http://www.eurekalert.org/pub_releases/2013-08/mu-cb081813.php

'Poisoning' corrosion brings stainless magnesium closer

In a discovery that could have major implications for the aerospace, automotive and electronics industries, scientists have found a way to dramatically reduce the corrosion rate of lightweight wonder metal magnesium: adding arsenic.

Weighing in at two thirds less than aluminium, magnesium is the lightest structural metal. It has many potential industrial applications, but uptake is severely restricted by its poor resistance to corrosion. Identification of methods to restrict magnesium corrosion is the first step in engineering such technology into functional alloys. For the first time, a group of researchers, led by Monash University's Associate Professor Nick Birbilis, have created a magnesium alloy with significantly reduced corrosion rates by adding a cathodic poison - arsenic. They found that the addition of very low levels of arsenic to magnesium retards the corrosion reaction by effectively 'poisoning' the reaction before it completes.

Once magnesium is available in a more stainless, or corrosion-resistant, form wider use will lead to significant weight and energy savings in transportation industries. It has been the subject of significant research efforts concentrating on developing light metals.

Associate Professor Birbilis, of the Monash Department of Materials Engineering, said the discovery would contribute to the birth of more stainless magnesium products by exploiting cathodic poisons.

"This is a very important and timely finding. In an era of light-weighting for energy and emissions reductions, there is a great demand for magnesium alloys in everything from portable electronics to air and land transportation," Associate Professor Birbilis said.

"Magnesium products are rapidly evolving to meet the demands of industry, but presently are hindered by high corrosion rates. The arsenic effect we discovered is now being trialled as a functional additive to existing commercial alloys. "Our breakthrough will help develop the next generation of magnesium products, which must be more stainless."

The research, conducted with the University of Wales and CSIRO, is published in the journal Electrochemistry Communications.

http://www.eurekalert.org/pub_releases/2013-08/w-edw081513.php

Experts describe ways to eliminate wasteful medical tests and procedures

Medical organizations are participating in a campaign to help clinicians and patients avoid wasteful and sometimes harmful medical interventions.

Recently, experts in pediatric and adult health from diverse geographic locations of the United States and from a mix of academic and non- academic settings shared their experiences, consulted their colleagues, and analyzed numerous studies in the medical literature to determine the top recommendations for improving healthcare value. Following these recommendations, which are outlined in a new study published today in the Journal of Hospital Medicine, will lower costs and lead to better care for patients.

Experts estimate that waste constitutes up to 20% of health care expenditures in the United States. To address this problem a number of national medical societies have joined the Choosing Wisely® campaign, with each creating a list of five common but sometimes unnecessary, tests, therapies, or procedures in their fields that patients and physicians should question and discuss. The Society of Hospital Medicine joined this effort in 2012, and it asked experts to create such lists regarding the care provided to hospitalized adults and children. In addition to including the Choosing Wisely lists for pediatric and adult hospitalists, the new articles provide details about the methodologies used to create them. The details can serve as a blueprint for other healthcare organizations interested in researching and developing lists of potentially over-used or harmful interventions. The recommendations – five for hospitalists and five for pediatric hospitalists – were published jointly by the American Board of Internal Medicine Foundation and the Society of Hospital Medicine in early 2013.

The top five recommendations proposed for hospitalized children are:

Don't order chest radiographs in children with asthma or bronchiolitis. This has the potential to decrease costs, reduce radiation exposure, and minimize the overuse of antibiotics due to false positive results.

Don't use bronchodilators in children with bronchiolitis because the agents have minimal or no treatment effects.

Don't use systemic corticosteroids in children under two years of age with a lower respiratory tract infection because the treatment is potentially harmful and provides little or no benefit.

Don't treat gastroesophageal reflux in infants routinely with acid suppression therapy, such as proton pump inhibitors. Studies show that such treatment is no more effective than placebo in infants, and it may cause side effects.

Don't use continuous pulse oximetry—a method for measuring oxygen saturation in the blood—routinely in children with acute respiratory illness unless they are on supplemental oxygen. Continuous monitoring of oxygen saturations in hospitalized infants with bronchiolitis may lead to overdiagnosis of hypoxemia, increased hospital duration, and the use of oxygen that is of no apparent benefit to the child.

"If pediatricians around the country adopt and follow these recommendations, the savings to our health care system could be in the millions, given the large number of hospitalized children this would affect," said lead researcher Ricardo Quinonez, MD, FAAP, FHM of the Children's Hospital of San Antonio and Baylor College of Medicine.

In an accompanying review, researchers also outlined the five recommendations adopted by the Society of Hospital Medicine regarding the care of adults. These recommendations include:

Do not place, or leave in place, urinary catheters for incontinence or convenience or monitoring of output for non-critically ill patients.

Do not prescribe medications for stress ulcer prophylaxis to medical inpatients unless at high risk for gastrointestinal complications.

Avoid transfusions of red blood cells for arbitrary hemoglobin or hematocrit thresholds and in the absence of symptoms or active coronary disease, heart failure, or stroke.

Do not order continuous telemetry monitoring outside of the intensive care unit without using a protocol that governs continuation.

Do not perform repetitive complete blood count and chemistry testing in the face of clinical and lab stability.

"These [pediatric and adult] lists are good starting points, and in fact many hospitalist groups, including our own, are using the Society of Hospital Medicine practices as a foundation for our waste reduction efforts," wrote Andrew Auerbach, MD, MPH, and Robert Wachter, MD, of the University of California, San Francsico, in an accompanying editorial. "The next challenge will be translating these recommendations into actionable measures and then clinical practice."

Through a grant from the American Board of Internal Medicine Foundation and supported by the Robert Wood Johnson Foundation, the Society of Hospital Medicine has already begun to promote the adoption of the recommendations for hospitalists and pediatric hospitalists. It will be educating hospitalists through a series of online webinars, presentations at regional meetings and a national competition to gather and promote the best case studies in implementing Choosing Wisely recommendations in hospitals. For more information, visit http://www.hospitalmedicine.org/choosingwisely.

http://phys.org/news/2013-08-newly-ocean-plume-major-source.html

Newly discovered ocean plume could be major source of iron

Scientists have discovered a vast plume of iron and other micronutrients more than 1,000 km long billowing from hydrothermal vents in the South Atlantic Ocean.

Phys.org - The finding, soon to be published in the journal Nature Geoscience, calls past estimates of iron abundances into question, and may challenge researchers' assumptions about iron sources in the world's seas. "This study and other studies like it are going to force the scientific community to reevaluate how much iron is really being contributed by hydrothermal vents and to increase those estimates, and that has implications for not only iron geochemistry but a number of other disciplines as well," says Mak Saito, a WHOI associate scientist and lead author of the study.

Saito and his team of collaborators—which includes WHOI researchers and a colleague affiliated with the University of Liverpool (U.K.)—didn't set out to find iron plumes in the South Atlantic. They set sail aboard the R/V Knorr in 2007 as part of the Cobalt, Iron and Micro-organisms from the Upwelling zone to the Gyre (or CoFeMUG, pronounced "coffee mug") expedition, which intended to map chemical composition and microbial life along the ship's route between Brazil and Namibia. As the scientists traveled the route, they sampled the seawater at frequent intervals and multiple depths along the way, and then stored the samples for in-depth analysis back on land.

Their route passed over the Mid-Atlantic Ridge, a band of mountains and valleys running along the Atlantic Ocean floor from the Arctic to the Antarctic where several of the Earth's major tectonic plates are slowly spreading apart. Hydrothermal vents, or fissures in the Earth's crust, are found along the ridge, but they haven't been extensively studied because slow-spreading ridges are thought to be less active than fast-spreading ones. Past studies using helium, which is released from the Earth's mantle through hydrothermal vents and is routinely used as an indicator of vent activity, have found little coming from mid-Atlantic vents, and researchers have assumed that means the vents spew little iron as well.

So Saito and his colleagues were surprised by what their samples revealed when later studied in the lab. Once filtered and analyzed, some of the seawater showed unexpectedly high levels of iron and manganese. When Abigail Noble, then a WHOI graduate student, and Saito plotted the sites where the iron-rich samples were

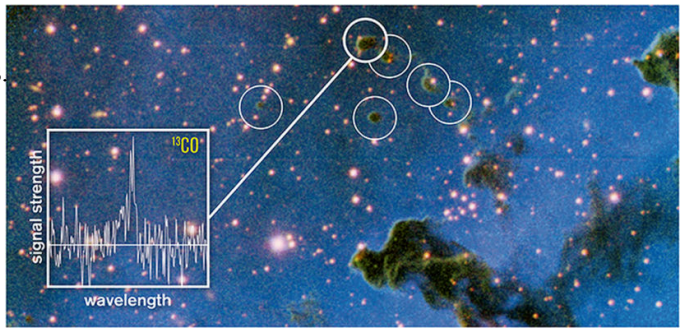
taken, they realized the samples formed a distinct plume—a cloud of nutrients ranging in depth from 1,500 to 3,500 meters that spanned more than 1,000 km of the South Atlantic Ocean.
"We had never seen anything like it," Saito says. "We were sort of shocked—there's this huge bull's-eye right in the middle of the South Atlantic Ocean. We didn't quite know what to do with it, because it went contrary to a lot of our expectations."
The plume's ratio of iron to helium was 80-fold higher than ratios reported for faster-spreading ridges in the southeastern Pacific Ocean.
The serendipitous discovery casts doubt on the assumption that slow-spreading ridges are iron-poor, and it raises questions about the use of helium as an indicator for iron flux in hydrothermal vents, Saito says.
"We've assumed that low helium means low iron, and our study finds that that's not true," Saito says. "There's actually quite a lot of iron coming out of these slow-spreading regions in the Atlantic, where people thought there would be little to none."
And that has profound implications, because iron is a critical element for ocean life. Iron is known to spur the growth of phytoplankton in many marine habitats, especially those important in the ocean's carbon cycle, which, in turn, impacts atmospheric carbon dioxide levels and Earth's climate. Because more than half the world's seafloor ridges are slow-spreading, the team's discovery suggests there may be far more iron from these locations than previously estimated.
"We need to understand where iron is in the ocean and where it's coming from to understand the role of iron in the marine carbon cycle with any confidence," Saito says.
Saito and his colleagues hope future studies will reveal the exact shape and extent of the plume, and just how much of its iron and other micronutrients persist and rise to the surface. Answering these lingering questions will help researchers truly understand how hydrothermal vents affect the ocean as a whole, Saito says.

http://phys.org/news/2013-08-free-floating-planets-born-free.html

Free-floating planets may be born free

Tiny, round, cold clouds in space have all the right characteristics to form planets with no parent star. New observations, made with Chalmers University of Technology telescopes, show that not all free-floating planets were thrown out of existing planetary systems. They can also be born free.

Previous research has shown that there may be as many as 200 billion free-floating planets in our galaxy, the Milky Way. Until now scientists have believed that such "rogue planets", which don't orbit around a star, must have been ejected from existing planetary systems. New observations of tiny dark clouds in space point out another possibility: that some free-floating planets formed on their own.
A team of astronomers from Sweden and Finland used several telescopes to observe the Rosette Nebula, a huge cloud of gas and dust 4600 light years from Earth in the constellation Monoceros (the Unicorn).



Astronomers have found that tiny, round, dark clouds called globulettes have the right characteristics to form free-floating planets. The graph shows the spectrum of one of the globulettes taken at the 20-metre telescope at Onsala Space Observatory. Radio waves from molecules of carbon monoxide (13CO) give information on the mass and structure of these clouds. **ESO/M. Mäkelä**

They collected observations in radio waves with the 20-metre telescope at Onsala Space Observatory in Sweden, in submillimetre waves with APEX in Chile, and in infrared light with the New Technology Telescope (NTT) at ESO's La Silla Observatory in Chile.
"The Rosette Nebula is home to more than a hundred of these tiny clouds – we call them globulettes", says Gösta Gahm, astronomer at Stockholm University, who led the project.
"They are very small, each with diameter less than 50 times the distance between the Sun and Neptune. Previously we were able to estimate that most of them are of planetary mass, less than 13 times Jupiter's mass. Now we have much more reliable measures of mass and density for a large number of these objects, and we have also precisely measured how fast they are moving relative to their environment", he says.
"We found that the globulettes are very dense and compact, and many of them have very dense cores. That tells us that many of them will collapse under their own weight and form free-floating planets. The most massive of them can form so-called brown dwarfs", says team member Carina Persson, astronomer at Chalmers University of Technology.
Brown dwarfs, sometimes called failed stars, are bodies whose mass lies between that of planets and stars.

The study shows that the tiny clouds are moving outwards through the Rosette Nebula at high speed, about 80 000 kilometres per hour.
"We think that these small, round clouds have broken off from tall, dusty pillars of gas which were sculpted by the intense radiation from young stars. They have been accelerated out from the centre of the nebula thanks to pressure from radiation from the hot stars in its centre", explains Minja Mäkelä, astronomer at the University of Helsinki.
According to Gösta Gahm and his team, the tiny dark clouds are being thrown out of the Rosette Nebula. During the history of the Milky Way, countless millions of nebulae like the Rosette have bloomed and faded away. In all of these, many globulettes would have formed.
"There are so many of them that they could be a significant source of the free-floating planets that have been discovered in recent years", he says.
Astronomers know of almost 900 planets which orbit around other stars than the Sun, but free-floating planets have also been found. Some have been discovered using a technique called microlensing, in which the planet is found when it passes in front of a background star, temporarily making it look brighter. This is an effect predicted by Einstein's theory of general relativity, in which the light from the star is bent when the planet passes in front of it, a so-called gravitational lens. Scientists have estimated that the number of free-floating planets in our galaxy may exceed 200 billion.
The study has been published in the article "Mass and motion of globulettes in the Rosette Nebula" in the July issue of the journal Astronomy & Astrophysics. The team observed radio waves from molecules of carbon monoxide using the 20-metre radio telescope at Onsala Space Observatory, Sweden, and submillimetre light with the telescope APEX at 5100 metres altitude in the Atacama desert in northern Chile. APEX is a collaboration between the Max Planck Institute for Radio Astronomy in Bonn, Germany, Onsala Space Observatory and ESO, with operations of the telescope entrusted to ESO. Observations in infrared light were made using the 3.58 metre New Technology Telescope (NTT) at ESO's La Silla Observatory.
More information: dx.doi.org/10.1051/0004-6361/201321547

http://www.eurekalert.org/pub_releases/2013-08/uow-mmc081913.php

Molten magma can survive in upper crust for hundreds of millennia

Reservoirs of silica-rich magma – the kind that causes the most explosive volcanic eruptions – can persist in Earth's upper crust for hundreds of thousands of years without triggering an eruption, according to new University of Washington modeling research.

That means an area known to have experienced a massive volcanic eruption in the past, such as Yellowstone National Park, could have a large pool of magma festering beneath it and still not be close to going off as it did 600,000 years ago.
"You might expect to see a stewing magma chamber for a long period of time and it doesn't necessarily mean an eruption is imminent," said Sarah Gelman, a UW doctoral student in Earth and space sciences.
Recent research models have suggested that reservoirs of silica-rich magma, or molten rock, form on and survive for geologically short time scales – in the tens of thousands of years – in the Earth's cold upper crust before they solidify. They also suggested that the magma had to be injected into the Earth's crust at a high rate to reach a large enough volume and pressure to cause an eruption.
But Gelman and her collaborators took the models further, incorporating changes in the crystallization behavior of silica-rich magma in the upper crust and temperature-dependent heat conductivity. They found that the magma could accumulate more slowly and remain molten for a much longer period than the models previously suggested.
Gelman is the lead author of a paper explaining the research published in the July edition of Geology. Co-authors are Francisco Gutiérrez, a former UW doctoral student now with Universidad de Chile in Santiago, and Olivier Bachmann, a former UW faculty member now with the Swiss Federal Institute of Technology in Zurich.
There are two different kinds of magma and their relationship to one another is unclear. Plutonic magma freezes in the Earth's crust and never erupts, but rather becomes a craggy granite formation like those commonly seen in Yosemite National Park. Volcanic magma is associated with eruptions, whether continuous "oozing" types of eruption such as Hawaii's Kilauea Volcano or more explosive eruptions such as Mount Pinatubo in the Philippines or Mount St. Helens in Washington state.
Some scientists have suggested that plutonic formations are what remain in the crust after major eruptions eject volcanic material. Gelman believes it is possible that magma chambers in the Earth's crust could consist of a core of partially molten material feeding volcanoes surrounded by more crystalline regions that ultimately turn into plutonic rock. It is also possible the two rock types develop independently, but those questions remain to be answered, she said.

