA and RNA, able to be sequenced.
Rogers said the team erred strongly on the conservative side in reporting its results, including only those sequences of which it could be absolutely certain were from the accretion ice, but there are a multitude of others he feels are probably from the lake, opening the door to additional investigation.
The DNA sequences they produced have been deposited in the National Center for Biotechnology GenBank database, and will be available to other researchers for further study.

http://www.huffingtonpost.com/2013/07/06/head-transplant-italian-neuroscientist_n_3533391.html

Human Head Transplants Now Possible, Italian Neuroscientist Says (VIDEO)

In a provocative new paper, an Italian neuroscientist outlines how to perform a complete human head transplant, arguing that such a surgical procedure is now within the realm of possibility.

Switching heads sounds pretty "Frankenstein," for sure. But for decades researchers have been trying the procedure on animals. In 1970, the first head "linkage" was achieved in a monkey. But no one knew how to hook up the transplanted head to the spinal cord.
Now Dr. Sergio Canavero of the Turin Advanced Neuromodulation Group says he knows how to solve that problem. "The greatest technical hurdle to such endeavor is of course the reconnection of the donor's and recipient's spinal cords," Dr. Canavero wrote in the paper. "It is my contention that the technology only now exists for such linkage. This paper sketches out a possible human scenario and outlines the technology to reconnect the severed cord (project GEMINI)."
He went on to say that several now-hopeless medical conditions might be addressed with the procedure, which would cost about $13 million.
Among the conditions that might be treated with a head transplant include muscular dystrophy and quadriplegia with widespread organ failure, according to U.S. News & World Report. And even some commenters on Reddit wrote they would be willing to donate their heads if given the option.
Dr. Canavero wrote in his paper that a clean-cut must be performed to disconnect and reconnect the donor's head at the spine. Then, special adhesives -- such as polyethylene glycol (PEG) -- would be used to fuse the donor's head and spine to the recipient. "It is this 'clean cut' the key to spinal cord fusion, in that it allows proximally severed axons to be 'fused' with their distal counterparts," Canavero wrote. And, a clean cut may allow the body to naturally repair the severed nerves.
But not everyone is convinced.
"It's complete fantasy, that you could use [PEG technology] in such a traumatic injury in an adult mammal," Dr. Jerry Silver, Case Western Reserve University neurologist, told CBSNews.com. "But to severe a head and even contemplate the possibility of gluing axons back properly across the lesion to their neighbors is pure and utter fantasy in my opinion... This is bad science, this should never happen."
Canavero's paper was published in the current issue of the journal Surgical Neurology International.

http://phys.org/news/2013-07-toxic-groundwater-fukushima.html

Toxic radiation 'in groundwater' at Fukushima

TEPCO will ask Japan's nuclear watchdog to green light two of seven units at the world's biggest nuclear plant in Niigata

TEPCO said last week it would ask Japan's nuclear watchdog for the green light to re-fire two of the seven units at the world's biggest Kashiwazaki Kariwa nuclear plant in Niigata prefecture, a move rebuked by local leaders.
Toxic radioactive substances have once again been detected in groundwater at the crippled Fukushima nuclear plant, its Japanese operator said on Sunday, the latest in a series of incidents at the tsunami-battered complex.

Tokyo Electric Power Co (TEPCO) said tests showed that tritium, a radioactive isotope of hydrogen used in glow-in-the-dark watches, was present at levels 10 times the permitted rate.

"From test samples on July 5... we detected a record high 600,000 becquerels per litre" of tritium, 10 times higher than the government guideline of 60,000 becquerels per litre, TEPCO said in a statement.

