http://medicalxpress.com/news/2011-11-als-drug-symptom-mortality-phase.html

Novel ALS drug slows symptom progression, reduces mortality in phase II trial

Treatment with a novel drug believed to prevent dysfunction of mitochondria appears to slow symptom progression in amyotrophic lateral sclerosis

Medical Xpress - Treatment with dexpramipexole - a novel drug believed to prevent dysfunction of mitochondria, the subcellular structures that provide most of a cell's energy – appears to slow symptom progression in the neurodegenerative disease amyotrophic lateral sclerosis (ALS). Promising results of a phase 2 trial of dexpramipexole are receiving advance online publication in Nature Medicine. Some preliminary results of the study were presented at the 2009 International Symposium on ALS/MND and the 2010 American Academy of Neurology annual meeting.

"Today there are only two FDA-approved drugs used to treat ALS – riluzole, which extends life about 10 percent, and Nuedexta, which treats the emotional instability that characterizes ALS and other neurological disorders," says Merit Cudkowicz, MD, director of the Massachusetts General Hospital (MGH) Neurology Clinical Trials Unit and ALS Center, lead author of the study. "We need more therapies to slow, halt and ultimately reverse the course of disease and also therapies to treat the symptoms."

Also known as Lou Gehrig's disease, ALS is a progressive neurodegenerative disease affecting motor neurons in the brain and spinal cord. Death of these nerve cells stops the transmission of neural impulses to muscle fibers, leading to weakness, paralysis and usually death from respiratory failure. Mitochondrial dysfunction is among several factors believed to underlie nerve cell death. Initially developed by Knopp Biosciences of Pittsburgh, dexpramipexole appears to protect neurons from mitochondrial dysfunction.

Several investigators from Knopp, which sponsored the study reported in the current article, collaborated with Cudkowicz and the Northeast ALS Consortium on the trial. Co-founded and co-directed by Cudkowicz, the Northeast ALS Consortium includes over 100 clinical sites throughout North America that work collaboratively on clinical trials and has established the infrastructure necessarily to quickly and efficiently bring forward new treatments for people with the disorder.

The progression of ALS can vary widely, with some patients surviving decades after diagnosis and others dying within a year. Therefore it can be quite challenging to develop phase 2 trials, which need both to test dosage levels and to determine potential effectiveness in small groups of participants over brief periods of time. To meet this challenge, the research team devised a two-stage study. In the first, 102 patients who had recently been diagnosed with ALS were randomized into four groups, receiving oral tablets of either a placebo or dexpramipexole at total daily dosages of either 50, 150 or 300 mg for 12 weeks. When that stage was completed, participants continuing in the trial received placebo only for four weeks and then were re-randomized into two different groups, receiving daily dosages of either 50 or 300 mg of the study drug for 24 weeks.

Results of the first stage showed that receiving dexpramipexole appeared to slow the progression of symptoms measured both by the ALS Functional Rating Scale and by pulmonary capacity. The protective effect was greatest in the 300 mg group – in whom symptom progression was approximately 30 percent slower than in the placebo group – and little effect was seen in those receiving 50 mg. The second stage had similar results, with slower disease progression and a reduced risk of death in participants receiving the higher dosage. While results were not generally statistically significant, due to the small size and short duration of the study, all data trends were dose responsive.

"Since individual participants could have been in different treatment groups in the first and second stages of the study, seeing the same dose-dependent differences at both stages gives us confidence in the data. In a way, this was two supportive studies in one trial design," says Cudkowicz. "Confirmation of these findings in the phase 3 clinical trial, which is currently ongoing, would give us even more confidence in this study design for phase 2 testing in ALS. We hope that adding this drug to the approved treatments for ALS would give patients a chance to stay healthier longer, with slower decline of function and increased survival." Cudkowicz is the Julieanne Dorn Professor of Neurology at Harvard Medical School. *Provided by Massachusetts General Hospital*

http://www.eurekalert.org/pub_releases/2011-11/nu-ncf112111.php

New culprit found in Lou Gehrig's disease

A second 'bad' gene is linked to damaged cell buildup, paralysis in ALS

CHICAGO - Following a major Northwestern Medicine breakthrough that identified a common converging point for all forms of amyotrophic lateral sclerosis (ALS and Lou Gehrig's disease), a new finding from the same scientists further broadens the understanding of why cells in the brain and spinal cord degenerate in the fatal disease.

Less than three months ago, Northwestern research found that the crucial recycling system for cells in the brain and spinal cord was broken in people with ALS. And one mutated gene had a key role. Like a loafing worker, it wasn't doing its job to recycle damaged cells. Now, scientists have discovered a second faulty gene - a new loafing worker - in the same recycling pathway. The finding is reported in Archives of Neurology.

"Now that we have two bad players, it shines more light on this broken pathway," said senior author Teepu Siddique, M.D., the Les Turner ALS Foundation/Herbert C. Wenske Professor of the Davee Department of Neurology and Clinical Neurosciences at Northwestern's Feinberg School and a neurologist at Northwestern Memorial Hospital. "This gives us a clear target to develop drug therapies to try to fix this problem. It strengthens our belief that this broken system is at the heart of ALS."

The new "bad player" is called sequestosome1. The previously identified mutated gene is ubiquilin2. Because these two genes aren't doing their jobs to recycle damaged proteins, those proteins – as well as sequestosome1 and ubiquilin2 - accumulate abnormally in the motor neurons in the spinal cord and cortical and hippocampal neurons in the brain. The protein accumulations resemble twisted skeins of yarn - characteristic of ALS - and cause the degeneration of the neurons.

In the new study, sequestosome1 genetic mutations were identified in 546 ALS patients; 340 with an inherited form of the disease, called familial, and 206 with a non-inherited form of the disease, called sporadic. About 90 percent of ALS is sporadic and 10 percent is familial. To date, mutations in about 10 genes, several of which were discovered at Northwestern, including SOD1 and ALSIN, account for about 30 percent of classic familial ALS, noted Faisal Fecto, M.D., study lead author and a PhD candidate in neuroscience at Feinberg.

ALS affects an estimated 350,000 people worldwide, including children and adults, with about 50 percent of people dying within three years of its onset. In the motor disease, people progressively lose muscle strength until they become paralyzed and can no longer move, speak, swallow and breathe. ALS/dementia targets the frontal and temporal lobes of the brain, affecting patients' judgment, the ability to understand language and to perform basic tasks like planning what to wear or organizing their day.

The discovery of the breakdown in protein recycling may also have a wider role in other neurodegenerative diseases, particularly the dementias. These include Alzheimer's disease and frontotemporal dementia as well as Parkinson's disease, all of which are characterized by aggregations of proteins, Siddique said. The removal of damaged or misfolded proteins is critical for optimal cell functioning, he noted.

The study was supported by the National Institute of Neurological Disorders and Stroke, the Les Turner ALS Foundation, the Herbert and Florence C. Wenske Foundation and other sources.

http://www.eurekalert.org/pub_releases/2011-11/isu-isu112111.php

Iowa State University scientists genetically increase algae biomass by more than 50 percent

Research at Iowa State University has led to discovery of a genetic method that can increase biomass in algae by 50 to 80 percent.

AMES, Iowa - The breakthrough comes from expressing certain genes in algae that increase the amount of photosynthesis in the plant, which leads to more biomass. Expressing genes means that the gene's function is turned on. "The key to this (increase in biomass) is combination of two genes that increases the photosynthetic carbon conversion into organic matter by 50 percent over the wild type under carbon dioxide enrichment conditions," said Martin Spalding, professor in the Department of Genetics, Development, and Cell Biology and associate dean for research and graduate studies in the College of Liberal Arts and Sciences.

Carbon enrichment conditions are those in which the algae has enough carbon dioxide. This patent-pending technology is available for licensing from the Iowa State University Research Foundation, which also provided technology development funds. This opens up possibilities for more and better biofuel development, according to Spalding. "There is no doubt in my mind that this brings us closer [to affordable, domestic biofuel]," said Spalding.

In nature, algae are limited from growing faster because they don't get enough carbon dioxide from the atmosphere, according to Spalding. In environments that have relatively low levels of carbon dioxide (CO2), such as air in earth's atmosphere, two genes in algae, LCIA and LCIB, are expressed - or turned on - to help capture and then channel more carbon dioxide from the air into the cells to keep the algae alive and growing. However, when algae are in environments with high carbon dioxide levels, such as in soil near plant roots that are expiring carbon dioxide, the two relevant genes shut down because the plant is getting enough carbon dioxide.