The new work suggests that molten magma reservoirs in the crust can persist for far longer than some scientists believe. Silica content is a way of judging how the magma has been affected by being in the crust, Gelman said. As the magma is forced up a column from lower in the Earth to the crust, it begins to crystallize. Crystals start to drop out as the magma moves higher, leaving the remaining molten rock with higher silica content.
"These time scales are in the hundreds of thousands, even up to a million, years and these chambers can sit there for that long," she said.
Even if the molten magma begins to solidify before it erupts, that is a long process, she added. As the magma cools, more crystals form giving the rock a kind of mushy consistency. It is still molten and capable of erupting, but it will behave differently than magma that is much hotter and has fewer crystals.
The implications are significant for volcanic "arcs," found near subduction zones where one of Earth's tectonic plates is diving beneath another. Arcs are found in various parts of the world, including the Andes Mountains of South America and the Cascades Range of the Pacific Northwest.
Scientists have developed techniques to detect magma pools beneath these arcs, but they cannot determine how long the reservoirs have been there. Because volcanic magma becomes more silica-rich with time, its explosive potential increases.
"If you see melt in an area, it's important to know how long that melt has been around to determine whether there is eruptive potential or not," Gelman said. "If you image it today, does that mean it could not have been there 300,000 years ago? Previous models have said it couldn't have been. Our model says it could. That doesn't mean it was there, but it could have been there."
The work was funded by the National Science Foundation and the National Scientific and Technological Research Commission of Chile.

http://www.medscape.com/viewarticle/809348?src=rss

Game Changers in Pediatric CPR

Three exciting new studies from the past year that may prove game changing in pediatric cardiac arrest and survival

Robert A. Berg, MD

I am Dr. Bob Berg. I am the Chief of Pediatric Critical Care at the Children's Hospital of Philadelphia (CHOP), and I am part of a large group of investigators that are interested in cardiac arrest, resuscitation, and saving children's lives. I would like to tell you about 3 very exciting new studies that have come out in the past year that I think are game changers in pediatric cardiac arrest and survival.
First and foremost is an article that was just published for which Saket Girotra served as first author and with which many of us at CHOP were involved.[1] The study was published in *Circulation: Cardiovascular Quality and Outcomes* in 2013. This study found, for the first time, that hospitals that were part of the American Heart Association's *Get With the Guidelines* resuscitation program, which includes CHOP, over the first decade of the 21st century had an 8% improvement in survival per year [in patients who experienced an in-hospital cardiac arrest]. This study shows that, when you focus on in-hospital cardiac arrest and optimal resuscitation, you really can save more lives. This is a big deal because in-hospital cardiac arrest occurs in about 6000 patients a year. About 200,000 in-hospital adults get cardiopulmonary resuscitation (CPR) every year. This is a large number of people and it is a major public health problem. So, first, we can save lives.
The second article was published in *Circulation* and Renee Matos was the first author; Vinay Nadkarni, I, and others at CHOP served as collaborators.[2] The study looked at the appropriate duration of CPR. In fact, we did not determine what was appropriate but instead examined the outcomes with different durations of CPR. In the past, it was thought that more than 15-20 minutes of CPR and a few doses of epinephrine was probably futile. After that point, we should stop. Many hospitals did. To our surprise, we found that 12% of children that had CPR provided in hospital for 35 minutes survived to discharge, and their neurologic outcomes were just as good as those children who had CPR for 10 minutes, with a return of spontaneous circulation. So, the exciting game changer is that prolonging CPR, at least for some children, can result in survival *and* survival with good neurologic outcome. I want to be clear that most patients that go that long do not survive. Twelve percent survival means 88% did not survive. There certainly was bias by those clinicians about why they went so long with these patients. However, regardless of the reason, it is very clear that doing CPR for more than a half-hour can result in good outcomes. Interestingly, there was a study in adults by Zachary Goldberger and others, in which I was a coauthor, which published in the *Lancet* in 2012, with very similar findings in adults.[3] In patients receiving more than 30 minutes of CPR, 9% survived and survived with good neurologic outcomes.

So, (1) we are improving survival for cardiac arrest in our hospitals, (2) prolonged duration can sometimes result in excellent outcomes, and (3) an exciting study that will be coming out soon in *Critical Care Medicine*

from the CHOP Research Group found that, nationally, pediatric cardiac arrests have shifted from the wards to the intensive care units (ICUs) to an amazing extent.[4] Now, 95% of in-hospital cardiac arrests, those that occur on a ward or in an ICU, occur in the ICU. What is the relevance of that? We have shifted these events from a ward setting, where it may be a while before somebody detects cardiac arrest and which may not have all the resources to provide the best CPR, to an ICU where there is immediate recognition and rapid response. ICUs are a pit-crew like Ferrari team, where everybody is changing the wheels and wiping the front of the car so that everything is done perfectly. We have shifted [these events] to the ICU where we can provide optimal care, and we believe that that is part of the reason why the survivals are improving in those other studies.
I want to leave you with this: There is exciting news with pediatric intensive care and pediatric cardiac arrest in hospitals. We now can [first and foremost] save more children's lives than we used to in the past. Second, one of the mechanisms for saving them is by doing CPR for a more prolonged period rather than quitting and being despondent too early. Third, we are shifting cardiac arrest from the ward to the ICUs where we can give the best of care.

1. Girotra S, Spertus JA, Li Y, Berg RA, Nadkarni VM, Chan PS; American Heart Association Get With the Guidelines–Resuscitation Investigators. Survival trends in pediatric in-hospital cardiac arrests: an analysis from Get With the Guidelines-Resuscitation. Circ Cardiovasc Qual Outcomes. 2013;6:42-49. Abstract

2. Matos RI, Watson RS, Nadkarni VM, et al. Duration of cardiopulmonary resuscitation and illness category impact survival and neurologic outcomes for in-hospital pediatric cardiac arrests. Circulation. 2013;127:442-451. Abstract

3. Goldberger ZD, Chan PS, Berg RA, et al. Duration of resuscitation efforts and survival after in-hospital cardiac arrest: an observational study. Lancet. 2012;380:1473-1481. Abstract

4. Berg RA, Sutton RM, Holubkov R, et al. Ratio of PICU versus ward cardiopulmonary resuscitation events is increasing. Crit Care Med. 2013 Aug 5. [Epub ahead of print]

http://www.sciencedaily.com/releases/2013/08/130819141641.htm

Computer Can Read Letters Directly from the Brain

Analysing MRI images of the brain with an elegant mathematical modelenabled researchers to reconstruct thoughts more accurately than ever before.

By analysing MRI images of the brain with an elegant mathematical model, it is possible to reconstruct thoughts more accurately than ever before. In this way, researchers from Radboud University Nijmegen have succeeded in determining which letter a test subject was looking at.
The journal Neuroimage has accepted the article, which will be published soon.
Functional MRI scanners have been used in cognition research primarily to determine which brain areas are active while test subjects perform a specific task. The question is simple: is a particular brain region on or off? A research group at the Donders Institute for Brain, Cognition and Behaviour at Radboud University has gone a step further: they have used data from the scanner to determine what a test subject is looking at.
The researchers 'taught' a model how small volumes of 2x2x2 mm from the brain scans -- known as voxels -- respond to individual pixels. By combining all the information about the pixels from the voxels, it became possible to reconstruct the image viewed by the subject. The result was not a clear image, but a somewhat fuzzy speckle pattern. In this study, the researchers used hand-written letters.

Prior knowledge improves model performance

'After this we did something new', says lead researcher Marcel van Gerven. 'We gave the model prior knowledge: we taught it what letters look like. This improved the recognition of the letters enormously. The model compares the letters to determine which one corresponds most exactly with the speckle image, and then pushes the results of the image towards that letter. The result was the actual letter, a true reconstruction.'
'Our approach is similar to how we believe the brain itself combines prior knowledge with sensory information. For example, you can recognise the lines and curves in this article as letters only after you have learned to read. And this is exactly what we are looking for: models that show what is happening in the brain in a realistic fashion. We hope to improve the models to such an extent that we can also apply them to the working memory or to subjective experiences such as dreams or visualisations. Reconstructions indicate whether the model you have created approaches reality.'

Improved resolution; more possibilities

'In our further research we will be working with a more powerful MRI scanner,' explains Sanne Schoenmakers, who is working on a thesis about decoding thoughts. 'Due to the higher resolution of the scanner, we hope to be able to link the model to more detailed images. We are currently linking images of letters to 1200 voxels in the brain; with the more powerful scanner we will link images of faces to 15,000 voxels.'

Sanne Schoenmakers, Markus Barth, Tom Heskes, Marcel van Gerven. Linear reconstruction of perceived images from human brain activity. NeuroImage, 2013; DOI: 10.1016/j.neuroimage.2013.07.043

http://www.eurekalert.org/pub_releases/2013-08/ip-nch081913.php

Novel Chinese herbal medicine JSK improves spinal cord injury outcomes in rats

Findings published in Restorative Neurology and Neuroscience

Amsterdam, NL - A new study published in Restorative Neurology and Neuroscience demonstrates that Chinese herbal medicine Ji-Sui-Kang (JSK), given systemically for three weeks after injury in rats, improved locomotor function, reduced tissue damage, and preserved the structure of neural cells compared to control rats. The report also includes data showing that JSK may first act to reduce inflammation and cell apoptosis and death, and boost local oxygen supply while, later on, it appears to restore function and promote tissue regeneration.

Although Chinese herbal medicines have traditionally been used for a variety of ailments, the rationale for their use relies more on anecdotal evidence than the results of modern-day controlled experiments.

"A number of anecdotal reports from Chinese medicine practitioners indicate that treatment with a novel herbal formulation, JSK, for periods of one week or three months improved functional recovery," explains co-lead investigator Shucui Jiang, MD, PhD, head of the Hamilton NeuroRestorative Group at McMaster University in Hamilton, Ontario, Canada. "Our present study provides an important and necessary foundation for further studies of JSK."

In this study rats began JSK treatment immediately after undergoing spinal cord injury. Within 7 days, hindlimb locomotor function was significantly better in JSK-treated rats compared to those receiving only saline. JSK-treated rats continued to have better motor function than controls throughout the 21-day test period and treated animals appeared to support their weight better and have more coordinated movements.

When the investigators looked at histological samples of the spinal cord, they found that the architecture of the spinal cord was better preserved in JSK-treated animals and the size of the injured area was significantly smaller 7 days after injury. JSK-treated animals also showed more intact axons and myelin in the injured areas compared to controls. Other encouraging signs were less deposition of fibrinogen in the injured areas of JSK-treated animals, a decrease in pro-inflammatory COX-2 expression, and fewer cell deaths at the lesion site (as measured by caspase-3 staining).

JSK also increased the expression of growth associated protein 43 (GAP43), a marker of neuronal development and axonal regeneration, and neuroglobulin, a protein found in cerebral neurons that is thought to help neurons survive and recover after trauma. "Our data suggest that JSK may enhance tissue recovery by reducing cell growth inhibitors and by promoting the proliferation of cells within the injured spinal cord," says co-lead investigator Michel P. Rathbone, MD, CHB, PhD, Professor, Division of Neurology, Department of Medicine, McMaster University, Hamilton, Ontario, Canada.

Other findings suggest JSK might help protect against injury caused by damage to spinal cord blood vessels. For instance, JSK increased vascular endothelial growth factor (VEGF), a protein involved in the formation and growth of blood vessels, down-regulated clotting-associated genes, and promoted factors that contribute to vasodilation.

The authors say that JSK targets multiple biochemical and cellular pathways that may help protect against the primary traumatic injury as well as subsequent secondary injuries that evolve over time.

The authors do not disclose the complete herbal composition of JSK for proprietary reasons. Some of its ingredients include Ginseng, Rhizoma (chuan xiong), Glycyrrhizae Radix (gan cao), Paeoniae Alba Radix (bai shao) and Cinnamomi Cortex (rou gui).

http://www.eurekalert.org/pub_releases/2013-08/kp-nrs081413.php

New risk score predicts 10-year dementia risk for type 2 diabetes patients

Researchers at Kaiser Permanente and the University Medical Centre Utrecht in the Netherlands have created the first risk score that predicts the 10-year individualized dementia risk for patients with type 2 diabetes, as reported in the inaugural issue of Lancet Diabetes & Endocrinology.

OAKLAND, Calif. - The researchers developed and validated the Diabetes-Specific Dementia Risk Score by examining data from nearly 30,000 patients with type 2 diabetes aged 60 and older over a 10-year period. They found eight factors that were most predictive of dementia -- including microvascular disease, diabetic foot and cerebrovascular disease -- and assigned each a value related to their association with dementia to create an overall score for patients. The researchers found that individuals in the lowest category of the 20-point risk score had a 5.3 percent chance of developing dementia over the next 10 years, while those in the highest category had a 73 percent chance. Compared with those in the lowest category, those in the highest were 37 times more likely to get dementia, according to the study.

"Patients with type 2 diabetes are twice as likely to develop dementia as those without the disease, but predicting who has the highest future risk is difficult," said Rachel Whitmer, PhD, an epidemiologist at the

Kaiser Permanente Division of Research in Oakland, California, who led the study. "While a few dementia risk scores exist, this is the first one that has been developed specifically for individuals with type 2 diabetes and encompasses diabetes-specific characteristics."
All predictors included in the Diabetes-Specific Dementia Risk Score are easy to obtain and based primarily on medical history, so the risk score can be calculated during a routine medical visit or with electronic health records. No labor-intensive or expensive tests, such as cognitive function or brain imaging, are required.
"This risk score is crucial for the care of patients with diabetes since they are particularly susceptible to dementia. It provides clinicians with an easy and efficient tool to assess their patients' chances of developing dementia over the next 10 years," Whitmer said. "Early detection of diabetes patients who are at increased future risk of dementia could help to develop and target preventive treatment."
According to the Centers for Disease Control and Prevention, more than 25 million children and adults in the United States have diabetes with type 2 diabetes in particular accounting for more than 90 percent of these cases. In addition to being a risk factor for dementia, diabetes is the leading cause of kidney failure, non-traumatic lower-limb amputations and new cases of blindness among adults in the United States.
"The risk score could be useful in the selection of high-risk patients for early intervention studies and for many applications of personalized medicine," said Geert Jan Biessels, MD, professor of neurology at the University Medical Centre Utrecht and co-author of the study. "Clinicians can use it to guide their decisions in terms of clinical attention to incipient cognitive impairment which makes people vulnerable to dangerous side-effects of diabetes treatment. The risk score will also help us to understand the causes of diabetes associated increased dementia risk, because we can examine those at high risk in early stages of the dementia process."
Additional authors on the study include Lieza G. Exalto, MD, of the Department of Neurology, University Medical Centre Utrecht, the Netherlands; Andrew J. Karter, PhD, of the Kaiser Permanente Division of Research, Oakland, Calif.; Elbert S. Huang, MD, of the Department of Internal Medicine, University of Chicago; Wayne J. Katon, MD, of the Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine; and Jerome R. Minkoff, MD, of the Kaiser Permanente Department of Endocrinology, Santa Rosa, Calif.
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The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

http://www.eurekalert.org/pub_releases/2013-08/uorm-cia081413.php

Copper identified as culprit in Alzheimer's disease

Copper appears to be one of the main environmental factors that trigger the onset and enhance the progression of Alzheimer's disease by preventing the clearance and accelerating the accumulation of toxic proteins in the brain. That is the conclusion of a study appearing today in the journal Proceedings of the National Academy of Sciences.