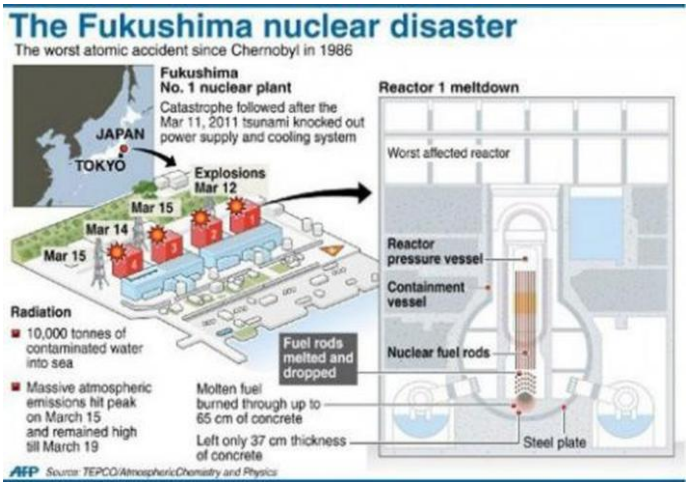
"We continue efforts to prevent further expansion of contamination by construction works... and will strengthen monitoring of pollution comprehensively," it said.

The new readings came after TEPCO said in late June that it had detected the highly toxic strontium-90, a by-product of nuclear fission that can cause bone cancer if ingested, at levels 30 times the permitted rate.

At the time it had detected tritium at around eight times the allowed level, or 500,000 becquerels per litre.

The substances, which were released by the meltdowns of reactors at the plant in the aftermath of the huge tsunami of March 2011, were not absorbed by soil and have made their way into underground water.

Subsoil water usually flows out to sea, meaning these two substances could normally make their way into the ocean, possibly affecting marine life and ultimately impacting humans who eat sea creatures.



Graphic on the March 11, 2011 nuclear disaster at Japan's Fukushima power station

Tokyo Electric Power Co (TEPCO) said on Sunday tests showed that tritium, a radioactive isotope of hydrogen used in glow-in-the-dark watches, was present at levels 10 times the permitted rate.

However, a TEPCO official said last month that seawater data showed no abnormal rise in the levels of either substance as the company believed the groundwater was largely contained by concrete foundations and steel sheets.

The revelations are the latest in a growing catalogue of mishaps at the crippled plant, more than two years after the worst nuclear disaster the world has seen in a generation.

TEPCO said last week it would ask Japan's nuclear watchdog for the green light to re-fire two of the seven units at the world's biggest Kashiwazaki Kariwa nuclear plant in Niigata prefecture, a move rebuked by local leaders.

Tens of thousands of people were forced from their homes by the threat of radiation after the tsunami and Fukushima disaster, with some still unable to return.

Although the nuclear accident is not officially recorded as having directly killed anyone, the natural disaster claimed more than 18,000 lives and was one of Japan's worst ever peacetime tragedies.

http://www.eurekalert.org/pub_releases/2013-07/epfd-cnf070513.php

Champion nano-rust for producing solar hydrogen

Water and some nano-structured iron oxide is all it takes to produce bubbles of solar hydrogen. EPFL and Technion scientists just discovered the champion structure to achieve this

In the quest for the production of renewable and clean energy, photoelectrochemical cells (PECs) constitute a sort of a Holy Grail. PECs are devices able of splitting water molecules into hydrogen and oxygen in a single operation, thanks to solar radiation. "As a matter of fact, we've already discovered this precious chalice, says Michael Grätzel, Director of the Laboratory of Photonics and Interfaces (LPI) at EPFL and inventor of dye-sensitized photoelectrochemical cells. Today we have just reached an important milestone on the path that will lead us forward to profitable industrial applications."

This week, Nature Materials is indeed publishing a groundbreaking article on the subject. EPFL researchers, working with Avner Rotschild from Technion (Israel), have managed to accurately characterize the iron oxide nanostructures to be used in order to produce hydrogen at the lowest possible cost. "The whole point of our approach is to use an exceptionally abundant, stable and cheap material: rust," adds Scott C. Warren, first author of the article.