The process is similar to a car driving up a hill. The accelerator - these two genes - is pressed and the engine works hard to climb a hill. But when going down an incline, the driver often lets up on the accelerator since

more gas isn't needed - the genes shut down. The two genes are expressed - essentially keeping algae's foot on the gas - even when they are in a carbon dioxide-rich environment and don't need additional carbon dioxide.

Research by Spalding's group shows that algae can be made to produce biomass with the accelerator floored, even in conditions where it would normally just coast, Spalding said. "Based on some prior research we had done, we expected to see an increase, probably in the 10 to 20 percent range" he said. "But we were surprised to see this big of an increase."

In experiments to get the algae type (Chlamydomonas reinhardtii) to produce more biomass, Spalding first expressed LCIA and LCIB separately. Each effort granted a significant 10 to 15 percent increase in biomass. When the two genes were expressed together, Spalding was surprised to see the 50 to 80 percent biomass increase. "Somehow these two genes are working together to increase the amount of carbon dioxide that's converted through photosynthesis into biomass by the algae under conditions where you would expect there would already be enough carbon dioxide," said Spalding.

The excess biomass naturally becomes starch through the photosynthesis process, and increases the biomass starch by around 80 percent. By using some existing mutated genes, Spalding can instruct the algae to make oil instead of starch. This process requires more energy and the process results in around a 50 percent increase in oil biomass.

Spalding's research was funded in part by grants from the Department of Agriculture's National Institute of Food and Agriculture and the Department of Energy, Advanced Research Projects Agency - Energy.

http://www.eurekalert.org/pub_releases/2011-11/uow-ing111611.php

Implanted neurons, grown in the lab, take charge of brain circuitry

Scientists report that neurons, forged in the lab from human embryonic stem cells and implanted into the brains of mice, can successfully fuse with the brain's wiring

MADISON - Among the many hurdles to be cleared before human embryonic stem cells can achieve their therapeutic potential is determining whether or not transplanted cells can functionally integrate into target organs or tissues.

Writing today (Monday, Nov. 21) in the Proceedings of the National Academy of Sciences, a team of Wisconsin scientists reports that neurons, forged in the lab from blank slate human embryonic stem cells and implanted into the brains of mice, can successfully fuse with the brain's wiring and both send and receive signals.

Neurons are specialized, impulse conducting cells that are the most elementary functional unit of the central nervous system. The 100 billion or so neurons in the human brain are constantly sending and receiving the signals that govern everything from walking and talking to thinking. The work represents a crucial step toward deploying customized cells to repair damaged or diseased brains, the most complex human organ.

"The big question was can these cells integrate in a functional way," says Jason P. Weick, the lead author of the new study and a staff scientist at the University of Wisconsin-Madison's Waisman Center. "We show for the first time that these transplanted cells can both listen and talk to surrounding neurons of the adult brain."

The Wisconsin team tested the ability of their lab grown neurons to integrate into the brain's circuitry by transplanting the cells into the adult mouse hippocampus, a well-studied region of the brain that plays a key role in processing memory and spatial navigation. The capacity of the cells to integrate was observed in live tissue taken from the animals that received the cell transplants.

Weick and colleagues also reported that the human neurons adopted the rhythmic firing behavior of many brain cells talking to one another in unison. And, perhaps more importantly, that the human cells could modify the way the neural network behaved.

A critical tool that allowed the UW group to answer this question was a new technology known as optogenetics, where light, instead of electric current, is used to stimulate the activity of the neurons.

"Previously, we've been limited in how efficiently we could stimulate transplanted cells. Now we have a tool that allows us to specifically stimulate only the transplanted human cells, and lots of them at once in a non-invasive way," says Weick.

Weick explains that the capacity to modulate the implanted cells was a necessary step in determining the function of implanted cells because previous technologies were too imprecise and unreliable to accurately determine what transplanted neurons were doing.

Embryonic stem cells, and the closely related induced pluripotent stem cells can give rise to all of the 220 types of tissues in the human body, and have been directed in the lab to become many types of cells, including brain cells.

The appeal of human embryonic stem cells and induced pluripotent cells is the potential to manufacture limitless supplies of healthy, specialized cells to replace diseased or damaged cells. Brain disorders such as Parkinson's disease and amyotrophic lateral sclerosis, more widely known as Lou Gehrig's disease, are conditions that scientists think may be alleviated by using healthy lab grown cells to replace faulty ones. Multiple studies over the past decade have shown that both embryonic stem cells and induced cells can alleviate deficits of these disorders in animal models.

The new study opens the door to the potential for clinicians to deploy light-based stimulation technology to manipulate transplanted tissue and cells. "The marriage between stem cells and optogenetics has the potential to assist in the treatment of a number of debilitating neurodegenerative disorders," notes Su-Chun Zhang, a UW-Madison professor of neuroscience and an author of the new PNAS report. "You can imagine that if the transplanted cells don't behave as they should, you could use this system to modulate them using light."

In addition to Weick and Zhang, the new PNAS report was co-authored by Yan Liu, also of UW-Madison's Waisman Center. The study was funded by the U.S. National Institutes of Health.

http://www.eurekalert.org/pub_releases/2011-11/uotw-neo111811.php

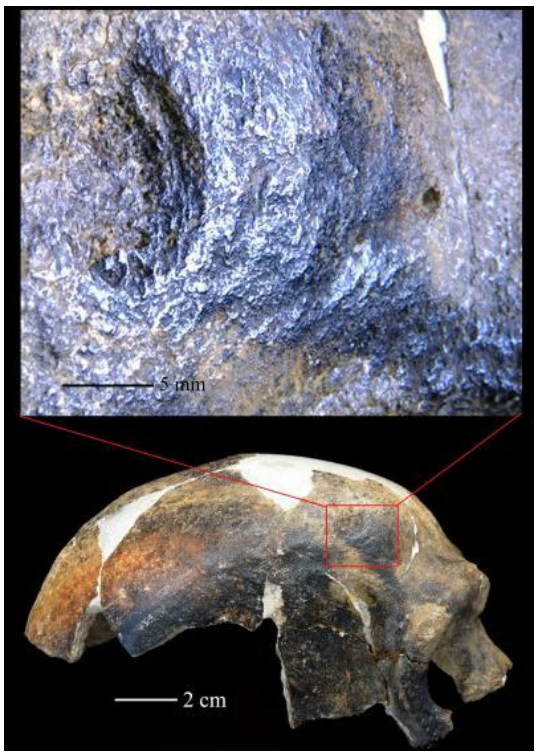
New evidence of interhuman aggression and human induced trauma 126,000 years ago

Maba cranium likely to have been struck forcibly with a blunt object

The study of a cranium of an East Asian human from the late Middle Pleistocene age from Maba, China, brings to the fore evidence that interhuman aggression and human induced trauma occurred 126,000 years ago.

The report, published on Monday, 21 November 2011, in the Proceedings of the National Academy of Sciences of the United States of America suggests that a 14mm ridged, healed lesion with bone depressed inward to the brain resulted from localised blunt force trauma due to an accident or, more probably, interhuman aggression.

"This wound is very similar to what is observed today when someone is struck forcibly with a heavy blunt object. As such it joins a small sample of Ice Age humans with probable evidence of humanly induced trauma, and could possibly be the oldest example of interhuman aggression and human induced trauma documented. Its remodelled, healed condition also indicates the survival of a serious brain injury, a circumstance that is increasingly documented for archaic and modern Homo through the Pleistocene," comments Prof. Lynne Schepartz from the School of Anatomical Sciences at the University of the Witwatersrand, one of the co-authors of the paper.



This is the right superolateral view of the Maba cranium showing the position (A) and detail (B) of the depressed lesion. **University of the Witwatersrand**

"It is not possible to assess whether the incident was accidental or intentional, or whether it resulted from a short-term disagreement, or premeditated aggression." Why is this study important?

"The identification of traumatic lesions in human fossils is of interest for assessing the relative risk of injury to different human groups, the location of trauma, and the behavioural implications," adds Schepartz.

"It also helps us to identify and understand some the earliest forms of interhuman aggression, and the abilities of Pleistocene humans to survive serious injury and post-traumatic disabilities. Maba would have needed social support and help in terms of care and feeding to recover from this wound."

The Maba cranium was discovered with the remains of other mammals in June 1958, in a cave at Lion Rock in Guangdong province, China. The Maba cranium and associated animal bones were unearthed at a depth of 1 metre by farmers removing cave sediments for fertiliser. The Maba cranium, which is housed in the Institute of Vertebrate Paleontology and Paleoanthropology at the Chinese Academy of Sciences, was analysed visually using stereomicroscopy and a high-resolution industrial CT scanner. This state-of-the-art imaging technology enabled the researchers to investigate the inner structure of the bone to verify that healing had occurred.