"It is clear that, over time, copper's cumulative effect is to impair the systems by which amyloid beta is removed from the brain," said Rashid Deane, Ph.D., a research professor in the University of Rochester Medical Center (URMC) Department of Neurosurgery, member of the Center for Translational Neuromedicine, and lead author of the study. "This impairment is one of the key factors that cause the protein to accumulate in the brain and form the plaques that are the hallmark of Alzheimer's disease."
Copper's presence in the food supply is ubiquitous. It is found in drinking water carried by copper pipes, nutritional supplements, and in certain foods such as red meats, shellfish, nuts, and many fruits and vegetables. The mineral plays an important and beneficial role in nerve conduction, bone growth, the formation of connective tissue, and hormone secretion.
However, the new study shows that copper can also accumulate in the brain and cause the blood brain barrier – the system that controls what enters and exits the brain – to break down, resulting in the toxic accumulation of the protein amyloid beta, a by-product of cellular activity. Using both mice and human brain cells Deane and his colleagues conducted a series of experiments that have pinpointed the molecular mechanisms by which copper accelerates the pathology of Alzheimer's disease.
Under normal circumstances, amyloid beta is removed from the brain by a protein called lipoprotein receptor-related protein 1 (LRP1). These proteins – which line the capillaries that supply the brain with blood – bind with the amyloid beta found in the brain tissue and escort them into the blood vessels where they are removed from the brain.
The research team – "dosed" normal mice with copper over a three month period. The exposure consisted of trace amounts of the metal in drinking water and was one-tenth of the water quality standards for copper established by the Environmental Protection Agency.
"These are very low levels of copper, equivalent to what people would consume in a normal diet." said Deane.

The researchers found that the copper made its way into the blood system and accumulated in the vessels that feed blood to the brain, specifically in the cellular "walls" of the capillaries. These cells are a critical part of the brain's defense system and help regulate the passage of molecules to and from brain tissue. In this instance, the capillary cells prevent the copper from entering the brain. However, over time the metal can accumulate in these cells with toxic effect.
The researchers observed that the copper disrupted the function of LRP1 through a process called oxidation which, in turn, inhibited the removal of amyloid beta from the brain. They observed this phenomenon in both mouse and human brain cells.
The researchers then looked at the impact of copper exposure on mouse models of Alzheimer's disease. In these mice, the cells that form the blood brain barrier have broken down and become "leaky" – a likely combination of aging and the cumulative effect of toxic assaults – allowing elements such as copper to pass unimpeded into the brain tissue. They observed that the copper stimulated activity in neurons that increased the production of amyloid beta. The copper also interacted with amyloid beta in a manner that caused the proteins to bind together in larger complexes creating logjams of the protein that the brain's waste disposal system cannot clear. This one-two punch, inhibiting the clearance and stimulating the production of amyloid beta, provides strong evidence that copper is a key player in Alzheimer's disease. In addition, the researchers observed that copper provoked inflammation of brain tissue which may further promote the breakdown of the blood brain barrier and the accumulation of Alzheimer's-related toxins.
However, because metal is essential to so many other functions in the body, the researchers say that these results must be interpreted with caution. "Copper is an essential metal and it is clear that these effects are due to exposure over a long period of time," said Deane. "The key will be striking the right balance between too little and too much copper consumption. Right now we cannot say what the right level will be, but diet may ultimately play an important role in regulating this process."
Additional contributors include first author Itender Singh and Abhay Sagare, Mireia Coma, David Perimutter, Robert Gelein, Robert Bell, Richard Deane, Elaine Zhong, Margaret Parisi, Joseph Ciszewski, and R. Tristan Kasper, all with URMC. The study was funded by the Alzheimer's Association, the National Institutes of Aging, and a pilot grant from the National Institute of Environmental Health Sciences.

http://www.eurekalert.org/pub_releases/2013-08/uoc--uss082013.php

UCLA study suggests iron is at core of Alzheimer's disease

Findings challenge conventional thinking about possible causes of disorder

Alzheimer's disease has proven to be a difficult enemy to defeat. After all, aging is the No. 1 risk factor for the disorder, and there's no stopping that.
Most researchers believe the disease is caused by one of two proteins, one called tau, the other beta-amyloid. As we age, most scientists say, these proteins either disrupt signaling between neurons or simply kill them. Now, a new UCLA study suggests a third possible cause: iron accumulation.
Dr. George Bartzokis, a professor of psychiatry at the Semel Institute for Neuroscience and Human Behavior at UCLA and senior author of the study, and his colleagues looked at two areas of the brain in patients with Alzheimer's. They compared the hippocampus, which is known to be damaged early in the disease, and the thalamus, an area that is generally not affected until the late stages. Using sophisticated brain-imaging techniques, they found that iron is increased in the hippocampus and is associated with tissue damage in that area. But increased iron was not found in the thalamus.
The research appears in the August edition of the Journal of Alzheimer's Disease.
While most Alzheimer's researchers focus on the buildup of tau or beta-amyloid that results in the signature plaques associated with the disease, Bartzokis has long argued that the breakdown begins much further "upstream." The destruction of myelin, the fatty tissue that coats nerve fibers in the brain, he says, disrupts communication between neurons and promotes the buildup of the plaques. These amyloid plaques in turn destroy more and more myelin, disrupting brain signaling and leading to cell death and the classic clinical signs of Alzheimer's.
Myelin is produced by cells called oligodendrocytes. These cells, along with myelin, have the highest levels of iron of any cells in the brain, Bartzokis says, and circumstantial evidence has long supported the possibility that brain iron levels might be a risk factor for age-related diseases like Alzheimer's. Although iron is essential for cell function, too much of it can promote oxidative damage, to which the brain is especially vulnerable.
In the current study, Bartzokis and his colleagues tested their hypothesis that elevated tissue iron caused the tissue breakdown associated with Alzheimer's disease. They targeted the vulnerable hippocampus, a key area of the brain involved in the formation of memories, and compared it to the thalamus, which is relatively spared by Alzheimer's until the very late stages of disease.

The researchers used an MRI technique that can measure the amount of brain iron in ferritin, a protein that stores iron, in 31 patients with Alzheimer's and 68 healthy control subjects.
In the presence of diseases like Alzheimer's, as the structure of cells breaks down, the amount of water increases in the brain, which can mask the detection of iron, according to Bartzokis.
"It is difficult to measure iron in tissue when the tissue is already damaged," he said. "But the MRI technology we used in this study allowed us to determine that the increase in iron is occurring together with the tissue damage. We found that the amount of iron is increased in the hippocampus and is associated with tissue damage in patients with Alzheimer's but not in the healthy older individuals — or in the thalamus. So the results suggest that iron accumulation may indeed contribute to the cause of Alzheimer's disease."
But it's not all bad news from this study, Bartzokis noted.
"The accumulation of iron in the brain may be influenced by modifying environmental factors, such as how much red meat and iron dietary supplements we consume and, in women, having hysterectomies before menopause," he said.
In addition, he noted, medications that chelate and remove iron from tissue are being developed by several pharmaceutical companies as treatments for the disorder. This MRI technology may allow doctors to determine who is most in need of such treatments.
Other authors of the study included Erika Raven, Po Lu, Todd Tishler and Panthea Heydari. Funding was provided by National Institutes of Health grants MH 0266029, AG027342 and T32 NS041231 and by the RCS Alzheimer's Foundation.

http://www.sciencedaily.com/releases/2013/08/130819102714.htm

How Shale Fracking Led to an Ohio Town's First 100 Earthquakes

Since records began in 1776, the people of Youngstown, Ohio had never experienced an earthquake. However, from January 2011, 109 tremors were recorded and new research in Geophysical Research-Solid Earth reveals how this may be the result of shale fracking.

In December 2010, Northstar 1, a well built to pump wastewater produced by fracking in the neighboring state of Pennsylvania, came online. In the year that followed seismometers in and around Youngstown recorded 109 earthquakes; the strongest being a magnitude 3.9 earthquake on December 31, 2011.
The study authors analyzed the Youngstown earthquakes, finding that their onset, cessation, and even temporary dips in activity were all tied to the activity at the Northstar 1 well. The first earthquake recorded in the city occurred 13 days after pumping began, and the tremors ceased shortly after the Ohio Department of Natural Resources shut down the well in December 2011.
Dips in earthquake activity correlated with Memorial Day, the Fourth of July, Labor Day, and Thanksgiving, as well as other periods when the injection at the well was temporarily stopped.
"In recent years, waste fluid generated during the shale gas production -- hydraulic fracturing, had been increasing steadily in United States. Earthquakes were triggered by these waste fluid injection at a deep well in Youngstown, Ohio during Jan. 2011 -- Feb. 2012. We found that the onset of earthquakes and cessation were tied to the activity at the Northstar 1 deep injection well. The earthquakes were centered in subsurface faults near the injection well. These shocks were likely due to the increase in pressure from the deep waste water injection which caused the existing fault to slip," said Dr. Won-Young Kim. "Throughout 2011, the earthquakes migrated from east to west down the length of the fault away from the well -- indicative of the earthquakes being caused by expanding pressure front."

http://www.medscape.com/viewarticle/809626?src=rss

New Lyme Culture Test Failed CDC Analysis

Eighty percent of the patient samples used to demonstrate a novel method of culturing Lyme disease spirochetes from serum contained gene sequences identical to those found in laboratory strains used to develop the test and were likely false positives, Centers for Disease Control and Prevention (CDC) researchers report in an article published online August 14 in the Journal of Clinical Microbiology.

Janis C. Kelly

"Taken together, our data and those of Sapi et al. indicate that laboratory contamination was the probable source of the borrelial DNA found in the patient samples. The vast majority of patient *pyrG* sequences (41/51) are indistinguishable from laboratory strains used by the investigators. The clinical relevance of the other *pyrG* sequences (10/51) is unclear; these findings also may be consistent with laboratory contamination," the authors write.
The CDC researchers warned that independent verification is critical for novel findings that contradict a large body of previous work and for tests that might lead to unnecessary antibiotic treatment.
"We caution clinicians and patients to wait for independent verification by scientifically sound methods before using this culture service for diagnostic purposes," they write.

The CDC research team, led by Barbara J.B. Johnson, PhD, from the Division of Vector-Borne Disease in Fort Collins, Colorado, were trying to understand why the majority of the spirochetes described in an article published earlier this year in the *International Journal of Medical Sciences* were related by *pyrG* gene sequences to species of Borrelia that had not previously been detected in North American patients other than those with a history of travel to Europe or Asia. The *pyrG* gene encodes CTP synthase, which interconverts UTP and CTP in pyrimidine biosynthesis.

The authors of the previous article had used 2 *B burgdorferi* reference strains (B31 and 297) and 2 Eurasian reference strains (*Borrelia afzelii* and *Borrelia garinii*) for method development and testing of culture medium.

To rule out the possibility that the sequence similarities were a result of laboratory contamination, the CDC researchers compared the *pyrG* sequences reported by Sapi et al. for 51 patient isolates to sequences for *B burgdorferi* B31 and 297 for *B afzelii*, and for *B garinii*, using the same primers used in the original study. Previously, *pyrG* gene sequence had been reported only for *B burgdorferi* strain B31, so Dr. Johnson's team sequenced the other 3 laboratory strains and deposited them in GenBank.

The analysis showed that 53% (27/51) of the patient-related sequences reported in the previous article were from samples infected by *B garinii* and 20 the 27 clones were identical to the *B garinii* reference strain. The other 7 *B garinii* sequences had either a single nucleotide polymorphism (n = 5), 2 differences (n = 1), or 3 differences (n = 1) from the laboratory strain.

Twenty-one (41%) of the 51 patients had nucleotide sequences related to *B burgdorferi*, and in 20 of these patients, the sequences matched the laboratory strain B31 exactly.

Two of the 51 patients had sequences closely related to *B afzelii*, which is not found in the United States.

"Eighty percent (41/51) of the reported patient-derived pyrG sequences are identical to one of the laboratory strains and an additional 12% (6/51) differ by only a single nucleotide across a 603bp region of the pyrG gene. Thus, false positivity due to laboratory contamination of patient samples cannot be ruled out and further validation of the proposed novel culture method is required," the authors conclude.

They also note that the patient cultures reported by Sapi et al. had been subjected to nested polymerase chain reaction, "a contamination-prone method that is unnecessary when bacteria are numerous enough to be seen by microscopy." The authors also point out that control samples from healthy blood donors had not been tested by polymerase chain reaction but had been classified as negative based only on dark field microscopy and antibody staining. *The authors have disclosed no relevant financial relationships.*

J Clin Microbiol. Published online August 14, 2013. Abstract

http://www.sciencedaily.com/releases/2013/08/130819182855.htm

Americans Diagnosed With Lyme Disease: Number May Be 10 Times More Than Reported

Preliminary estimates released by the Centers for Disease Control and Prevention indicate that the number of Americans diagnosed with Lyme disease each year is around 300,000.

The preliminary estimates were presented Sunday night in Boston at the 2013 International Conference on Lyme Borreliosis and Other Tick-Borne Diseases.

This early estimate is based on findings from three ongoing CDC studies that use different methods, but all aim to define the approximate number of people diagnosed with Lyme disease each year. The first project analyzes medical claims information for approximately 22 million insured people annually for six years, the second project is based on a survey of clinical laboratories and the third project analyzes self-reported Lyme disease cases from a survey of the general public.

Each year, more than 30,000 cases of Lyme disease are reported to CDC, making it the most commonly reported tick-borne illness in the United States. The new estimate suggests that the total number of people diagnosed with Lyme disease is roughly 10 times higher than the yearly reported number. This new estimate supports studies published in the 1990s indicating that the true number of cases is between 3- and 12-fold higher than the number of reported cases.

"We know that routine surveillance only gives us part of the picture, and that the true number of illnesses is much greater," said Paul Mead, M.D., M.P.H, chief of epidemiology and surveillance for CDC's Lyme disease program. "This new preliminary estimate confirms that Lyme disease is a tremendous public health problem in the United States, and clearly highlights the urgent need for prevention."

CDC continues to analyze the data in the three studies to refine the estimates and better understand the overall burden of Lyme disease in the United States and will publish finalized estimates when the studies are complete. Efforts are also underway at CDC and by other researchers to identify novel methods to kill ticks and prevent illness in people.

"We know people can prevent tick bites through steps like using repellents and tick checks. Although these measures are effective, they aren't fail-proof and people don't always use them," said Lyle R. Petersen, M.D., M.P.H, director of CDC's Division of Vector-Borne Diseases. "We need to move to a broader approach to tick reduction, involving entire communities, to combat this public health problem."
This community approach would involve homeowners trying to kill ticks in their own yards, and communities addressing a variety of issues. These issues include rodents that carry the Lyme disease bacteria, deer that play a key role in the ticks' lifecycle, suburban planning, and the interaction between deer, rodents, ticks, and humans. All must be addressed to effectively fight Lyme disease.
Most Lyme disease cases reported to CDC through national surveillance are concentrated heavily in the Northeast and upper Midwest, with 96 percent of cases in 13 states. Lyme disease is caused by the bacterium Borrelia burgdorferi and is transmitted to humans through the bite of infected blacklegged ticks. Typical symptoms include fever, headache, fatigue, and a characteristic skin rash called erythema migrans. If left untreated, infection can spread to joints, the heart, and the nervous system.
CDC recommends people take steps to help prevent Lyme disease and other tickborne diseases:
Wear repellent
Check for ticks daily
Shower soon after being outdoors
Call your doctor if you get a fever or rash
For more information on Lyme disease, visit www.cdc.gov/lyme.

http://www.bbc.co.uk/news/magazine-23756645#sa-ns_mchannel=rss&ns_source=PublicRSS20-sa

Can baking make you happier?

Baking is often associated with comfort food. Conjuring up homemade scones, chocolate brownies, macaroons or cupcakes has become a bit of a trend of late. But is there therapeutic value that is beneficial to mental health?