At the end of last year, Kevin Sivula, one of the collaborators at the LPI laboratory, presented a prototype electrode based on the same principle. Its efficiency was such that gas bubbles emerged as soon as it was under a light stimulus. Without a doubt, the potential of such cheap electrodes was demonstrated, even if there was still room for improvement.

By using transmission electron microscopy (TEM) techniques, researchers were able to precisely characterize the movement of the electrons through the cauliflower-looking nanostructures forming the iron oxide particles,

laid on electrodes during the manufacturing process. "These measures have helped us understand the reason why we get performance differences depending on the electrodes manufacturing process", says Grätzel.
By comparing several electrodes, whose manufacturing method is now mastered, scientists were able to identify the "champion" structure. A 10x10 cm prototype has been produced and its effectiveness is in line with expectations. The next step will be the development of the industrial process to large-scale manufacturing. A European funding and the Swiss federal government could provide support for this last part.
Evidently, the long-term goal is to produce hydrogen – the fuel of the future – in an environmentally friendly and especially competitive way. For Michael Grätzel, "current methods, in which a conventional photovoltaic cell is coupled to an electrolyzer for producing hydrogen, cost 15 € per kilo at their cheapest. We're aiming at a € 5 charge per kilo".

http://phys.org/news/2013-07-afar-scientists-oceans.html

Melting in the Afar helps scientists understand how oceans form

Lavas from the Afar Depression in Ethiopia, where three tectonic plates are spreading apart, have given scientists a new insight into how ocean basins form.

Erta Ale lava lake in the Afar region of Africa.

The Afar region is geologically unique, as it is the only place in the world where two continents are at the advanced stage of pulling away from each other. Geology tells us that when tectonic plates pull apart like this, the continental crusts usually gets thinner causing a depression to form between them. This often gets filled with a sea or, if the continents break apart altogether, a new ocean basin. By studying this so-called rifting process in the present, geologists hope to better understand how other ocean basins, like the North Atlantic, formed.

The Afar rift is home to numerous volcanoes and the magma the feeds these plays an important role in causing the crust to rift apart. UK and US researchers wanted to understand how and where the magma that causes the rifting in Afar is formed.
'Afar is the best example we currently have of advanced continental rifting – where flowing magma is forcing its way upwards causing the continents to break apart' explains Dr David Ferguson from the Lamont-Doherty Earth Observatory at Colombia University in the USA, who lead the research.
'In recent years we've seen some specific phases where we've seen lots of volcanic eruptions at the same time as lots of magma has intruded between the plates, forcing Africa and Arabia apart. Understanding how this magma is created is integral to understanding the process of tectonic rifting,' he adds.
Published today in Nature, the study found that the Earth's mantle layer directly beneath the rift valley is about 100 C hotter than the mantle beneath other continental regions. The hotter temperature means that there is a sustained supply of magma being created beneath Afar. This then moves upwards to the surface, feeding the many volcanoes at the surface.
'As the mantle is hotter it means it will melt much more easily and percolate up through the rocks. That explains why there are so many volcanoes,' says Dr Derek Keir from NERC's National Oceanography Centre, co-author on the study.
The researchers also found that the tectonic plates were thicker at the point where they were spreading than expected.
'If you take a continent and spread it apart, if the initial rift is 100km wide and then it extends to 400 km wide, like we saw at the Red Sea, it's opened by a factor of four times. So, you would expect the plates to be four times thinner - just like if you stretch a piece of toffee it gets thinner,' explains Keir.
'But here we see it's much thicker. We think that's because the plate cools as it extends and this maintains its thickness.'
The rift is approaching the age where it should form an oceanic basin, so it should be very thin by now.
'The thickness doesn't mean a new ocean basin won't form anytime soon but it does mean at some point the African plate will have to be thinned and stretched very quickly,' says Ferguson.
The team now hope to extend this study across entire regions, so that they can better understand how whole tectonic plates deform when continents break into two parts.
More information: www.nature.com/nature/journal/v499/n7456/full/nature12292.html