The co-authors of the paper are Xiu-Jie Wu and Wu Liu from the Institute of Vertebrate Paleontology and Paleoanthropology, Chinese Academy of Sciences, Beijing, China and Erik Trinkaus from the Department of Anthropology, Washington University, St. Louis, USA.

http://www.newscientist.com/article/dn21185-fetus-donates-stem-cells-to-heal-mothers-heart.html

Fetus donates stem cells to heal mother's heart

Mouse fetuses will give up stem cells to repair their mother's heart.

12:13 21 November 2011 by Andy Coghlan

Why wait to be born to develop a healing hand? Mouse fetuses will give up stem cells to repair their mother's heart. The discovery could explain why half the women who develop heart weakness during or just after pregnancy recover spontaneously.

Hina Chaudhry of the Mount Sinai School of Medicine in New York City mated normal female mice with males genetically engineered to produce a green-fluorescing protein in all their body cells. Half the resulting fetuses also produced the protein, making it easy to spot any fetal tissue in the mother.

Chaudhry's team inflicted a heart attack on the pregnant mice and killed them two weeks later to take a look at their hearts. They found some fluorescent cells in the mothers' damaged heart tissue, where they had accelerated repair by changing into new heart cells, including beating cardiomyocytes and blood vessel cells.

Chaudhry says that the phenomenon is an evolutionary mechanism: the fetus promotes its own survival by protecting its mother's heart. Because the cells are easy to obtain from the placenta and unlikely to cause immunological reactions, they could provide a new and potentially limitless source of stem cells for repairing damaged hearts.

"The study is the first to show conclusively that fetal cells contained in the placenta assist in cardiac tissue repair," says Jakub Tolar, director of stem-cell therapies at the University of Minnesota in Minneapolis.

"To date the mainstream stem-cell community has not paid much attention to fetal stem cells in the mother," says Diana Bianchi at Tufts University in Boston. "My hope is that this elegant paper will reawaken interest."

Previous research has identified fetal stem cells in other damaged organs of pregnant women, including the brain, liver, kidney and lung. Fetuses also produce cells that are known to protect the mother against breast cancer. *Journal reference: Circulation Research, DOI: 10.1161/circresaha.111.249037*

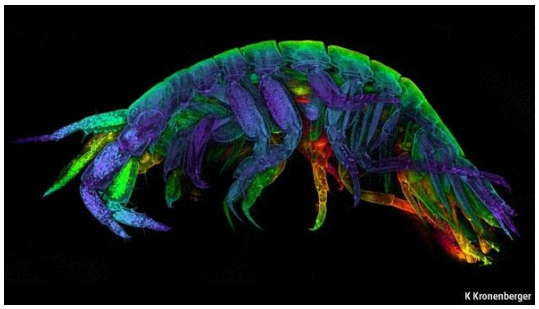
http://www.economist.com/node/21538659

Silk from the sea No sow's ear

A species of crustacean makes silk underwater

SPIDER silk is impressive stuff. Stronger than steel, flexible and exceedingly light. Barnacle glue is equally special. It holds an animal whose ancestors swam freely in the sea to rocks that are often battered by powerful waves. What, then, might a combination of the two achieve?

Fritz Vollrath, of Oxford University, hopes to find out. As he describes in N aturwissenschaften, he and his colleagues have found that a small marine crustacean called Crassicorophium bonellii produces a material which has the adhesive characteristics of barnacle glue and the structural properties of spider-silk fibres. It is water-resistant and flexible, but also somewhat sticky, and is employed by the animals to construct tubular homes in the sediments of the sea bed.



A spinster of rare beauty

Dr Vollrath's examination of Crassicorophium showed that the material is secreted by glands similar to those used by barnacles to make their cement. Given that Crassicorophium and barnacles are both crustaceans, albeit ones whose common ancestor lived 100m years ago, that suggests a single origin for the ability to make this type of goo. Indeed, it might explain the mystery of how barnacles settled down in first place. Possibly, a Crassicorophium-like ancestor used the material to anchor itself to rocks and feed on passing titbits by catching them with its legs, as modern barnacles do. (The protective plates presumably came later.)

To examine the relationship between the newly discovered goo and barnacle glue, Dr Vollrath's colleagues, Katrin Kronenberger and Cedric Dicko, took a look at the chemical composition of both. The proteins of barnacle glue, they discovered, are dominated by amino acids called proline and isoleucine. These like to form cross-links between protein molecules, and thus tend to hold such molecules together. Crassicorophium goo, by contrast, is dominated by lysine, glycine and aspartic acid. These encourage protein molecules to stretch out and form fibres.

In addition, whereas barnacles just ooze out their cement, Crassicorophium processes its material in a spider-like spinning duct. The goo emerges from holes in the crustacean's legs and is spun into gossamer filaments by being stuck to a surface and then pulled out as threads.

This way of spinning silk is remarkably similar to that used by spiders, which pull the material from their bodies using their legs. That similarity, though, is almost certainly the result of convergent evolution rather than a common origin, since the last joint ancestor of Crassicorophium and spiders lived way longer ago than the ancestor of Crassicorophium and barnacles.

Beyond its curiosity value, the discovery of Crassicorophium silk could have practical benefits. There is great interest, in biotechnological circles, in using silk more extensively as an industrial material. Its lightness, flexibility and strength would make it widely deployable. Adding Crassicorophium silk—or, at least, knowledge derived from its analysis—to the mix would extend that range. Dr Vollrath, for example, suggests that Crassicorophium silk's tolerance of salt water means it might find uses in medical applications where it would come into contact with salty bodily fluids. Thus, with luck, can curiosity-driven research of the most esoteric kind lead to good, solid human benefits.

http://www.sciencedaily.com/releases/2011/11/111121104509.htm

Tweaking a Gene Makes Muscles Twice as Strong

New Avenue for Treating Muscle Degeneration in People Who Can't Exercise

ScienceDaily - An international team of scientists has created super-strong, high-endurance mice and worms by suppressing a natural muscle-growth inhibitor, suggesting treatments for age-related or genetics-related muscle degeneration are within reach. The project was a collaboration between researchers at the Salk Institute for Biological Studies, and two Swiss institutions, Ecole Polytechnique Federale de Lausanne (EPFL) and the University of Lausanne.

The scientists found that a tiny inhibitor may be responsible for determining the strength of our muscles. By acting on a genome regulator (NCoR1), they were able to modulate the activity of certain genes, creating a strain of mighty mice whose muscles were twice a strong as those of normal mice.

"There are now ways to develop drugs for people who are unable to exercise due to obesity or other health complications, such as diabetes, immobility and frailty," says Ronald M. Evans, a professor in Salk's Gene Expression Lab, who led the Salk team. "We can now engineer specific gene networks in muscle to give the benefits of exercise to sedentary mice."

Johan Auwerx, the lead author from EPFL, says molecules such as NCoR1 are molecular brakes that decrease the activity of genes. Releasing the brake by mutation or with chemicals can reactivate gene circuits to provide more energy to muscle and enhance its activity.

In an article appearing in the journal Cell, the Salk researchers and their collaborators reported on the results of experiments done in parallel on mice and nematodes. By genetically manipulating the offspring of these species, the researchers were able to suppress NCoR1, which normally acts to inhibit the buildup of muscle tissues. In the absence of the inhibitor, the muscle tissue developed much more effectively. The mice with the mutation became true marathoners, capable of running faster and longer before showing any signs of fatigue. In fact, they were able to cover almost twice the distance run by mice that hadn't received the treatment. They also exhibited better cold tolerance.

Unlike previous experiments that focused on "genetic accelerators" this work shows that suppressing an inhibitor is a new way to build muscle. Examination under a microscope confirmed that the muscle fibers of the modified mice are denser, the muscles are more massive, and the cells in the tissue contain higher numbers of mitochondria - cellular organelles that deliver energy to the muscles. Similar results were also observed in nematode worms, allowing the scientists to conclude that their results could be applicable to a large range of living creatures.

The scientists have not yet detected any harmful side effects associated with eliminating the NCoR1 receptor from muscle and fat tissues. Although the experiments involved genetic manipulations, the researchers are already investigating potential drug molecules that could be used to reduce the receptor's effectiveness.

The researchers say their results are a milestone in our understanding of certain fundamental mechanisms of living organisms, in particular the little-studied role of corepressors - molecules that inhibit the expression of genes. In addition, they give a glimpse at possible long-term therapeutic applications.