By Farhana Dawood BBC News

"Baking helps lift my depression. It can't cure it but it helps," says John Whaite, last year's winner of The Great British Bake Off. He was diagnosed with manic depression eight years ago.
Whaite explains that baking is a way to turn manic, erratic negative energy into something constructive. He found it an effective way to manage his condition. "When I'm in the kitchen, measuring the amount of sugar, flour or butter I need for a recipe or cracking the exact number of eggs - I am in control. That's really important as a key element of my condition is a feeling of no control."
Whaite has eschewed prescribed medication but has tried other traditional treatments including talking therapy and exercise sessions. He's included a chapter on the recipes he uses to help lift his spirits in his latest cookbook and he's a supporter of The Depressed Cake Shop - a mental health charity initiative set up by the specialist food creative consultant Emma Thomas, aka Miss Cakehead.
The Depressed Cake Shop ran a series of pop-up cake stalls across the country earlier this month that sold only grey cakes. The stunt raised thousands of pounds for mental health charities and provided an unusual platform for people to discuss mental health issues.
Melanie Denyer, the host of London's Depressed Cake Shop in Brick Lane, says the success of the event was phenomenal. "For a lot of us involved in this project, mental illness and baking are linked. A lot of us turn to baking when we're feeling low. Some of us even started baking because they were ill and needed something simple as a focus. And there is genuinely something very therapeutic about baking.
"I have, for years, turned to my kitchen and cooked, savoury or sweet, because I get some relief in the creation of something that, in and of itself, is goodness, love, nurture - sometimes even beauty - when all I feel I am is ugliness, pain and a drain on all around me," she says.
Denyer has struggled with mental health problems for 15 years and was recently diagnosed with borderline personality disorder. She sees a psychiatrist and has taken anti-depressants.
"Getting treatment has not always been easy. Cooking and baking have, on occasion, very literally saved my life, giving me an outlet for emotions I couldn't handle. It has provided me with an alternative to self-harm."
East London NHS Foundation Trust is one mental health provider that has experimented in cooking therapies. Earlier this year they launched Recipes of Life, an integrated talking therapy with healthy cooking and eating sessions.
Dr Mark Salter, a consultant psychiatrist working in east London, says baking and cooking are good occupational therapies that help patients develop planning skills, short term memory and social skills - all of which suffer in mental illness. He says baking is particularly powerful because of its symbolism in our culture - associated with nurture and goodness.

But Dr Cosmo Hallstrom, fellow of the Royal College of Psychiatrists, cautions that it is difficult to measure the precise benefits of baking as a therapy.
"Any structured non-stressful activity will help depression and increase well-being. Traditional occupational therapies generally work on a physical or projection platform.
"For example, exercise sessions increase physical well-being and release endorphins that combat depression. Art therapy helps a patient project their depression through creating artwork; thereby helping a patient to better understand their condition. Baking can be seen as operating on both these platforms," he says.
There is a physical element to baking - kneading the dough or cutting out cookie shapes. But there is also a strong creative or artistic component - the intricate decoration of cakes or biscuits.
Baking can be therapeutic in different ways. Denyer likes to give away her baked treats. She says the act of making other people happy helps lift her spirits.
But Whaite warns that eating too many baked goods can undo some of the benefits. "There are two sides to the coin. You need to be careful you don't consume too much sugar or else you get a sugar high and then a slump."

http://www.eurekalert.org/pub_releases/2013-08/iu-rib081913.php

Researchers identify biomarkers for possible blood test to predict suicide risk

Indiana University School of Medicine researchers have found a series of RNA biomarkers in blood that may help identify who is at risk for committing suicide.

INDIANAPOLIS -- In a study reported Aug. 20 in the advance online edition of the Nature Publishing Group journal Molecular Psychiatry, the researchers said the biomarkers were found at significantly higher levels in the blood of both bipolar disorder patients with thoughts of suicide as well in a group of people who had committed suicide.
Principal investigator Alexander B. Niculescu III, M.D., Ph.D., associate professor of psychiatry and medical neuroscience at the IU School of Medicine and attending psychiatrist and research and development investigator at the Richard L. Roudebush Veterans Affairs Medical Center in Indianapolis, said he believes the results provide a first "proof of principle" for a test that could provide an early warning of somebody being at higher risk for an impulsive suicide act.
"Suicide is a big problem in psychiatry. It's a big problem in the civilian realm, it's a big problem in the military realm and there are no objective markers," said Dr. Niculescu, director of the Laboratory of Neurophenomics at the Institute of Psychiatric Research at the IU School of Medicine.
"There are people who will not reveal they are having suicidal thoughts when you ask them, who then commit it and there's nothing you can do about it. We need better ways to identify, intervene and prevent these tragic cases," he said.
Over a three-year period, Niculescu and his colleagues followed a large group of patients diagnosed with bipolar disorder, completing interviews and taking blood samples every three to six months. The researchers conducted a variety of analyses of the blood of a subset of participants who reported a dramatic shift from no suicidal thoughts to strong suicidal ideation. They identified differences in gene expression between the "low" and "high" states of suicidal thoughts and subjected those findings to a system of genetic and genomic analysis called Convergent Functional Genomics that identified and prioritized the best markers by cross-validation with other lines of evidence.
The researchers found that the marker SAT1 and a series of other markers provided the strongest biological "signal" associated with suicidal thoughts.
Next, to validate their findings, working with the local coroner's office, they analyzed blood samples from suicide victims and found that some of same top markers were significantly elevated.
Finally, the researchers analyzed blood test results from two additional groups of patients and found that high blood levels of the biomarkers were correlated with future suicide-related hospitalizations, as well as hospitalizations that had occurred before the blood tests. "This suggests that these markers reflect more than just a current state of high risk, but could be trait markers that correlate with long term risk," said Dr. Niculescu.
Although confident in the biomarkers validity, Dr. Niculescu noted that a limitation is that the research subjects were all male. "There could be gender differences," he said. "We would also like to conduct more extensive, normative studies, in the population at large."
In addition to extending the research to females to see if the same or other markers come into play, Dr. Niculescu and colleagues plan to conduct research among other groups, such as persons who have less impulsive, more deliberate and planned subtypes of suicide.
Nonetheless, Dr. Niculescu said, "These seem to be good markers for suicidal behavior in males who have bipolar mood disorders or males in the general population who commit impulsive violent suicide. In the future

we want to study and assemble clinical and socio-demographic risk factors, along with our blood tests, to increase our ability to predict risk.
"Suicide is complex: in addition to psychiatric and addiction issues that make people more vulnerable, there are existential issues related to lack of satisfaction with one's life, lack of hope for the future, not feeling needed, and cultural factors that make suicide seem like an option."
He said he hopes such biomarkers, along with other tools, including neuropsychological tests and socio-demographic checklists currently in development by his group, ultimately can help identify people who are at risk, leading to pre-emptive intervention, counseling, and saved lives.
"Over a million people each year world-wide die from suicide and this is a preventable tragedy".
Additional investigators contributing to the research were Helen Le-Niculescu, Daniel F. Levey, Mikias Ayalew, Nikita Jain, Laura Palmer, Miranda Gavrin, Evan Winiger, Sughanda Bhosrekar, Robert Schweitzer, Ganesh Shankar, Mike Yard, George Sandusky and Anantha Shekhar of the IU School of Medicine; Mark Radel, Elizabeth Belanger, Hillary Duckworth, Kyle Olesek, and Jeffery Vergo of the Indianapolis Veterans Administration Medical Center; Alfarena Ballew of the Marion County (Ind.) Coroner's Office and Nicholas J. Schork, Sunil M. Kurian, Daniel R. Salomon and of The Scripps Research Institute. The research was supported by an NIH Directors' New Innovator Award (1DP2OD007363) and a Veterans Administration Merit Award (1I01CX000139-01).

http://www.eurekalert.org/pub_releases/2013-08/vcu-iit082013.php

Ingredient in turmeric spice when combined with anti-nausea drug kills cancer cells

In a laboratory, preclinical study recently published by the journal Organic & Biomolecular Chemistry, Virginia Commonwealth University Massey Cancer Center researchers combined structural features from anti-nausea drug thalidomide with common kitchen spice turmeric to create hybrid molecules that effectively kill multiple myeloma cells.

Thalidomide was first introduced in the 1950s as an anti-nausea medication to help control morning sickness, but was later taken off the shelves in 1962 because it was found to cause birth defects. In the late 1990's the drug was re-introduced as a stand-alone or combination treatment for multiple myeloma. Turmeric, an ancient spice grown in India and other tropical regions of Asia, has a long history of use in herbal remedies and has recently been studied as a means to prevent and treat cancer, arthritis and Alzheimer's disease. According to the American Cancer Society, laboratory studies have shown that curcumin, an active ingredient in turmeric, interferes with several important molecular pathways and inhibits the formation of cancer-causing enzymes in rodents.
"Although thalidomide disturbs the microenvironment of tumor cells in bone marrow, it disintegrates in the body. Curcumin, also active against cancers, is limited by its poor water solubility. But the combination of thalidomide and curcumin in the hybrid molecules enhances both the cytotoxicity and solubility," says the study's lead researcher Shijun Zhang, assistant professor in the Department of Medicinal Chemistry at the VCU School of Pharmacy.
Compared to mixing multiple drugs, creating hybrid molecules can provide certain advantages. "Enhanced potency, reduced risk of developing drug resistance, improved pharmacokinetic properties, reduced cost and improved patient compliance are just a few of those advantages," says another of the study's researchers Steven Grant, M.D., Shirley Carter Olsson and Sture Gordon Olsson Chair in Oncology Research, associate director for translational research, program co-leader of Developmental Therapeutics and Cancer Cell Signaling research member at VCU Massey Cancer Center.
The hybrid molecules of turmeric and thalidomide created more than 15 compounds, each with a different effect. Scientists found that compounds 5 and 7 exhibited superior cell toxicity compared to curcumin alone or the combination of curcumin and thalidomide. Furthermore, the compounds were found to induce significant multiple myeloma cell death.
"Overall, the combination of the spice and the drug was significantly more potent than either individually, suggesting that this hybrid strategy in drug design could lead to novel compounds with improved biological activities," added Grant. "The results also strongly encourage further optimization of compounds 5 and 7 to develop more potent agents as treatment options for multiple myeloma."
Zhang and Grant collaborated on this study with Kai Liu from the Department of Medicinal Chemistry at the VCU School of Pharmacy; Jeremy Chojnacki, from the VCU Department of Medicinal Chemistry; Datong Zhang, from the School of Chemistry and Pharmaceutical Engineering at Shandong Polytechnic University in Jinan, Shandong; and Yuhong Du and Haian Fu, from the Department of Pharmacology and Emory Chemical Biology Discovery Center at Emory University in Atlanta, Georgia.
The full manuscript of this study is available at: http://pubs.rsc.org/en/content/articlepdf/2013/ob/c3ob40595h.

http://www.bbc.co.uk/news/uk-scotland-edinburgh-east-fife-23768427

Prickly weed in Scotland may be next superfood

Sea buckthorn, which grows in abundance around Scottish coasts, may be the next superfruit.

Despite often being viewed as an invasive prickly weed, the plant's bright orange berries are packed with vitamins, minerals and antioxidants.

Now, scientists from Edinburgh's Queen Margaret University are working on ways to use them in drinks and food. Sea buckthorn has more vitamin C than a kiwi and more vitamin E than a soya bean.

Previously, Scots have not exploited the nutritional benefits of Sea Buckthorn due to the problems associated with its harvesting and the often bitter taste of the berries. Popular in China, Norway and Russia, it is usually added to cereal and desserts.

Sea buckthorn has more vitamin C than a kiwi and more vitamin E than a soya bean

Sand dunes

It can normally be found growing in Scottish coastal areas near sand dunes, particularly in East Lothian.

If planted correctly it can help stabilise sand dunes next to golf courses, preserve areas of natural interest, and protect other plants by reducing salt spray produced by cars.

Since 2008, Queen Margaret University has been researching the nutritional properties of Sea Buckthorn and has run various trials for small food producers who are looking to enhance the nutritional content of their products while also adding a Scottish twist.

Graham Stoddart, owner of Cuddybridge, a small Scottish hand-pressed apple juice producer, said:

"Although, the properties of apple juice are well documented, the effects of Sea Buckthorn, with its excellent antioxidant properties, and its application for the fresh juice market when mixed with apples, have little or no documentation."

Cuddybridge presses a variety of apples throughout the year, but due to the seasonality of Sea Buckthorn, the combined Apple and Sea Buckthorn juice is only available as a fresh juice between September and February.

Dr Mary Warnock, senior lecturer in microbiology at Queen Margaret University, said: "Sea Buckthorn is literally bursting with potential.

"We are excited that our work in this area is changing the reputation of this undervalued plant to one which can add nutritional value to the Scottish diet."

http://bit.ly/14gJFKI

Doctors Bring Woman Back From the Dead

Vanessa Tanasio went into cardiac arrest and was declared clinically dead soon after arrival.

Aug 20, 2013 11:00 AM ET // by AFP

An Australian woman has lived to tell the tale after being brought back to life from being clinically dead for 42 minutes, doctors said on Monday.

Mother-of-two Vanessa Tanasio, 41, was rushed to Monash Medical Centre in Melbourne last week after a major heart attack, with one of her main arteries fully blocked.

She went into cardiac arrest and was declared clinically dead soon after arrival.

Doctors refused to give up and used a compression device called a Lucas 2 -- the only one of its kind in Australia -- to keep blood flowing to her brain while cardiologist Wally Ahmar opened an artery to unblock it.

Once unblocked, Tanasio's heart was shocked back into a normal rhythm.

"(I used) multiple shocks, multiple medications just to resuscitate her," Ahmar said.

"Indeed this is a miracle. I did not expect her to be so well."

Tanasio said she had no history of heart conditions and was grateful to be alive.

"I remember being on my couch, then the floor, then arriving at hospital, and then two days go missing," Tanasio said.

"I was dead for nearly an hour and only a week later I feel great. It's surreal."

The Lucas device physically compresses the chest, like during cardiopulmonary resuscitation (CPR), allowing doctors to work non-stop to put a stent into a blocked artery.

It is the first a time a patient has successfully used the device, which was donated to the medical center, for such a length of time in Australia, the hospital said.

Clinical death is a medical term for when someone stops breathing and their blood stops circulating.

http://www.medscape.com/viewarticle/809666?src=rss

Functional MRI Helps Nonresponsive Patients 'Talk'

Using functional MRI (fMRI), researchers have shown for the first time that patients who are nonresponsive because of severe brain injury can selectively focus their attention to follow commands and communicate.

Megan Brooks

"One patient who had maintained a clinical diagnosis of vegetative state over a 12-year period prior to scanning, and also subsequent to it, was able to use attention to correctly communicate answers to several binary (yes/no) questions. In this way, the patient demonstrated that he was aware of his identity and whereabouts," Lorina Naci, PhD, from The Brain and Mind Institute at Western University in London, Ontario, Canada, told Medscape Medical News.

"In 2 different hospital visits, five months apart, not only were we able to communicate with the patient but found that he was also aware of his environment, meaning he could maintain coherent thoughts and lead a rich mental life," Dr. Naci added. The study was published online August 12 in JAMA Neurology.

A Rich Mental Life

This group from the University of Western Ontario, with senior author Adrian M. Owen, PhD, previously reported http://archneur.jamanetwork.com/article.aspx?articleid=794212 using fMRI to have patients previously considered in a vegetative state apparently answer "yes" or "no" questions by visualizing themselves doing actions known to activate different parts of the brain. They have also previously reported using electroencephalography (EEG) at the bedside for this purpose, although their interpretation of their findings was later challenged by another group.

Their current report involved a convenience sample of 3 patients: 2 diagnosed as being in a minimally conscious state and 1 diagnosed as being in a vegetative state. All 3 patients were entirely behaviorally nonresponsive to repeated independent neurologic bedside examinations.

The researchers had all patients undergo fMRI while being asked to selectively attend to auditory stimuli, which would convey their ability to follow commands and communicate.

Indeed, they found that all 3 patients could follow a simple command (to count or relax); their brain images showed "significantly more activation following the instruction to count than relax," the investigators say.

"The significant brain activity observed for each patient during the command-following task confirmed that he understood and followed the commands and was able to pay attention to some words while ignoring others that were irrelevant for the task," they write.

In addition, in the communication task during fMRI, 1 of the patients in a minimally conscious state and the patient in the vegetative state were also able to correctly answer yes/no questions, such as "Are you in a hospital?" or "Are you in a supermarket?"

"Convincing" Data

This novel fMRI technique "takes communication with some patients who are assumed to be in a vegetative state to the next level," Dr. Naci told Medscape Medical News. "It will make detecting who is conscious and who is not faster and more reliable, and for those who are conscious, communicating their wishes will be much easier."

She cautioned that more study is needed. "In this study, we establish a proof of principle that some entirely behaviorally nonresponsive patients can use selective attention to communicate. We are now undertaking patient cohort studies to determine what proportion of nonresponsive patients retain these high-level cognitive abilities and can successfully use this technique," Dr. Naci said.

The data here are "convincing," writes James L. Bernat, MD, from the Geisel School of Medicine at Dartmouth in Hanover, New Hampshire, in 1 of 2 editorials published with the study.