"This could be used to combat muscle weakness in the elderly, which leads to falls and contributes to hospitalizations," Auwerx says. "In addition, we think that this could be used as a basis for developing a treatment for genetic muscular dystrophy." He added that if these results are confirmed in humans, there's no question they will attract interest from athletes as well as medical experts.

http://www.sciencenews.org/view/generic/id/336359/title/Coffee_delivers_jolt_deep_in_the_brain

Coffee delivers jolt deep in the brain

Caffeine strengthens electrical signals in rats' hippocampus

By Laura Sanders

Most caffeine addicts would tell you that coffee sharpens the mind. It turns out that in rodents, a single dose of caffeine does indeed strengthen brain cell connections in an underappreciated part of the brain, scientists report online November 20 in Nature Neuroscience. A clearer idea of caffeine's effect on the brain could allow scientists to take advantage of its stimulating effects and perhaps even alleviate some symptoms of brain disorders. "Caffeine is something people are very interested in," says neuroscientist Susan Masino of Trinity College in Hartford, Conn., who was not involved in the study.

So far, most of caffeine's effects have been illuminated by studies using doses much higher than an average person's morning cup of joe, says study coauthor Serena Dudek of the National Institute of Environmental Health Sciences in Research Triangle Park, N.C.

Dudek and her team looked at the effects of smaller hits of caffeine on a small part of the hippocampus. In humans, this seahorse-shaped structure is buried deep in the brain behind the ears. After feeding rats the equivalent of two human cups of coffee (two milligrams of caffeine per kilogram of body weight), the team measured the strength of nerve cells' electrical messages in slices of brain tissue. Nerve cells in this particular nook — a brain region called CA2 - got a major jolt from caffeine, showing a bigger burst of electrical activity when researchers stimulated the cells. Nerve cells in a neighboring part of the hippocampus didn't show this sensitivity.

And the higher the caffeine dose, the stronger the effect. A caffeine dose 10 times higher - a dose reached by only die-hard caffeine consumers - caused an even bigger response in nerve cells in the CA2 region.

The team found similar effects when they applying caffeine directly to CA2 nerve cells in a dish, a result that rules out effects from post-caffeine changes in blood flow. After five minutes of caffeine exposure, the synapses stayed amped up for three hours. "We don't know what it looks like in humans, but in rodents, we think this is the area most sensitive to caffeine," Dudek says.

These strengthened synapses in the hippocampus may have a role in learning and memory, which makes sense because one of the main jobs of the hippocampus is to form spatial memories. (After navigating London's labyrinthine roads for years, for instance, cab drivers have larger hippocampi than normal folks.)

Though the results are the first to establish CA2 as a caffeine hot spot, it's too early to say how the research will apply to people, says psychologist Harris Lieberman of the U.S. Army Research Institute of Environmental Medicine in Natick, Mass. "It's hard to jump from these kinds of studies to direct application to humans."

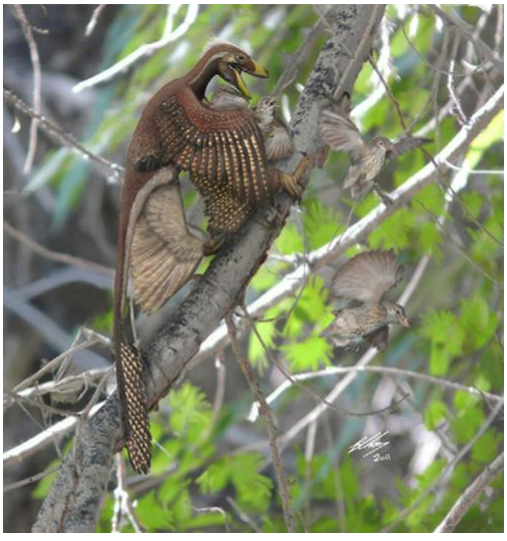
http://www.newscientist.com/article/dn21182-first-evidence-that-dinosaurs-ate-birds.html

First evidence that dinosaurs ate birds

Palaeontologists have found a fossil bird preserved where the stomach of a dinosaur would have been

20:00 21 November 2011 by Freya Boardman-Pretty

The world was a dangerous place for the first birds. Palaeontologists have found a fossil bird preserved where the stomach of a dinosaur would have been – the first direct evidence that dinos preyed on their feathered relatives.



Palaeontologists have long suspected that birds made up part of the predatory dino diet, but proof has been lacking. No longer: Jingmai O'Connor and colleagues at the Chinese Academy of Sciences in Beijing found the near-intact skeleton of a primitive bird nestling suspiciously inside a fossilised predator.

The bird belonged to an extinct group called Enantiornithes and was lying in the ribcage of an early Cretaceous winged theropod called Microraptor gui. They were part of the prehistoric ecosystem known as the Jehol biota, which existed in what is now China and has also yielded numerous spectacular feathered dinosaurs.

The bird skeleton was nearly intact, suggesting it was swallowed whole as live prey rather than scavenged.

(Image: Brian Choo, IVPP)

Not only do the remains provide clues as to how and what the dinosaur ate, but also where it hunted. The bird's feet were adapted for perching, suggesting it lived in trees. Microraptor had four wings, which may have allowed it to glide between trees to hunt prey there, says O'Connor's team.

Luis Chiappe at the Natural History Museum of Los Angeles County says we need to be cautious about reaching that kind of conclusion, however. "The fact that Enantiornithes are largely viewed as arboreal animals doesn't mean that they didn't frequent the ground – like most living arboreal birds, from parrots to woodpeckers," he says.

Journal reference: Proceedings of the National Academy of Sciences, DOI: 10.1073/pnas.1117727108

http://www.newscientist.com/article/dn21194-soft-food-may-lead-to-a-mouth-with-too-many-teeth.html

Soft food may lead to a mouth with too many teeth

Teenagers facing the purgatory of braces to fix their misaligned teeth might be able to blame bread for their predicament.

20:00 21 November 2011 by Bob Holmes

Noreen von Cramon-Taubadel at the University of Kent, UK, measured the shape of 295 human lower jaws from museum specimens. Those that came from agricultural societies were smaller, on average, than those that came from hunter-gatherer societies – although all carried the same number of teeth.

The differences persisted even after she accounted for the effects of climate, geography and random genetic variation. "Our mouths are now slightly too short for the amount of teeth we have," she says.

The likeliest explanation is that agricultural diets, which contain large amounts of ground grains, tend to be softer and easier to chew than the wild plant and meat-rich diets of hunter-gatherers. Indeed, animal experiments have shown that the lower jaw grows more slowly in individuals fed a softer diet (Science, DOI: 10.1126/science.7123221). If the same applies to humans it may explain why dental crowding is so common today, von Cramon-Taubadel speculates.

More work is needed to prove the link, though. "The work demonstrates it is possible for diet to affect facial shape," says Timothy Weaver, a biological anthropologist at the University of California, Davis. That's different from demonstrating that this is what actually happens in humans, he adds.

Journal reference: Proceedings of the National Academy of Sciences, DOI: 10.1073/pnas.1113050108

http://www.eurekalert.org/pub_releases/2011-11/uom-cpl112111.php

Chemistry professor links feces and caffeine

Abnormal levels of caffeine in water indicate human contamination

Researchers led by Prof. Sébastien Sauvé of the University of Montreal's Department of Chemistry have discovered that traces of caffeine are a useful indicator of the contamination of our water by sewers. "E coli bacteria is commonly used to evaluate and regulate the levels of fecal pollution of our water from storm water discharge, but because storm sewers systems collect surface runoff, non-human sources can contribute significantly to the levels that are observed," Sauvé explained. "Our study has determined that there is a strong correlation between the levels of caffeine in water and the level of bacteria, and that chemists can therefore use caffeine levels as an indicator of pollution due to sewerage systems."

The researchers took water samples from streams, brooks and storm sewer outfall pipes that collect storm waters across the Island of Montreal, and analyzed them for caffeine, fecal coliforms, and a third suspected indicator, carbamazepine. Shockingly, all the samples contained various concentrations of these contaminants, which would suggest that contamination is widespread in urban environments. Carbamazepine is an anti-seizure drug which is also increasingly used for various psychiatric treatments, and the researchers thought it might be a useful indicator because it degrades very slowly. However, unlike with caffeine, no correlation was found.

Caffeine degrades within a few weeks to 2-3 months in the environment and is very widely consumed. The presence of caffeine is also a sure indicator of human sewage contamination, as agriculture and industry do not tend to release caffeine into the environment. The team also noted that the data suggest that Montreal's storm water collection system is widely contaminated by domestic sewers. On the other hand, the researchers observed high levels of fecal coliforms but little or no caffeine in some of the samples, which they attribute to urban wildlife. "This data reveals that any water sample containing more than the equivalent of ten cups of coffee diluted in an Olympic-size swimming pool is definitely contaminated with fecal coliforms," Sauvé said. "A caffeine sampling program would be relatively easy to implement and might provide a useful tool to identify sanitary contamination sources and help reduce surface water contamination within an urban watershed."

About this study: *"Fecal coliforms, caffeine and carbamazepine in stormwater collection systems in a large urban area" was published online in Chemosphere on November 8, 2011.*

http://www.eurekalert.org/pub_releases/2011-11/w-pri111811.php

Paracetamol: Repeated ingestion of slightly too much can be fatal - recognize and treat quickly

Repeatedly taking slightly too much paracetamol over time can cause a dangerous overdose that is difficult to spot, but puts the person at danger of dying.

Patients may not come to hospital reporting the overdose, but because they feel unwell. This clinical situation needs to be recognized and treated rapidly because these patients are at even greater danger than people who take single overdoses. These so-called staggered overdoses can occur when people have pain and repeatedly take a little more paracetamol than they should. "They haven't taken the sort of single-moment, one-off massive overdoses taken by people who try to commit suicide, but over time the damage builds up, and the effect can be fatal," says Dr Kenneth Simpson who publishes the findings of a recent research project in the British Journal of Clinical Pharmacology.

The problem is that doctors normally assess how much danger an overdose patient is in when they arrive at hospital by taking a blood sample and finding out how much paracetamol is present. In the case of a single dose overdose, the blood sample gives valuable information, but people with staggered overdoses may have low levels of paracetamol in their blood even though they are at high risk of liver failure and death.

Working in the University of Edinburgh and the Scottish Liver Transplantation Unit, Scotland, Dr Simpson and his team analysed data from 663 patients who had been admitted to the Royal Infirmary of Edinburgh between 1992 and 2008 with paracetamol-induced liver injury. They found that 161 had taken a staggered overdose, usually to relieve a variety of common pains, such as abdominal or muscular pains, headache and toothache.

"On admission, these staggered overdose patients were more likely to have liver and brain problems, require kidney dialysis or help with breathing and were at a greater risk of dying than people who had taken single overdoses," says Simpson. The problem is also worse for people who arrive at hospital more than a day after taking an overdose - they are also at high risk of dying or needing a liver transplant. "Staggered overdoses or patients presenting late after an overdose need to be closely monitored and considered for the paracetamol antidote, N-acetylcysteine, irrespective of the concentration of paracetamol in their blood," says Simpson.

Because measuring the paracetamol in the blood is such a poor assessment of the patient's status in staggered overdoses or delayed presentation, he believes that doctors urgently need to find new ways of assessing whether a patient can be sent home, need medical treatment to counteract the paracetamol, or need to be considered for a liver transplant.

http://www.bbc.co.uk/news/uk-england-leeds-15828266

Julie McCabe in coma after 'hair dye allergic reaction'

A woman from West Yorkshire has been left brain-damaged and in a coma, apparently after suffering a severe reaction while dyeing her hair.

Julie McCabe, 38, from Keighley, is on a life-support machine following the incident at her home on 30 October. Her family believe she collapsed because of an allergic reaction to a chemical widely used in hair dyes.

Her father Keith Miller said she was struggling to breathe and was taken to Airedale General Hospital. Mr Miller, 63, from Shipley, said: "She dyed her hair. She couldn't breathe so we'd rushed her down to the hospital and her heart stopped during that journey. "So they revived her in hospital but the damage had been done by then."

He believes the chemical para-phenylenediamine (PPD) in her hair dye caused his daughter's condition.

'Unlikely to recover' In 2007, an article in the British Medical Journal by St John's Institute of Dermatology in London warned PPD could trigger allergic reactions. However there is not yet any proven link between the chemical in the dye and Mrs McCabe's illness. Doctors believe Mrs McCabe is unlikely to recover.

Mr Miller has instructed a lawyer to highlight the dangers of the chemical.

Lawyer Greg Almond said: "We would encourage people to carry out a test absolutely every time they dye their hair and that's probably the best way to prevent it at the minute. "But we would call on the government to take a much stronger line with this and to introduce either an outright ban on this particular chemical or to force restriction on sale."

L'Oreal 'concerned'

Mr Miller said: "Knowing my daughter she's a strong little character and if anyone can [recover] she can."

Mrs McCabe was using a L'Oreal Preferences hair dye.

Mr Miller said his daughter had dyed her hair regularly for several years and had used the L'Oreal product in the past. He believes she did a skin test before using the dye. In a statement, the cosmetics company said: "L'Oreal was extremely concerned to hear about this serious situation.

"We do not know the details of the case so it would be inappropriate for us to comment further, however we will do everything we can to assist this lady's family and medical team with information they might need to establish what happened."

http://news.discovery.com/tech/batteries-last-week-after-15-minute-charge-111122.html

Batteries Last a Week After 15-Minute Charge

Imagine if your phone's battery could hold a single charge for a week after being plugged in for only 15 mintues.

By Nic Halverson | Tue Nov 22, 2011 10:03 AM ET

According to some engineers at Northwestern University, this is no stretch of the imagination. They've created an electrode for lithium-ion batteries that extends their lasting life by ten times after only charging them for one-tenth of the time it normally takes.

"We have found a way to extend a new lithium-ion battery's charge life by 10 times," wrote Harold H. Kung, in a paper published in the journal Advanced Energy Materials. Kung is professor of chemical and biological engineering at Northwestern's McCormick School of Engineering and Applied Science. "Even after 150 charges, which would be one year or more of operation, the battery is still five times more effective than lithium-ion batteries on the market today."

Lithium-ion batteries in our devices have two major flaws: limited energy capacity and a slower-than-molasis recharge rate. This electrode eliminates these problems. Here's how:

When you're charging your device, lithium ions are being sent back and forth from the ends of the battery - the anode and the cathode. When all the ions make it to the anode, the glass is full, so to speak. Once you start using your device, the ions begin trickling back to the cathode until your battery is dead.

Because the anode can only accommodate one lithium atom for every six carbon atoms, battery charge density is hindered. Scientists have tried replacing the carbon with silicon because it can accomodate more lithium. But silicon expands and retracts during charging, which causes the battery to lose its charge very quickly.

Kung and his colleagues solved this problem by sandwiching the silicon between sheets of graphene, which is a form of carbon. This stabilized the silicon and maximized the amount of lithium ions that could travel between the two sheets. Kung's team also sped up the recharge rate by poking microscopic holes in the graphene sheets. This gave the ions a shorter secondary route to the anode, drastically reducing charge times by 10 times. Expect the technology to hit marketplaces within the next three to five years.

In celebration of our batteries becoming harder, better, faster and stronger, let's all boogie to some Daft Punk, shall we?

http://www.sciencedaily.com/releases/2011/11/111122133326.htm

Blocked Holes Can Enhance Rather Than Stop Light Going Through

A research team has found that placing a metal cap over a small hole in a metal film does not stop the light at all, but rather enhances its transmission.

ScienceDaily - Conventional wisdom would say that blocking a hole would prevent light from going through it, but Princeton University engineers have discovered the opposite to be true. A research team has found that placing a metal cap over a small hole in a metal film does not stop the light at all, but rather enhances its transmission.

In an example of the extraordinary twists of physics that can occur at very small scales, electrical engineer Stephen Chou and colleagues made an array of tiny holes in a thin metal film, then blocked each hole with an opaque metal cap. When they shined light into the holes, they found that as much as 70 percent more light came through when the holes were blocked than when they were open.

"The common wisdom in optics is that if you have a metal film with very small holes and you plug the holes with metal, the light transmission is blocked completely," said Chou, the Joseph Elgin Professor of Engineering. "We were very surprised."

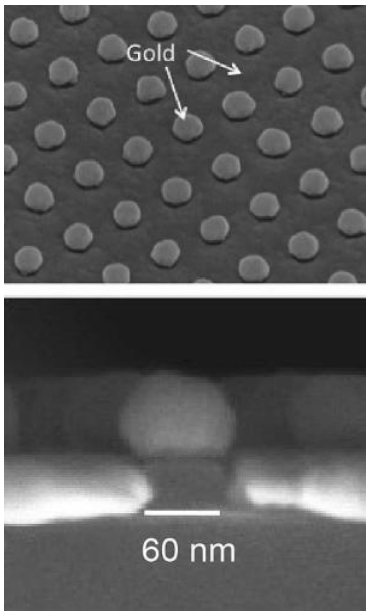
Chou said the result could have significant implications and uses. For one, he said, it might require scientists and engineers to rethink techniques they have been using when they want to block all light transmission. In very sensitive optical instruments, such as microscopes, telescopes, spectrometers and other optical detectors, for example, it is common to coat a metal film onto glass with the intention of blocking light. Dust particles, which are unavoidable in metal film deposition, inevitably create tiny holes in the metal film, but these holes have been assumed to be harmless because the dust particles become capped and surrounded by metal, which is thought to block the light completely.