He thinks patients discovered by fMRI studies to have been wrongly diagnosed as being in vegetative state "deserve our efforts to reassure them that we know they are aware, to establish a reliable communication system to the fullest extent possible, and to adequately address their medical, emotional, and palliative care needs just as we currently do with our awake and aware but profoundly paralyzed patients with LIS [locked-in syndrome]."

Another implication of the study is the need to incorporate fMRI and other valid functional neuroimaging and electroencephalographic data documenting evidence of awareness into current diagnostic criteria for the syndrome of vegetative state, Dr. Bernat says.

"Once there is general acceptance that the fMRI data from the studies published during the past 7 years conclusively demonstrate at least some level of awareness in the subset of patients with these findings, these data should be accepted as evidence that the patient's diagnosis is MCS [minimally conscious state], not VS [vegetative state]," Dr. Bernat writes.

This study also highlights the need to "optimize the design, data acquisition, and signal processing in experimental fMRI paradigms to generate valid and consistent data that accurately record the conscious activity of patients with severe brain damage," he adds.

A Paradigmatic Shift?

In a second, separate editorial, Kenneth M. Heilman, MD, from the Department of Neurology, University of Florida College of Medicine in Gainesville, says the finding that fMRI may be used to communicate with patients who have a total locked-in syndrome "may lead to a paradigmatic shift such that with the further development of prostheses, these unfortunate patients, as well as patients with other forms of locked-in syndromes, will be able to open the door to end their isolation."

"Cortically controlled motor prostheses are being developed to restore functions lost by the damage caused by neurological diseases and injuries. Several studies have already shown encouraging results, but barriers to clinical translation still remain," Dr. Heilman writes.

The study was supported by the DECODER Project, the European Commission in the 7th Framework Programme, the James S. McDonnell Foundation, and the Canada Excellence Research Chairs Program. The authors and editorial writers have disclosed no relevant financial relationships.

http://bit.ly/14Uuanp

China calls an end to harvesting organs from prisoners

If you go to China for an organ transplant, the organ may well have come from an executed prisoner. Not for much longer, perhaps.

19:52 20 August 2013 by Michael Slezak

China has announced that it will phase out the practice from November, when hospitals licensed for transplantation will stop using organs harvested from executed prisoners. "I am confident that before long all accredited hospitals will forfeit the use of prisoner organs," Huang Jiefu, who heads the health ministry's organ transplant office, told Reuters.

Maria Fiatarone Singh of the University of Sydney, Australia, says the announcement is little reason for optimism. Until 2005, China denied the practice existed. Then in 2006, it passed legislation aimed to stop such organ trafficking. But Fiatarone Singh says they did not act on the new legislation until 2010, when a "small pilot programme" was set up to recruit non-prisoners.

World Health Organization organ donation guidelines require informed consent be given without coercion. "If you are in a situation where you are incarcerated and there are people who have power over your life and freedom, then it's considered coercive," says Fiatarone Singh.

Executed to order?

Yang Chunhua of the First Affiliated Hospital of Sun Yat-sen University in Guangdong Province admitted in a state-owned newspaper that until very recently, consent from prisoners had not been gained prior to their execution.

Meanwhile, the Taipei Times recently reported that, according to Taiwanese government figures, almost 2000 Taiwanese citizens had travelled to China between 2000 and 2011 to buy organs.

"It's very clear that what's been happening is that people are being executed to order," says Fiatarone Singh. It's inconceivable that someone could go to China and then just by chance a prisoner would be executed. And just by chance their blood type matches yours."

Amnesty International says the numbers of executed prisoners in China is a state secret, but estimates that China probably executes more people than the rest of the world combined.

http://bit.ly/14huHnO

First Pre-Clinical Gene Therapy Study to Reverse Rett Symptoms

New research suggests replacing mutated genes with healthy ones may eventually be a feasible option to treat the most disabling of the autism spectrum disorders

The concept behind gene therapy is simple: deliver a healthy gene to compensate for one that is mutated. New research published today in the Journal of Neuroscience suggests this approach may eventually be a feasible option to treat Rett Syndrome, the most disabling of the autism spectrum disorders. Gail Mandel, Ph.D., a Howard Hughes Investigator at Oregon Health and Sciences University, led the study. The Rett Syndrome Research Trust, with generous support from the Rett Syndrome Research Trust UK and Rett Syndrome Research & Treatment Foundation, funded this work through the MECP2 Consortium.

In 2007, co-author Adrian Bird, Ph.D., at the University of Edinburgh astonished the scientific community with proof-of-concept that Rett is curable, by reversing symptoms in adult mice. His unexpected results catalyzed labs around the world to pursue a multitude of strategies to extend the pre-clinical findings to people.

Today's study is the first to show reversal of symptoms in fully symptomatic mice using techniques of gene therapy that have potential for clinical application.
Rett Syndrome is an X-linked neurological disorder primarily affecting girls; in the US, about 1 in 10,000 children a year are born with Rett. In most cases symptoms begin to manifest between 6 and 18 months of age, as developmental milestones are missed or lost. The regression that follows is characterized by loss of speech, mobility, and functional hand use, which is often replaced by Rett's signature gesture: hand-wringing, sometimes so intense that it is a constant during every waking hour. Other symptoms include seizures, tremors, orthopedic and digestive problems, disordered breathing and other autonomic impairments, sensory issues and anxiety. Most children live into adulthood and require round-the-clock care.
The cause of Rett Syndrome's terrible constellation of symptoms lies in mutations of an X-linked gene called MECP2 (methyl CpG-binding protein). MECP2 is a master gene that regulates the activity of many other genes, switching them on or off.
"Gene therapy is well suited for this disorder," Dr. Mandel explains. "Because MECP2 binds to DNA throughout the genome, there is no single gene currently that we can point to and target with a drug. Therefore the best chance of having a major impact on the disorder is to correct the underlying defect in as many cells throughout the body as possible. Gene therapy allows us to do that."
Healthy genes can be delivered into cells aboard a virus, which acts as a Trojan horse. Many different types of these Trojan horses exist. Dr. Mandel used adeno-associated virus serotype 9 (AAV9), which has the unusual and attractive ability to cross the blood-brain barrier. This allows the virus and its cargo to be administered intravenously, instead of employing more invasive direct brain delivery systems that require drilling burr holes into the skull.
Because the virus has limited cargo space, it cannot carry the entire MECP2 gene. Co-author Brian Kaspar of Nationwide Children's Hospital collaborated with the Mandel lab to package only the gene's most critical segments. After being injected into the Rett mice, the virus made its way to cells throughout the body and brain, distributing the modified gene, which then started to produce the MeCP2 protein.
As in human females with Rett Syndrome, only approximately 50% of the mouse cells have a healthy copy of MECP2. After the gene therapy treatment 65% of cells now had a functioning MECP2 gene.
The treated mice showed profound improvements in motor function, tremors, seizures and hind limb clasping. At the cellular level the smaller body size of neurons seen in mutant cells was restored to normal. Biochemical experiments proved that the gene had found its way into the nuclei of cells and was functioning as expected, binding to DNA.
One Rett symptom that was not ameliorated was abnormal respiration. Researchers hypothesize that correcting this may require targeting a greater number of cells than the 15% that had been achieved in the brainstem.
"We learned a critical and encouraging point with these experiments -- that we don't have to correct every cell in order to reverse symptoms. Going from 50% to 65% of the cells having a functioning gene resulted in significant improvements," said co-author Saurabh Garg.
One of the potential challenges of gene therapy in Rett is the possibility of delivering multiple copies of the gene to a cell. We know from the MECP2 Duplication Syndrome that too much of this protein is detrimental.
"Our results show that after gene therapy treatment the correct amount of MeCP2 protein was being expressed. At least in our hands, with these methods, overexpression of MeCP2 was not an issue," said co-author Daniel Lioy.
Dr. Mandel cautioned that key steps remain before clinical trials can begin. "Our study is an important first step in highlighting the potential for AAV9 to treating the neurological symptoms in Rett. We are now working on improving the packaging of MeCP2 in the virus to see if we can target a larger percentage of cells and therefore improve symptoms even further," said Mandel. Collaborators Hélène Cheval and Adrian Bird see this as a promising follow up to the 2007 work showing symptom reversal in Rett mice. "That study used genetic tricks that could not be directly applicable to humans, but the AAV9 vector used here could in principle deliver a gene therapeutically. This is an important step forward, but there is a way to go yet."
"Gene therapy has had a tumultuous road in the past few decades but is undergoing a renaissance due to recent technological advances. Europe and Asia have gene therapy treatments already in the clinic and it's likely that the US will follow suit. Our goal now is to prioritize the next key experiments and facilitate their execution as quickly as possible. Gene therapy, especially to the brain, is a tricky undertaking but I'm cautiously optimistic that with the right team we can lay out a plan for clinical development. I congratulate the Mandel and Bird labs on today's publication, which is the third to be generated from the MECP2 Consortium in a short period of time," said Monica Coenraads, Executive Director of the Rett Syndrome Research Trust and mother of a teenaged daughter with the disorder.

http://www.eurekalert.org/pub_releases/2013-08/uoy-rrh082113.php

Researchers reveal hunter-gatherers' taste for spice

Our early ancestors had a taste for spicy food, new research led by the University of York has revealed.

Archaeologists at York, working with colleagues in Denmark, Germany and Spain, have found evidence of the use of spices in cuisine at the transition to agriculture. The researchers discovered traces of garlic mustard on the charred remains of pottery dating back nearly 7,000 years.

The silicate remains of garlic mustard (Alliaria petiolata) along with animal and fish residues were discovered through microfossil analysis of carbonised food deposits from pots found at sites in Denmark and Germany. The pottery dated from the Mesolithic-Neolithic transition from hunter-gathering to agriculture.

Previously scientists have analysed starches which survive well in carbonised and non-carbonised residues to test for the use of spices in prehistoric cooking. But the new research, which is reported in PLOS ONE, suggests that the recovery of phytoliths – silicate deposits from plants -- offers the additional possibility to identify leafy or woody seed material used as spices, not detectable using starch analysis. Phytoliths charred by cooking are more resilient to destruction.

Lead researcher Dr Hayley Saul, of the BioArCH research centre at at the University of York, said: "The traditional view is that early Neolithic and pre-Neolithic uses of plants, and the reasons for their cultivation, were primarily driven by energy requirements rather than flavour. As garlic mustard has a strong flavour but little nutritional value, and the phytoliths are found in pots with terrestrial and marine animal residues, our findings are the first direct evidence for the spicing of food in European prehistoric cuisine.

"Our evidence suggests a much greater antiquity to the spicing of foods in this region than is evident from the macrofossil record, and challenges the view that plants were exploited by hunter-gatherers and early agriculturalists solely for energy requirements, rather than taste."

The research was funded by the UK Arts and Humanities Research Council.

The research also involved scientists at the Institució Catalana de Recerca i Estudis Avançats, Institución Milá i Fontanals, Spanish National Research Council, Barcelona, Spain; the Danish Agency for Culture, Copenhagen, Denmark; the Institute of Prehistoric and Protohistoric Archaeology, University of Kiel, Kiel, Germany. And Stiftung Schleswig-Holsteinische Landesmuseen, Schloß Gottorf, Schleswig, Germany.

http://www.eurekalert.org/pub_releases/2013-08/cums-mvd082113.php

MERS virus discovered in bat near site of outbreak in Saudi Arabia

First study of MERS animal host in Saudi Arabia; led by Columbia University, EcoHealth Alliance, and the Ministry of Health of the Kingdom of Saudi Arabia

A 100% genetic match for Middle East Respiratory Syndrome (MERS) has been discovered in an insect-eating bat in close proximity to the first known case of the disease in Saudi Arabia. The discovery points to the likely animal origin for the disease, although researchers say that an intermediary animal is likely also involved.

Led by team of investigators from the Center for Infection and Immunity (CII) at Columbia University's Mailman School of Public Health, EcoHealth Alliance, and the Ministry of Health of the Kingdom of Saudi Arabia, the study is the first to search for an animal reservoir for MERS in Saudi Arabia, and the first to identify such a reservoir by finding a genetic match in an animal.

Results appear online in Emerging Infectious Diseases, a journal of the U.S. Centers for Disease Control and Prevention.

"There have been several reports of finding MERS-like viruses in animals. None were a genetic match. In this case we have a virus in an animal that is identical in sequence to the virus found in the first human case. Importantly, it's coming from the vicinity of that first case," says W. Ian Lipkin, MD, director of the Center for Infection and Immunity and a co-author of the study.

This is an Egyptian Tomb Bat (Taphozous perforatus) being examined by researchers. One of this type of bat was found to have Middle East Respiratory Syndrome in a study in Saudi Arabia. **Jonathan H. Epstein/EcoHealth Alliance**

MERS was first described in September 2012 and continues to spread. Close to 100 cases have been reported worldwide, 70 of them from Saudi Arabia. The causative agent, a new type of coronavirus, has been determined; however, the origin of the virus has been unknown until now.

Over a six-week period during field expeditions in October 2012 and April 2013, the researchers collected more than 1,000 samples from seven bat species in regions where cases of MERS were identified in Bisha, Unaizah, and Riyadh. Extensive analysis was performed using polymerase chain reaction and DNA sequencing revealed the presence of a wide range of alpha and beta coronaviruses in up to a third of bat samples. One fecal sample

from an Egyptian Tomb Bat (Taphozous perforatus) collected within a few kilometers of the first known MERS victim's home contained sequences of a virus identical to those recovered from the victim.
Bats are the reservoirs of viruses that can cause human disease including rabies, Hendra, Nipah, Marburg, and SARS. In some instances the infection may spread directly from bats to humans through inadvertent inhalation of infected aerosols, ingestion of contaminated food, or, less commonly, a bite wound. In other instances bats can first infect intermediate hosts. The researchers suggest that the indirect method for transmission is more likely in MERS.
"There is no evidence of direct exposure to bats in the majority of human cases of MERS," says Ziad Memish, MD, Deputy Minister of Health, Kingdom of Saudi Arabia, and lead author of the study. "Given that human-to-human transmission is inefficient, we speculate that an as-yet-to-be determined intermediate host plays a critical role in human disease." "We are continuing to look for evidence of the virus in wildlife and domestic animals, and investigating the mechanisms by which the virus causes human disease," adds Dr. Lipkin. "This is but the first chapter in a powerful collaboration amongst partners committed to global public health."
In the coming days, the group will be reporting the results of its investigation into the possible presence of MERS in camels, sheep, goats, and cattle.
The current study, titled "Coronavirus diversity and evidence for MERS-CoV infection in bats in Saudi Arabia" appears online in the journal Emerging Infectious Diseases: http://wwwnc.cdc.gov/eid/article/19/11/13-1172_article.htm.

http://www.eurekalert.org/pub_releases/2013-08/aafc-poh081913.php

Poor oral health linked to cancer-causing oral HPV infection

Poor oral health, including gum disease and dental problems, was found to be associated with oral human papillomavirus (HPV) infection, which causes about 40 percent to 80 percent of oropharyngeal cancers, according to a study published in Cancer Prevention Research, a journal of the American Association for Cancer Research.

PHILADELPHIA - "Poor oral health is a new independent risk factor for oral HPV infection and, to our knowledge, this is the first study to examine this association," said Thanh Cong Bui, Dr.P.H., postdoctoral research fellow in the School of Public Health at the University of Texas Health Sciences Center in Houston. "The good news is, this risk factor is modifiable — by maintaining good oral hygiene and good oral health, one can prevent HPV infection and subsequent HPV-related cancers."
The researchers found that among the study participants, those who reported poor oral health had a 56 percent higher prevalence of oral HPV infection, and those who had gum disease and dental problems had a 51 percent and 28 percent higher prevalence of oral HPV infection, respectively. In addition, the researchers were able to associate oral HPV infections with number of teeth lost.
Similar to genital HPV infection, oral HPV infection can be of two kinds: infection with low-risk HPV types that do not cause cancer, but can cause a variety of benign tumors or warts in the oral cavity, and infection with high-risk HPV types that can cause oropharyngeal cancers.
Bui, Christine Markham, Ph.D., and colleagues used data from the 2009-2010 National Health and Nutrition Examination Survey (NHANES) conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention. This survey consisted of a nationally representative sample of about 5,000 people recruited each year, located in counties across the United States.
The researchers identified 3,439 participants aged 30 to 69 years from NHANES, for whom data on oral health and the presence or absence of 19 low-risk HPV types and 18 high-risk HPV types in the oral cavity were available. Oral health data included four measures of oral health: self-rating of overall oral health, presence of gum disease, use of mouthwash to treat dental problems within past seven days of the survey, and number of teeth lost. They examined data on age, gender, marital status, marijuana use, cigarette smoking, and oral sex habits, among others, which influence HPV infection.
The researchers found that being male, smoking cigarettes, using marijuana, and oral sex habits increased the likelihood of oral HPV infection. They also found that self-rated overall oral health was an independent risk factor for oral HPV infection, because this association did not change regardless of whether or not the participants smoked or had multiple oral sex partners.
Because HPV needs wounds in the mouth to enter and infect the oral cavity, poor oral health, which may include ulcers, mucosal disruption, or chronic inflammation, may create an entry portal for HPV, said Bui. There is, however, currently not enough evidence to support this, and further research is needed to understand this relationship, he said.
"Although more research is needed to confirm the causal relationship between oral health and oral HPV infection, people may want to maintain good oral health for a variety of health benefits," said Bui. "Oral hygiene is fundamental for oral health, so good oral hygiene practices should become a personal habit."

http://www.eurekalert.org/pub_releases/2013-08/uon-ssl082013.php

Schizophrenia symptoms linked to faulty 'switch' in brain

Scientists at The University of Nottingham have shown that psychotic symptoms experienced by people with schizophrenia could be caused by a faulty 'switch' within the brain.