"This assumption is wrong - the plug may not stop the leakage but rather greatly enhance it," Chou said.

He explained that in his own field of nanotechnology, light is often used in a technique called photolithography to carve ultrasmall patterns in silicon or other materials. Thin metal film patterns on a glass plate serve as a mask, directing light through certain locations of the plate and blocking other locations. Given the new finding, engineers ought to examine whether the mask blocks the light as expected, Chou said.

Conversely, Chou said, the newly discovered "blocking" technique might be used in situations when a boost in light transmission is desired. In near-field microscopy, for example, scientists view extremely fine details by passing light through a hole as tiny as billionths of a meter in diameter. With the new technique, the amount of light passing through the hole - and thus the amount of information about the object being viewed - can be increased by blocking the hole.

Chou and colleagues stumbled on the phenomenon of enhanced light transmission through a blocked hole in their research on developing ultrasensitive detectors that sense minute amounts of chemicals, with uses ranging from medical diagnostics to the detection of explosives. These detectors use a thin metal film with an array of holes and metal disks to boost faint signals produced when laser light encounters a molecule, allowing much greater sensitivity in identifying substances.



These electron microscope images show an experiment demonstrated that blocking a hole in a thin metal film could cause more light to pass through the hole than leaving the hole unblocked. The top image shows an array of holes with gold caps, each of which is 40 percent bigger than the hole on which it sits. The bottom image shows a cross-section view of one hole with the cap sitting on top. The hole covered with the cap allows more light to be transmitted through the film than a hole without the cap. (Credit: Image courtesy of Stephen Chou)

In one of their experimental detectors, the researchers studied transmission of light through an array of tiny holes that were 60 nanometers (billionths of a meter) in diameter and 200 nanometers apart in a gold film that was 40 nanometers thick. Each tiny hole was capped with a gold disk that was 40 percent larger than the hole. The disks sat on top of the holes with a slight gap between the metal surface and the disks.

The researchers pointed a laser at the underside of the film and tested to see if any of the laser light went through the holes, past the caps, and could be detected on the other side. To their surprise, they found that the total light transmission was 70 percent higher with the holes blocked by the metal disks than without blockers. The researchers repeated the same experiment shining the light in the opposite direction - pointing at the side with the caps and looking for transmitted light under the film - and found the same results.

"We did not expect more light to get through," Chou said. "We expected the metal to block the light completely."

Chou said the metal disk acts as a sort of "antenna" that picks up and radiates electromagnetic waves. In this case, the metal disks pick up light from one side of the hole and radiate it to the opposite side. The waves travel along the surface of the metal and leap from the hole to the cap, or vice versa depending on which way the light is traveling. Chou's research group is continuing to investigate the effect and how it could be applied to enhance the performance of ultrasensitive detectors.

The researchers published their findings Oct. 7 in the journal Optics Express, and it quickly became one of the most downloaded papers. In addition to Chou, the team included graduate student Wen-Di Li and postdoctoral researcher Jonathan Hu in the Department of Electrical Engineering. The work is sponsored in part by the Defense Advanced Research Agency and the National Science Foundation.

http://nyti.ms/tgMp1D

In Body's Shield Against Cancer, a Culprit in Aging May Lurk

Until recently, few people gave much thought to senescent cells. They are cells that linger in the body even after they have lost the ability to divide.

By NICHOLAS WADE

But on Nov. 2, in what could be a landmark experiment in the study of aging, researchers at the Mayo Clinic reported that if you purge the body of its senescent cells, the tissues remain youthful and vigorous. The experiment was just in mice, and it cleared the cells with a genetic technique that cannot be applied to people. Like all critical experiments, it needs to be repeated in other labs before it can be accepted with confidence.

But the startling result is plausible because it ties together an emerging body of knowledge about senescent cells. And it raises the possibility that attacks on the cells might postpone the diseases of aging and let people live out more of their life span in good health.

Senescent cells were discovered 50 years ago in a classic experiment by the biologist Leonard Hayflick. He found that human cells cultured in glassware do not multiply indefinitely, as was then assumed, but can divide only 50 or so times before lapsing into senescence. But the finding was not followed up for many years; researchers assumed that it was something that occurred only in the laboratory, or that even if cells did become senescent in the body, there were too few to make a difference.

Only in the last few years have researchers come to realize that senescent cells do occur naturally and that they play central roles in both cancer and aging. Simple organisms live short lives and do not need cell division. More complex animals live longer because their tissues are renewable. In humans, the cells lining the gut are renewed every five days. Red blood cells last 120 days. Even bone cells slowly turn over, with the result that the entire skeleton is renewed every 10 years or so. But the price for renewable tissues is cancer: If cells are capable of division, any damage to their control systems can lead to unconstrained growth. The body has therefore evolved two major systems to curb the risk of cancer - cell senescence and cell death.

Both systems are set in motion by illicit cell divisions, like those caused by a virus; by damage to DNA; or by activation of tumor-causing genes. Senescence can also be caused when cells run out of telomeres, the caps at the end of the chromosomes that get shorter at each cell division. This route to senescence, discovered in the 1990s, underlies the process observed by Dr. Hayflick.

Cells thrown into senescence do not divide again but hang about in tissues until they are cleared by the immune system. In cell death, a cell is forced to set off a built-in suicide mechanism.

Researchers do not yet understand why there are two systems, or how the body chooses whether to assign a damaged cell to senescence or to death. But a benefit of senescence is that suspect cells can continue to perform vital functions, said Daniel Peeper, an expert on senescence at the Netherlands Cancer Institute in Amsterdam. Moles, for instance, are collections of senescent cells that continue to produce melanin and defend the skin from ultraviolet rays.

Senescent cells thus seem to be a benign byproduct of the body's defense against cancer. But researchers have developed growing suspicions of a less benign aspect: the cells' culpability in aging.

Senescent cells accumulate throughout life, probably because the immune system sweeps them away less efficiently as a person ages. Larger and flatter than normal cells, they are especially common in tissues showing signs of aging, like arthritic knees or the plaque in the arteries.

And despite being termed senescent, the cells are very active: They convert themselves into factories that churn out 100 different kinds of growth factors, along with cytokines, the inflammatory agents that stimulate the immune system. The evolutionary reason for this activity may be to provoke the immune system to attack patches of premalignant and malignant cells. But the process turns out to have some untoward side effects.

As it happens, many aging tissues show signs of chronic inflammation, which can foster age-related diseases, including arthritis, Alzheimer's and cancer. The relationship between aging and inflammation has so far been a mystery. "Does aging drive inflammation, or does something else cause chronic inflammation, which in turn drives aging?" Judith Campisi of the Buck Institute for Age Research asked in a review in the journal Cell last year.

The Mayo Clinic researchers, a team led by Jan M. van Deursen and Dr. James L. Kirkland, have come up with a clear and dramatic answer to this question in a mouse study: It's the senescent cells that inflame the tissues and cause them to age.

Senescence is induced in most cells by the activation of two genes, known as p53 and p16-INK4a, that are the guardians and enforcers of proper cell division. When they detect any damage in the cell's controls, they force it into either senescence or death. The role of p16-INK4a is to block the cell from dividing. The Mayo team genetically engineered a strain of mice in which whenever a cell became senescent by switching on its p16-INK4a gene, it also primed a cell suicide device. The Mayo team used a special drug to activate this device and clear the mice of all their senescent cells.

The researchers showed that mice purged of senescent cells could run much longer on a treadmill, had larger fat deposits — fat disappears from the skin as people age, causing wrinkles — and developed cataracts much later. Much the same effect was seen in a second experiment, in which dosing did not start until the mice were middle-aged, except that cataracts that had already formed could not be reversed.

The experiment "strongly suggests that accumulation of senescent cells does contribute to aging, and they show that by eliminating senescent cells they could delay premature aging," Dr. Peeper said.

The finding was made in a strain of mice that age fast and usually die of heart arrhythmia. So despite their healthier tissues, the mice purged of senescent cells died at the usual age of heart problems. Dr. van Deursen's team is now testing to see whether normal mice will live longer when purged of senescent cells.

The treatment was started when the normal mice were a year old, and they have now been treated for five months. Next month they will run treadmill tests to see if they are in better shape than a comparison group of untreated mice, Dr. van Deursen said. The genetic method used to purge mice of senescent cells cannot be used in people. Instead of trying to remove senescent cells from elderly people, Dr. Peeper believes, it may be more effective to identify which of the factors that the senescent cells secrete are the source of their ill effects and to develop drugs that block these factors.

But Dr. van Deursen thinks it would be better to go after the senescent cells themselves. In his view it should be easy enough by trial and error to find chemicals that selectively destroy senescent cells, just like the targeted chemicals now used to treat certain kinds of cancer. And unlike the cancer cells, which proliferate so fast that they soon develop resistance, the senescent cells cannot replicate, so they should be easy targets.

Several companies and individuals have already approached the Mayo Clinic to explore developing such drugs. “They think it’s possible, and they are very enthusiastic,” Dr. van Deursen said. “So I can guarantee that there will be initiatives to find drugs that kill senescent cells and mimic the system that we have developed in the mouse.” Suppose such drugs are developed and retard aging of the tissues in humans just as the mouse experiments suggest can be done. Would people live forever?

The answer is no, Dr. van Deursen says, because many other kinds of damage are incurred by DNA and proteins in cells throughout the body. But the senescent cells make the situation much worse with their inflammatory hormones.

“If you remove the senescent cells you improve things considerably, but you can’t reverse the process or completely stop the aging because it has other causes,” Dr. van Deursen said. “Personally I think we can slow aging down, and over time we will become more and more successful.

“Aging is a fate that no one can escape, but now we can maybe intervene a bit.”

http://nyti.ms/vMm3qQ

Trauma: To Highlight Benefits of a Clotting Drug, a Cartoon Figure Dies a Messy Death

Dr. Ian Roberts of had his 22-year-old nephew create Tranman, whom he let bleed to death on YouTube to demonstrate the benefits of tranexamic acid, a cheap generic drug that helps blood clot

By DONALD G. McNEIL Jr.

Dr. Ian Roberts of the London School of Hygiene and Tropical Medicine had his 22-year-old nephew create a Claymation cartoon figure, Tranman, whom he ***let bleed to death on YouTube*** to demonstrate the benefits of tranexamic acid, a cheap generic drug that helps blood clot.

Car crashes, farm machinery accidents and acts of violence are major killers of the world’s poor; 90 percent of trauma deaths are in poor or middle-income countries, and they are skyrocketing as car ownership increases.

Last year, a trial led by Dr. Roberts comparing 20,000 trauma patients at hospitals in 40 countries showed that a prompt injection of tranexamic acid could reduce hemorrhage deaths by 30 percent.

The British and American Armies were so impressed that they have just added the drug to their combat injury protocols, Dr. Roberts said in an interview.

But few civilian doctors have noticed. A recent survey of British hospitals cited last week in the medical journal The Lancet showed that only 12 of 412 accident victims likely to benefit had received the drug.

Low-profit generic drugs do not get big advertising budgets, so Dr. Roberts commissioned the cartoon, which he is recording in many languages to reach doctors in China, India, Brazil, Russia and Africa.

Tranman’s cartoonishly messy death “will no doubt appeal to the ‘South Park’ generation,” the Lancet editors said, expressing a hope that the word will spread.

http://medicalxpress.com/news/2011-11-heart-disease-long-term-benefit-statins.html

Heart disease: Long-term study proves benefit of statins

Statins safely reduce the risk of cardiovascular illness even years after treatment is stopped, according to a probe into the popular cholesterol-busters published on Wednesday.

Statins work by blocking a liver enzyme that makes fatty molecules which line arterial walls and boost the danger of heart disease and strokes. With worldwide annual sales of more than 20 billion dollars, the drugs have been dubbed "the aspirin of the 21st century" because of their benefit and wide use.

But lingering questions persist about their long-term safety for the heart, liver and cancer risk. Researchers at the Heart Protection Study Collaborative Group in Oxford looked at 20,536 patients at risk of cardiovascular disease who were randomly allocated 40mg daily of simvastatins or a dummy look-alike over more than five years.

During this period, those who took the statins saw a reduction in "bad" LDL cholesterol and a 23-percent reduction in episodes of vascular ill-health compared to the placebo group.

The monitoring of the volunteers continued for a further six years after the trial ended. The benefits persisted throughout this monitoring period among those volunteers who stopped taking the statins, the investigators found. In addition, there was no emergence of any health hazard among those who had taken, or were continuing to take, the drugs. A large number of cancers (nearly 3,500) developed during this follow-up period, but there was no difference in cancer incidence between the statin and placebo groups.

"The persistence of benefit we observed among participants originally allocated simvastatin during the subsequent six-year post-trial period is remarkable," said one of the investigators, Richard Bulbulia.

"In addition, the reliable evidence of safety, with no excess risk of cancer or other major illnesses during over 11 years follow-up, is very reassuring for doctors who prescribe statins and the increasingly large numbers of patients who take them long-term to reduce their risk of vascular disease."

A previous investigation in November 2010 found that long-term use of statins was less risky than thought for people with non-alcoholic fatty liver disease (NAFLD), a common liver ailment.

http://www.eurekalert.org/pub_releases/2011-11/epfd-fr112311.php

Finger (mal)formation reveals surprise function of desert DNA

Explaining the diversity of leg shapes in the animal kingdom and hereditary defects in finger formation

Scientists from the EPFL and the University of Geneva have discovered a genetic mechanism that defines the shape of our members in which, surprisingly, genes play only a secondary role. The research published in Cell, online the 23rd of November, shows the mechanism is found in a DNA sequence that was thought, incorrectly, to play no role. This long string has seven enhancers which, when combined with one another, modulate the activity of the genes responsible for the formation of the fingers – an important fundamental discovery for the field of genetics. The discovery could notably help better understand anomalies that are transmitted from generation to generation such as welded fingers or extra or abnormally short fingers (Kantaputra syndrome) even if the genes appear perfectly normal.

Turbos on the genome

DNA is composed of only about 2% genes. But it has other types of sequences, such as enhancers that increase the activity of certain genes at key moments. "The discovery we have made is that the group of genes involved in finger growth is modulated by seven enhancers, not just one, and they combine through contact," says Thomas Montavon, lead author of the article and researcher at the EPFL.

When the fingers in the embryo begin to take shape, the string of DNA folds and the enhancers, located on different parts of the string, come into contact. They then bring together various proteins that stimulate the activity of the genes, and the fingers start to grow. If one of these seven enhancers is missing, the fingers will be shorter, or abnormally shaped. When two are missing, the defects are even more pronounced. Without enhancers, the genes work slowly, and generate only the beginnings of fingers.

How does the DNA fold in exactly the right way so that the enhancers will correctly do their job? The recently discovered process remains largely unexplained. "In other tissues, such as the brain, the string of DNA folds differently," says Denis Duboule, director of the study and researcher at both the EPFL and the University of Geneva. "To our knowledge, it is only in the fingers that it adopts this shape."

An explanation for evolutionary diversity

Statistically, the seven enhancers involved in finger growth create seven opportunities for a mutation to occur. The flexibility of this mechanism, with no known equivalent to date, causes not only hereditary malformations, but also the many variations in the hands, legs and other appendages in nature. "Just think of some ungulates, which walk on a single finger, or the ostrich, which has only two, and the human hand, of course" explains Denis Duboule.

Other genetic processes may also function on the basis of a similar principle. This could explain the diversity of the products of evolution, in areas other than the fingers, according to Denis Duboule. "When a mutation occurs on a gene, for instance in cystic fibrosis, it is often binary. This amounts to an 'all or nothing' situation. With the mechanism we have discovered, it is a 'more or less' situation. It is combined, it is modulated."

This research is carried out within the National Center of Competence in Research (NCCR) Frontiers in Genetics. The NCCRs are an initiative of the Swiss government to stimulate research and education in key areas. http://www.frontiers-in-genetics.org

Vidéo (interview with Denis Duboule) : ***http://www.youtube.com/watch?v=jrFG34HPqN8***

http://www.eurekalert.org/pub_releases/2011-11/src-gsc112311.php

Genetic study confirms: First dogs came from East Asia

Researchers at Sweden's KTH Royal Institute of Technology say they have found further proof that the wolf ancestors of today's domesticated dogs can be traced to southern East Asia

Researchers at Sweden's KTH Royal Institute of Technology say they have found further proof that the wolf ancestors of today's domesticated dogs can be traced to southern East Asia - findings that run counter to theories placing the cradle of the canine line in the Middle East.

Dr Peter Savolainen, KTH researcher in evolutionary genetics, says a new study released Nov. 23 confirms that an Asian region south of the Yangtze River was the principal and probably sole region where wolves were domesticated by humans. Data on genetics, morphology and behaviour show clearly that dogs are descended from wolves, but there's never been scientific consensus on where in the world the domestication process began. "Our analysis of Y-chromosomal DNA now confirms that wolves were first domesticated in Asia south of Yangtze River - we call it the ASY region - in southern China or Southeast Asia", Savolainen says.