In a study published today in the leading journal Neuron, they have demonstrated that the severity of symptoms such as delusions and hallucinations which are typical in patients with the psychiatric disorder is caused by a disconnection between two important regions in the brain — the insula and the lateral frontal cortex.

The breakthrough, say the academics, could form the basis for better, more targeted treatments for schizophrenia with fewer side effects.

The four-year study, led by Professor Peter Liddle and Dr Lena Palaniyappan in the University's Division of Psychiatry and based in the Institute of Mental Health, centred on the insula region, a segregated 'island' buried deep within the brain, which is responsible for seamless switching between inner and outer world.

Dr Lena Palaniyappan, a Wellcome Trust Research Fellow, said: "In our daily life, we constantly switch between our inner, private world and the outer, objective world. This switching action is enabled by the connections between the insula and frontal cortex. This switch process appears to be disrupted in patients with schizophrenia. This could explain why internal thoughts sometime appear as external objective reality, experienced as voices or hallucinations in this condition. This could also explain the difficulties in 'internalising' external material pleasures (e.g. enjoying a musical tune or social events) that result in emotional blunting in patients with psychosis. Our observation offers a powerful mechanistic explanation for the formation of psychotic symptoms."

Several brain regions are engaged when we are lost in thought or, for example, remembering a past event. However, when interrupted by a loud noise or another person speaking we are able to switch to using our frontal cortex area of the brain, which processes this external information. With a disruption in the connections from the insula, such switching may not be possible.

The Nottingham scientists used functional MRI (fMRI) imaging to compare the brains of 35 healthy volunteers with those of 38 schizophrenic patients. The results showed that whereas the majority of healthy patients were able to make this switch between regions, the patients with schizophrenia were less likely to shift to using their frontal cortex.

The insular and frontal cortex form a sensitive 'salience' loop within the brain — the insular should stimulate the frontal cortex while in turn the frontal cortex should inhibit the insula — but in patients with schizophrenia this system was found to be seriously compromised. The results suggest that detecting the lack of a positive influence from the insula to the frontal cortex using fMRI could have a high degree of predictive value in identifying patients with schizophrenia. The results of the study offer vital information for the development of more effective treatments for the condition.

Schizophrenia is one of the most common serious mental health conditions affecting around 1 in 100 people. Its onset occurs most commonly in a patient's late teens or early 20s which can have devastating consequences for their future. Scientists remain unsure what causes schizophrenia but believe it could be a combination of a genetic predisposition to the condition combined with environmental factors. Drug use is known to be a key trigger – people who use cannabis, or stimulant drugs, are three to four times more likely to go on to develop recurrent psychotic symptoms.

It is also believed that underdevelopment of the brain in the womb caused by complications in the mother's pregnancy and in early childhood linked to issues such as malnutrition could play a key part. Previous observations from this research group have also uncovered the presence of unusually smooth folding patterns of the brain over the insula region in patients, suggesting an impairment in the normal development of this structure in schizophrenia.

At present, treatment involves a combination of antipsychotic medications, psychological therapies and social interventions. Currently, only one in five patients with schizophrenia achieve complete recovery and many patients who develop the condition in the long-term struggle to find a treatment that is 100 per cent effective in managing their condition. Antipsychotic drugs, though effective in a number of patients, have poor acceptance rates due to the side effect burden meaning that many patients stop taking them in the longer run, leading to recurrence of disabling symptoms.

Researchers in Nottingham are also looking at a technique called TMS – transcranial magnetic stimulation — which uses a powerful magnetic pulse to stimulate the brain regions that are malfunctioning.

Despite the fact that the insular region is buried so deeply within the brain that TMS would usually be ineffective, the results of the Nottingham study suggest that the loop between the insular and the frontal cortex

could be exploited for TMS– if a pulse is delivered to the frontal lobe it could stimulate the insula and reset the 'switch'.
Other future treatment options could include the use of a compassion-based meditation therapy called mindfulness, which may have the potential to 'reset' the switching function of the insula and can promote physical changes within the brain. Meditation over a long period of time has been shown to increase the folding patterns within the insula area of the brain. These ideas are in its early stages at present, but may deliver more focussed treatment approaches in the longer term.
This study was funded with a £614,000 grant from the Medical Research Council (MRC) and a research fellowship from the Wellcome Trust to Dr. Palaniyappan. The research was conducted with support from the Institute of Mental Health, a partnership between University of Nottingham and Nottinghamshire Healthcare NHS Trust. The paper, Neural Primacy of the Salience Processing System in Schizophrenia, is available online on Neuron's website at http://dx.doi.org/10.1016/j.neuron.2013.06.027 (after the embargo has lifted).

http://bit.ly/1aDPghY

Sniffing Out New Strategies in the Fight against Alzheimer's Disease

Despite barriers of blood, brain and bureaucracy, intranasal insulin may emerge as a promising treatment for pathological memory loss

By Caitlin Shure | Wednesday, August 21, 2013 | 2

The newest chemical under investigation for managing Alzheimer's disease (AD) is actually not new at all. Insulin, the therapeutic hormone all-too familiar to individuals with diabetes, has been around for decades. In fact December will mark 90 years since its discoverers earned the Nobel Prize in Physiology or Medicine for the extraction of insulin for clinical use. Yet to say that insulin has been under our noses all these years wouldn't exactly be correct. Because if it had been under our noses, we might have sensed its neurologic benefits sooner.
The latest insulin therapy is not delivered via injection like its diabetes-treating counterparts, nor does it come in the form of a pill or a patch like the cholinesterase inhibitors often prescribed to patients with AD. Instead this novel therapeutic enters the body through the nose—the only entry point that gives insulin a chance of reaching the brain.
A large peptide molecule, insulin from the blood cannot float easily into the brain because the blood brain barrier (BBB), a sort of neuroprotective moat, prevents its transport. Fortified by cellular guards called tight junctions, the BBB rejects many pharmacologic hopefuls, allowing entrance only to certain types of substances. Namely small or lipophilic molecules can be administered orally (or via injection, or through the skin) and as long as the relevant chemicals end up in the blood stream, they can casually saunter across the BBB and act on the brain. Large and cumbersome, insulin does not have this luxury and must therefore take a more creative route across the moat. The nose, conspicuous and sometimes even goofy, provides that creative route. Yet it's a route that, for many years, researchers were hesitant to take.
"They would say things like, 'Well, why would there be a blood brain barrier if all you had to do was put something in the nose and it would go to the brain?'" says William H. Frey II, Ph.D., Research Director at HealthPartners Center for Memory & Aging. As of 1989 Frey had been "in the Alzheimer's deal" for over a decade. At that time he was conducting clinical trials of a neurotrophic factor (a therapeutic protein) to treat AD and, because of the seeming insurmountability of the BBB, the work had been less than fruitful. "It became clear to me that, once again, this neurotrophic factor was not getting effectively into the brain," he says. So Frey decided to sleep on it. "I went to sleep and I had a dream. And this is how I discovered the intranasal method of getting around the blood brain barrier," he says. "It had been known since the early 1900s that a number of different viruses that got into the nose would travel up the olfactory nerves and the trigeminal nerves—both of these are nerves that go directly from the nasal mucosa right into the brain. The idea that came to me in this dream in 1989 was: if bad things can do it, why can't good things do it?"

The newest intranasal delivery devices differ from conventional sprays (such as those used for allergies) in that they are designed to specifically target the upper portion of the nasal cavity. For example the "Precision Olfactory Device" in this picture projects aerosolized drugs towards nerve fibers at the top of the nose, allowing more efficient transport across the blood brain barrier. **Impel NeuroPharma**

When Frey revisited the idea upon waking, it registered as simultaneously intuitive and absurd—a logical fantasy like so many dreams. Despite pushback from his colleagues ("Pretty much people thought that I was crazy," he says), Frey decided to pursue the development of an intranasal (IN) system to deliver drugs to the

brain. Awake as ever, his first step was to obtain a patent for his new technique. Here he would meet the first of many hurdles—barriers—in bringing his dream to fruition.

"The patent office said that they didn't believe that it would work, that I couldn't patent it because it didn't makes sense," Frey says. Yet Frey and others continued experimenting with IN delivery (mostly in rodents), and showed that drugs administered in this fashion reliably reached the central nervous system. "By the time four years had gone by, there were so many published papers showing that this did work, the patent office said, 'Well, we won't give you the patent, because it's obvious that this would work," Frey says. In 1997, however, the patent office landed somewhere between "nonsense" and "obvious" and Frey's request was granted. Technically the patent covered any drug or therapeutic protein delivered to the brain via the nose. Working at an Alzheimer's research center, however, Frey had a special interest in AD and had reason to focus on insulin as a pharmacologic candidate. Like other cells, neurons need insulin in order to absorb glucose and obtain energy; and research had shown deficits in glucose uptake and utilization in the brains of patients with AD. Thus, investigators had suspected a connection between insulin and AD for some time, but prior to the emergence of IN therapy this association was clinically moot.

Frey's invention did not lead to the widespread therapeutic use of IN insulin that he might have hoped for. Researchers continued experimenting with the drug, but they did not have sufficient funding for the type of large-scale clinical trials that would bring it to market. The pharmaceutical industry hadn't entirely ignored the IN method: biotech firm Chiron bought the patent almost immediately after it went public in 1997. But when Chiron changed leadership and decided to go into the business of flu vaccines, the patent was relegated to nothing more than impotent intellectual property. Eventually Chiron was bought by Novartis pharmaceuticals, "but they had a strict policy: they don't develop generic drugs," says Frey, "so they didn't do anything with it." Frey came to realize that pharmaceutical companies generally were not inclined to pour money into clinical trials for a drug they didn't own. The quality that made IN delivery so exciting—a new way to use old drugs—also made it unattractive from a business perspective. And though Novartis' ownership would not preclude government-funded development of IN, reviewers at the National Institutes of Health (NIH) were hesitant to explore novel technology and remained narrowly focused on attempts to improve cholinesterase inhibitors. "Even though I had the patent, even though all these papers had come out…the NIH basically wouldn't fund anything on intranasal," says Frey. "They didn't believe in intranasal."

Of course, with time and proper inspiration nonbelievers can be converted. In May 2012 the NIH and the Obama administration announced the allocation of $7.9 million specifically for clinical trials of IN insulin. The NIH's amended stance on the drug comes as part of an ambitious national initiative to effectively prevent and treat AD by 2025—a goal that, Frey speculates, puts pressure on the government to seek new avenues of research. "Jeez, we spent all this money for 35 years and what have we got to show for it? Nothing?" Frey mocks gently. "Let's look around and see if anything's working…Oh! What's this? Intranasal insulin?"

The funding also follows an enhanced understanding of how insulin may mediate disease progression: The hormone seems to interact with amyloid-β (Aβ), the peptide comprising toxic amyloid plaques characteristic of AD. Studies suggest that insulin protects against Aβ's neurodegenerative effects and that Aβ interferes with normal insulin signaling. Confirming this relationship are promising therapeutic results from a team of researchers led by neuropsychologist Suzanne Craft of Wake Forest Baptist Medical Center. In a 2011 study Craft and her colleagues demonstrated improved memory and cognition among individuals with AD or amnestic mild cognitive impairment (MCI) after IN insulin treatment. In this trial, insulin therapy was also associated with reduced loss of glucose uptake and utilization in brain areas linked to disease.

Funded by the new NIH resources, Craft, along with the Alzheimer's Disease Cooperative Study, a national research consortium, is now planning phase II and III clinical trials to evaluate the safety and efficacy of the medication. Quaintly titled "SNIFF," or Study of Nasal Insulin to Fight Forgetfulness, Craft's investigation will examine the cognitive effects of IN insulin versus placebo in 240 participants with either AD or MCI. In addition to tests of memory, researchers will measure biological correlates of disease such as neural atrophy and cerebrospinal fluid biomarkers.

If the trials go well IN insulin could be available to patients are early as 2017—perhaps sooner if a pharmaceutical company jumps on board to expedite the process. Frey is excited about this prospect, but cautious not to oversell the drug. "I'm not claiming that intranasal insulin is going to solve the entire problem of the disease or that it's going to cure everyone who has the disease or help everybody or anything," he clarifies. "I'm only saying, let's not be stupid. Let's stop just looking at one thing. Here's something that seems to help. Let's develop this and see what good [it] can do for people."

http://scitechdaily.com/drug-candidate-sr9009-increases-exercise-endurance/

Drug Candidate SR9009 Increases Exercise Endurance

Drug Candidate Leads to Improved Endurance

A new drug candidate, SR9009, has been shown to significantly increase exercise endurance in animal models. Researchers believe these findings may lead to better treatments for people suffering from conditions that acutely limit exercise tolerance.

An international group of scientists has shown that a drug candidate designed by scientists from the Florida campus of The Scripps Research Institute (TSRI) significantly increases exercise endurance in animal models. These findings could lead to new approaches to helping people with conditions that acutely limit exercise tolerance, such as obesity, chronic obstructive pulmonary disease (COPD) and congestive heart failure, as well as the decline of muscle capacity associated with aging.

The study was published in the journal Nature Medicine.

The drug candidate, SR9009, is one of a pair of compounds developed in the laboratory of TSRI Professor Thomas Burris and described in a March 2012 issue of the journal Nature as reducing obesity in animal models. The compounds affect the core biological clock, which synchronizes the rhythm of the body's activity with the 24-hour cycle of day and night.

The compounds work by binding to one of the body's natural molecules called Rev-erbα, which influences lipid and glucose metabolism in the liver, the production of fat-storing cells and the response of macrophages (cells that remove dying or dead cells) during inflammation.

In the new study, a team led by scientists at the Institut Pasteur de Lille in France demonstrated that mice lacking Rev-erbα had decreased skeletal muscle metabolic activity and running capacity. Burris' group showed that activation of Rev-erbα with SR9009 led to increased metabolic activity in skeletal muscle in both culture and in mice. The treated mice had a 50 percent increase in running capacity, measured by both time and distance.

"The animals actually get muscles like an athlete who has been training," said Burris. "The pattern of gene expression after treatment with SR9009 is that of an oxidative-type muscle— again, just like an athlete."

The authors of the new study suggest that Rev-erbα affects muscle cells by promoting both the creation of new mitochondria (often referred to as the "power plants" of the cell) and the clearance of those mitochondria that are defective.

The study, "Rev-Erbα Modulates Skeletal Muscle Oxidative Capacity by Regulating Mitochondrial Biogenesis and Autophagy" was led by Estelle Woldt and Yasmine Sebti (first authors) and Bart Staels and Hélène Duez (senior authors) of Institut Pasteur de Lille, France. Other contributors include Christian Duhem, Jérôme Eeckhoute, Charlotte Paquet, Stéphane Delhaye and Philippe Lefebvre of Institut Pasteur de Lille, France; Laura Solt, Youseung Shin, Thomas Burris and Theodore M. Kamenecka of TSRI; Steve Lancel and Rémi Nevière of Université Lille Nord de France; and Matthijs K.C. Hesselink, Gert Schaart and Patrick Schrauwen of Maastricht University Medical Center, Maastricht, the Netherlands.

The study was supported by a Marie Curie International Reintegration Grant (FP7), the European Commission (FP7) consortium Eurhythdia, Région Nord Pas-de-Calais/FEDER, a CPER "starting grant," the European Genomic Institute for Diabetes (ANR-10-LABX-46), an unrestricted ITMO/Astra Zeneca grant, a joint Société Francophone du Diabète MSD research fellowship, Research Grant from the European Foundation for the Study of Diabetes, National Institutes of Health grant (MH093429 and DK080201) and a VICI Research grant for innovative research from the Netherlands Organization for Scientific Research (918.96.618).

Publication: Estelle Woldt, et al., "Rev-erb-α modulates skeletal muscle oxidative capacity by regulating mitochondrial biogenesis and autophagy," Nature Medicine 19, 1039–1046, 2013; doi:10.1038/nm.3213

http://www.sciencenews.org/view/generic/id/352613/description/Bacteria_can_cause_pain_on_their_own

Bacteria can cause pain on their own

Microbes caused discomfort in mice by activating nervous system, not immune response

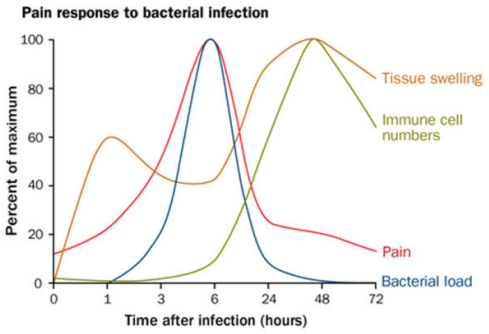
By Cristy Gelling

Bacteria can directly trigger the nerves that sense pain, suggesting that the body's own immune reaction is not always to blame for the extra tenderness of an infected wound. In fact, mice with staph-infected paws showed signs of pain even before immune cells had time to arrive at the site, researchers report online August 21 in Nature.

"Most people think that when they get pain during infection it's due to the immune system," says coauthor Isaac Chiu of Boston Children's Hospital and Harvard Medical School. Indeed, immune cells do release pain-causing molecules while fighting off invading microbes. But in recent years scientists have started uncovering evidence that bacteria can also cause pain.

Chiu and his colleagues stumbled on this idea when they grew immune cells and pain-sensing cells together in a dish. The researchers were trying to activate the immune cells by adding bacteria to the mix but were surprised

to see an immediate response in the nerve cells instead. This made them suspect that nerve cells were sensing the bacteria directly.
To take a closer look at a real infection, the team injected the back paws of mice with Staphylococcus aureus, a bacterium that causes painful sores in humans. The researchers measured how tender the infected area was by poking it with flexible filaments of plastic. If the mouse didn't like being prodded, it would lift its paw, giving a sensitive measure of each infection's ouch factor.



The mice's paws were most sensitive when bacterial cell numbers were at their peak, six hours after infection. By the time the immune response caught up, at 48 hours after infection, the pain had largely ebbed away. The researchers identified two protein factors released by S. aureus that could trigger nerve cells in dishes and that were also painful when injected into the mice.

Mice with infected paws were most sensitive to being prodded when bacterial numbers were at their highest, not when the immune response was peaking. **Chiu et al.**

These factors seemed to be more important than the immune system in making mouse paws achy, since mice with faulty immune responses were at least as tender as normal mice, the researchers report. However, pain from immune reactions might play a more significant role in other kinds of infections, Chiu cautions, since not all bacterial species are as good as S. aureus at evading the immune system.
The team guessed that the nerves were helping to alert the immune system to the presence of bacteria, but when they tested this idea, they got a surprise. "We saw the opposite of what we expected," Chiu says. When the researchers infected mice that lacked pain-sensing nerve cells, even more immune cells rushed to the site of infection than in normal mice. This implies that the nerve cells normally suppress the immune system, Chiu says.
Chiu doesn't know why pain should dampen the body's defenses against pathogens but speculates that when tissue is damaged by injury, an overenthusiastic immune system may need to be held back. Bacteria like S. aureus might take advantage of pain's anti-immune effects to avoid detection, he suggests, "but it's an open question."
Kevin Tracey, an immunologist and president of the Feinstein Institute for Medical Research in Manhasset, N.Y., says the results fit with his own studies that show nerve signals can put the brakes on immune responses. "It's a beautiful study," Tracey says. "It's important because it shows that in order to understand the immune system, you really have to understand the nervous system."
I.M. Chiu et al. Bacteria activate sensory neurons that modulate pain and inflammation. Nature. Published online August 21, 2013. doi:10.1038/nature12479. [Go to]

http://bit.ly/12pHu6h

Star twinkles could help pin down planet sizes

Starlight captured by the Kepler space telescope has revealed that the amount a star flickers is tied to its size

18:00 21 August 2013 by Maggie McKee

Twinkle, twinkle little star – and show us just how little you are. Starlight captured by the Kepler space telescope has revealed that the amount a star flickers is tied to its size, offering a better way to measure a wide variety of stars and their associated planets. Unfortunately, that may be mixed news for seekers of Earth-sized worlds.
Kepler was designed to spot transits, the periodic dips in a star's brightness indicating that a planet has passed in front of it. The telescope's vigil required exquisite targeting precision, and key parts of its steering system are now broken, ending the telescope's main mission as an exoplanet hunter. But you haven't heard the last of Kepler. Two years' worth of data still need inspecting, including information about the thousands of stars in its field of view.
Figuring out the properties of stars is vital to planet surveys. When a planet transits a star, the amount of light it blocks is used to calculate its size. That can help to pinpoint whether it is rocky like Earth or gassy like Jupiter – as long as the star's size is known. Simply looking at a star's colour can reveal whether it is small and compact like our sun or big and bloated like a red giant, the type of star the sun will swell into in about 5 billion years. But such estimates are crude, with uncertainties of more than 90 per cent.
Much more accurate size and mass measurements, boasting uncertainties of just 2 per cent, come from studying vibrations within the star called starquakes. However this technique, known as asteroseismology, can be used only on bright stars, because it requires teasing out subtle periodic variations in a star's light.

Getting granular

Fabienne Bastien of Vanderbilt University in Tennessee and colleagues used Kepler data to watch instead for flickers in starlight due to short-lived convection cells, or granules, on the star's surface. These are bright regions where hot plasma wells up, surrounded by darker boundaries where it cools and falls back down.

They began with a sample of about 500 stars whose size and mass were already known, thanks to asteroseismology measurements made by Kepler. They found a clear pattern: bigger, more bloated stars flicker more. That's probably because each granule spans some two dozen times the width of the Earth in a giant star, compared to just a fraction of the Earth's diameter in a compact star.

"What we see over time is the combined effect of this network of bright granules flickering on and off," says team member Keivan Stassun, also of Vanderbilt.

The method provides stellar size and mass estimates with uncertainties of about 25 per cent – a vast improvement over colour-based estimates, says Stassun. So far, the flicker technique has been used to find the size and mass of about 1000 stars that do not have asteroseismology measurements, and it could be used to gauge the sizes of 50,000 more stars already studied by Kepler, Stassun says.

Fewer Earths

How will that affect the count of Earth-sized worlds? Kepler's principal investigator William Borucki expects the current pool of candidates to shrink. He suspects we may have been underestimating the size of stars, and therefore the planets that they host, so many worlds currently deemed "Earth-like" may turn out to be too big.

"Based on previous experience, there is a significant chance that star sizes will increase when we have a more accurate method," he says.

Unfortunately, Kepler's pointing is probably no longer precise enough to measure the subtle flicker or asteroseismology signals from sun-like stars, says Jørgen Christensen-Dalsgaard of Aarhus University in Denmark, who leads a consortium of researchers who analyse Kepler's starquake data.

Still, the flicker method could be put to use on NASA's next planet hunter, the Transiting Exoplanet Survey Satellite (TESS), due to launch in 2017. "Our hope is that TESS will be able to do what Kepler has done, but over the entire sky," says Stassun.

Journal reference: Nature, DOI: 10.1038/nature12419

http://www.medscape.com/viewarticle/809724?src=rss

Psychedelic Drugs No Risk to Mental Health, Possibly Beneficial

Using classic psychedelic drugs does not raise the risk for mental health problems; on the contrary, it may offer some protection, new research suggests.

Megan Brooks

Among 130,152 representative US adults, including 21,967 reported psychedelic drug users, researchers found no significant link between lifetime use of lysergic acid diethylamide (LSD), psilocybin, mescaline, or peyote and an increased rate of mental health problems.

Rather, in several cases, psychedelic drug use was associated with a lower rate of mental health problems, Teri S. Krebs, PhD, and Pål-Ørjan Johansen, PhD, of the Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, report. The findings were published online August 19 in *PLoS One*.

Lower Rates of Distress

"We were not particularly surprised. Overall, there is a lack of evidence that psychedelics cause lasting mental health problems," Dr. Krebs told *Medscape Medical News*.

More than 30 million Americans have used LSD, psilocybin, or mescaline at some time in their lives. Some case reports of mental illness in people who had used psychedelics fueled some concern of a link. But there are "many potential biases of relying on individual anecdotes," Dr. Krebs said. "In particular, mental illness is rather common, and symptoms often appear in the early 20s, which is the same time that people often first use psychedelics."

In the current population study, after adjusting for other risk factors, there was no link between psychedelic drug use and a range of mental health outcomes, including serious psychologic distress, mental health treatment, symptoms of 8 psychiatric disorders (panic disorder, major depressive episode, mania, social phobia, general anxiety disorder, agoraphobia, posttraumatic stress disorder, and nonaffective psychosis), and 7 specific symptoms of nonaffective psychosis.

In fact, lifetime use of psilocybin or mescaline and past-year use of LSD were associated with lower rates of serious psychologic distress. Lifetime use of LSD was also significantly associated with a lower rate of outpatient mental health treatment and psychiatric medicine prescription.

"We cannot exclude the possibility that use of psychedelics might have a negative effect on mental health for some individuals or groups, perhaps counterbalanced at a population level by a positive effect on mental health

in others," the authors note. Nevertheless, "recent clinical trials have also failed to find any evidence of any lasting harmful effects of psychedelics."

Less Harmful

"This is an important analysis," Matthew W. Johnson, PhD, of the Behavioral Pharmacology Research Unit, Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, in Baltimore, Maryland, who was not involved in the study, *told Medscape Medical News*.

"Although there is evidence suggesting beneficial effects of psychedelics in well-controlled clinical research, that does not address the occurrence of psychiatric adverse effects in the population. It is very interesting to know that these drugs are not associated with adverse mental health outcomes at the population level," Dr. Johnson said.

"However, as the authors note, it is certainly possible that individual recreational users experience harms. This analysis would just suggest that this may be limited in scope, and possibly offset by some individuals also receiving benefit at the population level," he added.

This study "chimes very much with what we know already about psychedelics — that they are essentially much less harmful than other illicit substances," Mark Bolstridge, BSc, MRCPsych, Centre for Neuropsychopharmacology, Imperial College London, United Kingdom, told *Medscape Medical News*.

"Having personally worked in mental health and trained in psychiatry, I am yet to see any individual suffering from significant mental health problems as a result of using psychedelics. Alcohol, amphetamines, and cannabis, yes, but never psychedelics," said Dr. Bolstridge, who was not involved in the study.

Dr. Krebs noted that "psychedelics interact with a specific type of serotonin receptor in the brain and may stimulate the formation of new connections and patterns. They generally seem to open an individual to an awareness of new perspectives and opportunities for action. People often report deeply personally and spiritually meaningful experiences with psychedelics," she said.

Researchers at Imperial College London have found that healthy adults recall memories much more vividly while under the influence of psilocybin, and functional magnetic resonance imaging (fMRI) data reveal a neurobiological basis for this effect, as reported by *Medscape Medical News*.

Their research also shows that psilocybin has potential in the treatment of depression, anxiety, and possibly cluster headaches.

Debunking Myths

"We know categorically that psychedelics taken in a controlled clinical environment with appropriate support almost certainly never lead to any recurring or enduring mental health problems," Dr. Bolstridge said.

"All in all, I think the [new] paper is an important addition to the scientific literature, and it can only help in dispelling the myths surrounding these much maligned substances and in reinforcing the case for continued investigations into how these fascinating compounds work in the brain," Dr. Bolstridge said.

"In particular, [it can help in] attempting to determine whether they can prove effective in helping those patients incapacitated by ongoing mental health problems and who are little helped by conventional psychiatric treatments," he added.

Dr. Krebs said clinical trials looking at the potential benefits of psilocybin in alcoholism and smoking cessation are also under way. Last year, she and Dr. Johansen published a meta-analysis of randomized controlled trials of LSD in alcoholism, which provided evidence for a beneficial effect of LSD for treating alcohol dependency.

The study was supported by the Research Council of Norway. The authors, Dr. Johnson, and Dr. Bolstridge report no relevant financial relationships.

PLoS One. Published online August 19, 2013. Full article

http://nyti.ms/16hEPsz

As Humans Change Landscape, Brains of Some Animals Change, Too

A new study suggests that the brains of several small mammals, including those of the little brown bat, have grown bigger as humans have altered the animals' living conditions.

By CARL ZIMMER

Evolutionary biologists have come to recognize humans as a tremendous evolutionary force. In hospitals, we drive the evolution of resistant bacteria by giving patients antibiotics. In the oceans, we drive the evolution of small-bodied fish by catching the big ones.

In a new study, a University of Minnesota biologist, Emilie C. Snell-Rood, offers evidence suggesting we may be driving evolution in a more surprising way. As we alter the places where animals live, we may be fueling the evolution of bigger brains.

Dr. Snell-Rood bases her conclusion on a collection of mammal skulls kept at the Bell Museum of Natural History at the University of Minnesota. Dr. Snell-Rood picked out 10 species to study, including mice, shrews,

bats and gophers. She selected dozens of individual skulls that were collected as far back as a century ago. An undergraduate student named Naomi Wick measured the dimensions of the skulls, making it possible to estimate the size of their brains.

Two important results emerged from their research. In two species — the white-footed mouse and the meadow vole — the brains of animals from cities or suburbs were about 6 percent bigger than the brains of animals collected from farms or other rural areas. Dr. Snell-Rood concludes that when these species moved to cities and towns, their brains became significantly bigger. Dr. Snell-Rood and Ms. Wick also found that in rural parts of Minnesota, two species of shrews and two species of bats experienced an increase in brain size as well.

Dr. Snell-Rood proposes that the brains of all six species have gotten bigger because humans have radically changed Minnesota. Where there were once pristine forests and prairies, there are now cities and farms. In this disrupted environment, animals that were better at learning new things were more likely to survive and have offspring.

Studies by other scientists have linked better learning in animals with bigger brains. In January, for example, researchers at Uppsala University in Sweden described an experiment in which they bred guppies for larger brain sizes. The big-brained fish scored better on learning tests than their small-brained cousins.

Animals colonizing cities and towns have to learn how to find food in buildings and other places their ancestors hadn't encountered. "We're changing rural populations, too," Dr. Snell-Rood said. As forests get cut for timber or farming, for example, bats may have to travel farther to find food and still be able to navigate home to roost. Big brains may have benefited them as well.

Other scientists not involved in the research hailed it as the first report of significant changes in brain size in animals outside of labs. "I think the results are exciting and deserving of much follow-up work," said Jason Munshi-South, an evolutionary biologist at Fordham University.

Dr. Munshi-South and other researchers see a need to test Dr. Snell-Rood's hypothesis in new ways, so as to rule out alternative explanations. If she's right, for example, then the same trend she observed in Minnesota should exist in museum collections of skulls from other heavily developed regions of the world.

It should also be possible to continue the research in labs, by breeding small-brained rural mammals with their big-brained cousins. By studying their offspring, scientists could study the genes involved in producing different brain sizes. They could even give the animals tests to see just how much life in a human-dominated world has changed how their brains work.

But the ultimate breeding experiment to test Dr. Snell-Rood's hypothesis may not be possible outside the movie set for "Jurassic Park." "What would be really cool would be to raise populations from 1900," said Dr. Snell-Rood with a laugh, "but we can't really do that."

http://www.sciencedaily.com/releases/2013/08/130822091026.htm

Breast Is Best: Good Bacteria Arrive from Mum's Gut Via Breast Milk

Scientists have discovered that important 'good' bacteria arrive in babies' digestive systems from their mother's gut via breast milk.

Although this does confirm that when it comes to early establishment of gut and immune health, 'breast is best', a greater understanding of how babies acquire a population of good bacteria can also help to develop formula milk that more closely mimics nature.

The study, published today (22 August) in Environmental Microbiology, which is a journal of the Society for Applied Microbiology (SfAM), was led by Professor Christophe Lacroix at the Institute for Food, Nutrition and Health, ETH-Zurich, Switzerland.

Professor Lacroix said: "We are excited to find out that bacteria can actually travel from the mother's gut to her breast milk. "A healthy community of bacteria in the gut of both mother and baby is really important for baby's gut health and immune system development."

The Zurich team found the same strains of Bifidobacterium breve and several types of Clostridium bacteria, which are important for colonic health, in breast milk, and maternal and/or neonatal faeces. Strains found in breast milk may be involved in establishing a critical nutritional balance in the baby's gut and may be important to prevent intestinal disorders.

Professor Lacroix continued "We're not sure of the route the bacteria take from gut to breast milk but, we have used culture, isolation, sequencing and fingerprinting methods to confirm that they are definitely the same strains."

Future research will hopefully complete the picture of how bacteria are transferred from mother to neonate. With a more thorough knowledge, we can decide which bacterial species will be most important as probiotics in formula. But until then, for neonates at least, the old adage is true, breast is best.

http://www.sciencedaily.com/releases/2013/08/130822091021.htm

Flu Shot May Halve Heart Attack Risk in Middle Aged With Narrowed Arteries

The flu shot seems to almost halve the risk of heart attacks in middle aged people with narrowed arteries, finds research published in the journal Heart.

Those aged 50 to 64 are not currently routinely included in national flu vaccination programmes in either the UK or Australia. But the findings prompt the Australian authors to suggest that further exploration of extending the schedule may be warranted.

The researchers wanted to find out if flu is an unrecognised, but clinically important, contributing factor to increased heart attack risk. Published evidence suggests that flu boosts the risk of death from all causes as well as the risk of admission to hospital for cardiovascular and respiratory problems.

They therefore assessed 559 patients over the age of 40 who were referred to a tertiary hospital during consecutive winters in 2008-10. Some 275 of these patients had sustained a heart attack and 284 had not.

Nose and throat swabs and blood samples taken at admission and 4-6 weeks later showed that around one in eight (12.4%; 34) of the heart attack patients had recently had flu, compared with just under 7% (18) in the comparison group. Half of all the patients had had the flu jab that year.

Flu had not been diagnosed in around one in 10 of those who had the infection, indicating that it may be missed in hospital patients with other clinical problems, say the authors.

A recent respiratory infection was more common among those patients who'd had a heart attack and doubled the risk.

But after taking account of other influential factors, such as age, high cholesterol, and smoking, flu did not increase heart attack risk. But vaccination against the infection did seem to be protective, decreasing the risk of a heart attack by 45%.

Previous research suggests that infections such as flu might encourage blood to thicken or prompt an inflammatory response in arteries that are already diseased, so sparking the development of a blockage.

Extending the flu vaccination programme to 50 to 64 year olds has been mooted before, but not considered to be cost effective, say the authors. However, cardiovascular disease, which causes a great deal of illness and death in older adults, wasn't taken into consideration in these estimates, they add.

"As such, even a small effect of influenza vaccination in preventing [heart attacks] may have significant population health gains," they write.

They call for the issues to be explored further, and at the very least say that doctors should be aware that flu is an underlying and poorly diagnosed condition in hospital patients and that the flu jab seems to lessen the risk of a heart attack in susceptible patients.

C. R. MacIntyre, A. E. Heywood, P. Kovoor, I. Ridda, H. Seale, T. Tan, Z. Gao, A. L. Katelaris, H. W. D. Siu, V. Lo, R. Lindley, D. E. Dwyer. Ischaemic heart disease, influenza and influenza vaccination: a prospective case control study. Heart, 2013; DOI: 10.1136/heartjnl-2013-304320

http://www.sciencedaily.com/releases/2013/08/130822105040.htm

Engaging in a Brief Cultural Activity Can Reduce Implicit Prejudice

Social connection sparks interest in another culture; Acting on this interest improves attitudes toward that cultural group.

A small cue of social connection to someone from another group -- such as a shared interest -- can help reduce prejudice immediately and up to six months later, according to new research published in Psychological Science, a journal of the Association for Psychological Science.

"Our research shows that even a brief opportunity to take part in another group's culture can improve intergroup attitudes even months later," says psychological scientist and lead researcher Tiffany Brannon of Stanford University.

Decades of research in psychology show that extended relationships between people from different groups -- such as between roommate pairs and long-standing friends -- can improve attitudes toward other groups.

Even small cues like a common birthday have been shown to bring people together and lead them to share common goals and motivations. Brannon and Stanford professor Gregory Walton wanted to investigate whether such small cues might impact people's engagement with, and attitudes toward, other groups.

In the first experiment, White Canadian participants expressed greater interest in Chinese culture when their body posture was subtly mimicked by a Chinese Canadian peer in a getting-to-know-you conversation than when the peer held a neutral position. They also completed more tickets for a drawing to win Chinese cultural products, like Chinese films.

The next two experiments examined the link between social connection, cultural engagement, and prejudice.

White and Asian American participants showed less implicit prejudice against Latinos after they got to know a Latina peer with whom they had a common interest, such as the same favorite book, and after they worked with her on a group activity that incorporated elements of Mexican culture.
Importantly, participants showed no reduction in prejudice when they worked with the Latina peer on a project related to a non-Mexican cultural group, suggesting the importance of engaging in the peer's culture. Moreover, participants only showed reduced prejudice when they felt they had freely chosen the topic of the group activity.
Surprisingly, the effects of the brief laboratory interaction lasted over time. Participants who had connected with the Latina peer and who had freely chosen the group activity topic not only expressed greater interest in interacting with Mexican Americans, but also had somewhat more positive attitudes toward illegal Mexican immigrants in an unrelated survey six months later.
"It was impressive that a short interaction in a laboratory could facilitate more positive implicit attitudes immediately and better attitudes in the long-term," observe Brannon and Walton. "The right kind of intergroup interactions, even if brief, can have lasting benefits."
Taken together, the new findings inform policies that aim to use multicultural experiences to improve intergroup relations:
"Often, the expression of distinctive cultural interests by minority-group members is seen as risky, as an invitation to be perceived through the lens of a stereotype," the researchers note. "The present research highlights the benefits that can arise when minority group members are encouraged to express and share positive aspects of their culture in mainstream settings."
This research is important in diverse countries like the U.S., Brannon and Walton argue, because people from different backgrounds routinely come in to contact with one another at workplaces, schools, and in other social institutions. But it's important to note that the effects depend on people feeling they have freely chosen to participate and engage in cultural activities:
"Our research suggests how diverse cultural interactions and experiences can improve intergroup attitudes and relationships," say Brannon and Walton. "But it also suggests one way it can be done badly: Making people feel obligated to take part in multicultural activities can reduce their benefits."
T. N. Brannon, G. M. Walton. Enacting Cultural Interests: How Intergroup Contact Reduces Prejudice by Sparking Interest in an Out-Group's Culture. Psychological Science, 2013; DOI: 10.1177/0956797613481607

http://www.sciencedaily.com/releases/2013/08/130822194145.htm

Single Injection May Revolutionize Melanoma Treatment

A new study at Moffitt Cancer Center could offer hope to people with melanoma, the deadliest form of skin cancer.

Researchers are investigating whether an injectable known as PV-10 can shrink tumors and reduce the spread of cancer.
PV-10 is a solution developed from Rose Bengal, a water-soluble dye commonly used to stain damaged cells in the eye.
Early clinical trials show PV-10 can boost immune response in melanoma tumors, as well as the blood stream.
"Various injection therapies for melanoma have been examined over the past 40 years, but few have shown the promising results we are seeing with PV-10," said Shari Pilon-Thomas, Ph.D., assistant member of Moffitt's Immunology Program.
In the initial study, researchers injected a single dose of PV-10 into mice with melanoma.
The result was a significant reduction in the skin cancer lesions, as well as a sizable reduction in melanoma tumors that had spread to the lungs.
The researchers said the dye solution appeared to produce a robust anti-tumor immune response and may be safer than existing immunological agents.
"We are currently in the middle of our first human clinical trial of PV-10 for advanced melanoma patients.
In addition to monitoring the response of injected melanoma tumors, we are also measuring the boost in the anti-tumor immune cells of patients after injection," explained Amod A. Sarnaik, M.D., assistant member of Moffitt's Cutaneous Oncology Program.
The initial study appears in PLOS ONE. It was supported by a sponsored research agreement with Provectus Pharmaceuticals, Inc., developer of PV-10.
Paul Toomey, Krithika Kodumudi, Amy Weber, Lisa Kuhn, Ellen Moore, Amod A. Sarnaik, Shari Pilon-Thomas. Intralesional Injection of Rose Bengal Induces a Systemic Tumor-Specific Immune Response in Murine Models of Melanoma and Breast Cancer. PLoS ONE, 2013; 8 (7): e68561 DOI: 10.1371/journal.pone.0068561

http://www.sciencedaily.com/releases/2013/08/130823090947.htm

Receptor May Aid Spread of Alzheimer's and Parkinson's in Brain

Scientists at Washington University School of Medicine in St. Louis have found a way that corrupted, disease-causing proteins spread in the brain, potentially contributing to Alzheimer's disease, Parkinson's disease and other brain-damaging disorders.

The research identifies a specific type of receptor and suggests that blocking it may aid treatment of theses illnesses. The receptors are called heparan sulfate proteoglycans (HSPGs).

"Many of the enzymes that create HSPGs or otherwise help them function are good targets for drug treatments," said senior author Marc I. Diamond, MD, the David Clayson Professor of Neurology. "We ultimately should be able to hit these enzymes with drugs and potentially disrupt several neurodegenerative conditions."

The study is available online in the Proceedings of the National Academy of Sciences.

Over the last decade, Diamond has gathered evidence that Alzheimer's disease and other neurodegenerative diseases spread through the brain in a fashion similar to conditions such as mad cow disease, which are caused by misfolded proteins known as prions.

Proteins are long chains of amino acids that perform many basic biological functions. A protein's abilities are partially determined by the way it folds into a 3-D shape. Prions are proteins that have become folded in a fashion that makes them harmful.

Prions spread across the brain by causing other copies of the same protein to misfold.

Among the most infamous prion diseases are mad cow disease, which rapidly destroys the brain in cows, and a similar, inherited condition in humans called Creutzfeldt-Jakob disease.

Diamond and his colleagues have shown that a part of nerve cells' inner structure known as tau protein can misfold into a configuration called an amyloid. These corrupted versions of tau stick to each other in clumps within the cells. Like prions, the clumps spread from one cell to another, seeding further spread by causing copies of tau protein in the new cell to become amyloids.

In the new study, first author Brandon Holmes, an MD/PhD student, showed that HSPGs are essential for binding, internalizing and spreading clumps of tau. When he genetically disabled or chemically modified the HSPGs in cell cultures and in a mouse model, clumps of tau could not enter cells, thus inhibiting the spread of misfolded tau from cell to cell.

Holmes also found that HSPGs are essential for the cell-to-cell spread of corrupted forms of alpha-synuclein, a protein linked to Parkinson's disease.

"This suggests that it may one day be possible to unify our understanding and treatment of two or more broad classes of neurodegenerative disease," Diamond said.

"We're now sorting through about 15 genes to determine which are the most essential for HSPGs' interaction with tau," Holmes said. "That will tell us which proteins to target with new drug treatments."

B. B. Holmes, S. L. DeVos, N. Kfoury, M. Li, R. Jacks, K. Yanamandra, M. O. Ouidja, F. M. Brodsky, J. Marasa, D. P. Bagchi, P. T. Kotzbauer, T. M. Miller, D. Papy-Garcia, M. I. Diamond. Heparan sulfate proteoglycans mediate internalization and propagation of specific proteopathic seeds. Proceedings of the National Academy of Sciences, 2013; 110 (33): E3138 DOI: 10.1073/pnas.1301440110

http://www.eurekalert.org/pub_releases/2013-08/jhm-run082013.php

Researchers uncover new biological target for combating Parkinson's disease

Compounds already exist to potentially treat both inherited and non-inherited cases

Researchers at Johns Hopkins and elsewhere have brought new clarity to the picture of what goes awry in the brain during Parkinson's disease and identified a compound that eases the disease's symptoms in mice. Their discoveries, described in a paper published online in Nature Neuroscience on August 25, also overturn established ideas about the role of a protein considered key to the disease's progress.

"Not only were we able to identify the mechanism that could cause progressive cell death in both inherited and non-inherited forms of Parkinson's, we found there were already compounds in existence that can cross into the brain and block this from happening," says Valina Dawson, Ph.D., the director of the Stem Cell Biology and Neuroregeneration Programs at the Johns Hopkins University School of Medicine's Institute for Cell Engineering (ICE). "While there are still many things that need to happen before we have a drug for clinical trials, we've taken some very promising first steps."

Dawson and her husband, Ted Dawson, M.D., Ph.D., the director of ICE, have collaborated for decades on studies of the molecular chain of events that leads to Parkinson's. One of their findings was that the function of an enzyme called parkin, which malfunctions in the disease, is to tag a bevy of other proteins for destruction by the cell's recycling machinery. This means that nonfunctional parkin leads to the buildup of its target proteins, and the Dawsons and others are exploring what roles these proteins might play in the disease.

In the new study, the Dawsons collaborated with Debbie Swing and Lino Tessarollo of the National Cancer Institute, to develop mice whose genes for a protein called AIMP2 could be switched into high gear. AIMP2 is one of the proteins normally tagged for destruction by parkin, so the genetically modified mice enabled the research team to put aside the effects of defective parkin and excesses of other proteins and look just at the consequences of too much AIMP2.

The consequences were that the mice developed symptoms similar to those of Parkinson's as they aged, the group found. As in Parkinson's patients, the brain cells that make the chemical dopamine were dying. Since AIMP2 is known for its role in the process of making new proteins, the researchers thought the cell death was caused by problems with this process. But when graduate student Yunjong Lee looked at the efficiency of protein-making in the affected mice, everything appeared normal.

Looking for an alternative explanation, Lee tested how cells with excess AIMP2 responded to compounds blocking various paths to cell death, and found that the AIMP2 was activating a self-destruct pathway called parthanatos, discovered and named by the Dawsons years ago for the for poly(ADP-ribose), or "PAR," and the Greek word thanatos, which means "messenger of death."

The Dawsons had previously seen parthanatos set off after events like traumatic injuries or stroke — not by chronic disease. And there were more surprises to come. Lee found that AIMP2 triggered parthanatos by directly interacting with a protein called PARP1, which was long thought to respond only to DNA damage — not to signals from other proteins. Valina Dawson notes that AIMP2 is actually the second protein found to activate PARP1, but the idea that PARP1 is only involved in detecting and responding to DNA damage is still firmly entrenched in her field.

Since the Dawsons had been studying PARP1 for some time, they knew of compounds drug companies had designed to block this enzyme. Such drugs are already in the process of being tested to protect healthy cells during cancer treatment. Crucially, two of these compounds can cross over the blood-brain barrier that keeps many drugs from affecting brain cells. The research team used a compound that blocks PARP1, and Lee tested it on the mice with too much AIMP2. "Not only did the compound protect dopamine-making neurons from death, it also prevented behavioral abnormalities similar to those seen in Parkinson's disease," Lee says.

Though the results are encouraging, Valina Dawson cautions that there are hurdles that will need to be overcome before either of the brain-accessible compounds has a chance to make it into clinical trials. More extensive animal testing will need to be done, and with mice whose Parkinson's symptoms don't arise from genetically amped-up AIMP2 production. In addition, Dawson explains, in order for trials on any Parkinson's drugs to run effectively, measurable markers of the disease's severity need to be found. Ted Dawson and others at Johns Hopkins say they are now working on a separate project to do just that.

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Other authors of the study are Senthilkumar S. Karuppagounder, Joo-Ho Shin, Yun-Il Lee, Han Seok Ko, Haisong Jiang, Sung-Ung Kang, Byoung Dae Lee, Ho Chul Kang and Donghoon Kim, all of the Johns Hopkins University School of Medicine.