The Y data supports previous evidence from mitochondrial DNA. "Taken together, the two studies provide very strong evidence that dogs originated in the ASY region", Savolainen says.

Archaeological data and a genetic study recently published in Nature suggest that dogs originate from the Middle East. But Savolainen rejects that view. "Because none of these studies included samples from the ASY region, evidence from ASY has been overlooked," he says.

Peter Savolainen and PhD student Mattias Oskarsson worked with Chinese colleagues to analyse DNA from male dogs around the world. Their study was published in the scientific journal Heredity.

Approximately half of the gene pool was universally shared everywhere in the world, while only the ASY region had the entire range of genetic diversity. "This shows that gene pools in all other regions of the world most probably originate from the ASY region", Savolainen says.

"Our results confirm that Asia south of the Yangtze River was the most important - and probably the only - region for wolf domestication, and that a large number of wolves were domesticated", says Savolainen.

In separate research published recently in Ecology and Evolution, Savolainen, PhD student Arman Ardalan and Iranian and Turkish scientists conducted a comprehensive study of mitochondrial DNA , with a particular focus on the Middle East. Because mitochondrial DNA is inherited only from the mother in most species, it is especially useful in studying evolutionary relationships.

"Since other studies have indicated that wolves were domesticated in the Middle East, we wanted to be sure nothing had been missed. We find no signs whatsoever that dogs originated there", says Savolainen.

In their studies, the researchers also found minor genetic contributions from crossbreeding between dogs and wolves in other geographic regions, including the Middle East. "This subsequent dog/wolf hybridisation contributed only modestly to the dog gene pool", Savolainen explains.

KTH researchers Peter Savolainen, Mattias Oskarsson och Arman Ardalan work at the Science for Life Laboratory (SciLifeLab http://www.scilifelab.se), a collaboration involving KTH Royal Institute of Technology, Stockholm University, Karolinska Institutet and Uppsala University.

http://www.eurekalert.org/pub_releases/2011-11/jhmi-rst112311.php

Researchers surprised to find fatty liver disease poses no excess risk for death

Condition prevalent among those with heart disease and obesity

Non-alcoholic fatty liver disease (NAFLD) is a common condition associated with obesity and heart disease long thought to undermine health and longevity. But a new study by Johns Hopkins researchers suggests the condition does not affect survival. A report on the study was published online last week in BMJ, the British medical journal.

"Physicians have considered fatty liver disease a really worrisome risk factor for cardiovascular disease," says study leader Mariana Lazo, M.D., Ph.D., a postdoctoral fellow at the Johns Hopkins University School of Medicine's Welch Center for Prevention, Epidemiology, and Clinical Research. "Our data analysis shows this doesn't appear to be the case. We were surprised to say the least because we expected to learn by how much non-alcoholic fatty liver disease increased the risk of death and instead found the answer was not at all."

Using health information collected from 11,371 Americans between 1994 and 1998 and followed for up to 18 years as part of the Third National Health and Nutrition Examination Survey (NHANES III), the researchers checked liver enzyme levels and ultrasound tests for evidence of NAFLD, and ultimately looked at death rates associated with NAFLD. The participants ranged in age from 20 to 74 during the data collection years. Because the ultrasounds were originally taken to assess gallbladder health, Lazo and colleagues from Johns Hopkins

looked at each recording to determine the presence of fat in each person's liver. People whose livers are 5 percent fat or more are considered to have NAFLD.

The Johns Hopkins team found no increase in mortality among those with NAFLD, which was identified in approximately 20 percent of the NHANES participants. At the end of the follow-up period, mortality from all causes was 22 percent, or 1,836 individuals. Cardiovascular disease was the cause of death for 716 participants, cancer for 480 and liver disease for 44.

Although the researchers found no increase in deaths, Lazo says further study is needed to determine whether more advanced NAFLD has serious long-term consequences for the liver, a vital organ that turns what we eat and drink into nutrients and filters harmful substances from the blood.

NAFLD, which some researchers have called the nation's next epidemic, is characterized by the liver's inability to break down fats and fatty build up in the organ. Found in roughly one in three Americans, it is most prevalent in those who are obese, and those with diabetes and cardiovascular disease. The spectrum of disease ranges from simple fat build-up to inflammation to the scarring and poor liver function that characterize cirrhosis. Chronic liver disease has long been associated with long-term alcohol consumption, but as the name suggests, NAFLD is found in those who are not heavy drinkers.

"We don't yet know why mortality is not affected or whether there might be some actual protective effect of non-alcoholic fatty liver disease," she says, "but it looks like the liver's ability to accumulate fat may somehow shield the body from the detrimental effects of other health problems such as obesity and diabetes," she says.

There is no treatment for NAFLD, other than lifestyle changes, including weight loss, and only a liver biopsy can determine how serious NAFLD is. Lazo says she hopes new methods are developed that more easily identify more advanced stages of NAFLD, which may not be harmless.

Still, she says, her research suggests that with respect to long-term survival of people with non-alcoholic fatty liver disease, "it may not matter if you have the disease or not."

The research was supported by grants from the National Institute of Diabetes and Digestive Diseases and the American Diabetes Association.

Other Johns Hopkins researchers involved in the study include Ruben Hernaez, M.D., Ph.D.; Susanne Bonekamp, Ph.D.; Ihab R. Kamel, M.D., Ph.D.; Frederick L. Brancati, M.D.; Eliseo Guallar, M.D., M.P.H.; and Jeanne M. Clark, M.D., M.P.H. For more information: http://www.jhsph.edu/welchcenter/

http://bit.ly/vaTTkY

Our ancestors speak out after 3 million years

An unlikely experiment using plastic tubes and puffs of air is helping to recreate the first sounds uttered by our distant ancestors

23 November 2011 by Charles Harvey

Listen to simulations of our ancestors' first sounds

YOU may think humanity's first words are lost in the noise of ancient history, but an unlikely experiment using plastic tubes and puffs of air is helping to recreate the first sounds uttered by our distant ancestors.

Many animals communicate with sounds, but it is the variety of our language that sets us apart. Over millions of years, changes to our vocal organs have allowed us to produce a rich mix of sounds. One such change was the loss of the air sac - a balloon-like organ that helps primates to produce booming noises.

All primates have an air sac except humans, in whom it has shrunk to a vestigial organ. Palaeontologists can date when our ancestors lost the organ, as the tissue attaches to a skeletal feature called the hyoid bulla, which is absent in humans. "Lucy's baby", an Australopithecus afarensis girl who lived 3.3 million years ago, had a hyoid bulla; but by the time Homo heidelbergensis arrived on the scene 600,000 years ago, air sacs were a thing of the past.

To find out how this changed the sounds produced, Bart de Boer of the University of Amsterdam in the Netherlands created artificial vocal tracts from shaped plastic tubes. Air forced down them produced different vowel sounds, and half of the models had an extra chamber to mimic an air sac.

De Boer played the sounds to 22 people and asked them to identify the vowel. If they got it right, they were asked to try again, only this time noise was added to make it harder to identify the sound. If they got it wrong, noise was reduced.

He found that those listening to tubes without air sacs could tolerate much more noise before the vowels became unintelligible.

The air sacs acted like bass drums, resonating at low frequencies, and causing vowel sounds to merge; Lucy's baby would have had a greatly reduced vocabulary. Even simple words - such as "tin" and "ten" - would have sounded the same to her.

Observations of soldiers from the first world war corroborate de Boer's findings. Poison gas enlarged the vestigial air sacs of some soldiers, who are said to have had speech problems that made them hard to comprehend.

De Boer's study provides clear evidence supporting the idea that the need to produce complex sounds to communicate better made air sacs shrink, says Ann MacLarnon of the University of Roehampton in London. More sounds meant more information could be shared, giving those who lacked air sacs a better chance of survival in a dangerous world.

De Boer found that air sacs also interfered with the workings of the vocal cords, making consonants trickier. Only once they had gone could words like "perpetual", requiring rapid changes in sound, be produced. What, then, might our ancestors' first words have been? With air sacs, vowels tend to sound like the "u" in "ugg". But studies suggest it is easier to produce a consonant plus a vowel, and "d" is easier to form with "u". "Drawing it all together, I think it is likely cavemen and cavewomen said 'duh' before they said 'ugg'," says de Boer.

http://bit.ly/taRMMW

'Lethal' radiation doses can be treated with drugs

Mice can survive lethal effects of high radiation doses that are usually fatal when given a double-drug therapy - even when they get the drugs 24 hours after exposure.

19:00 23 November 2011 by Jessica Hamzelou

Because these drugs are known to be safe in people, it could be worth stockpiling them in preparation for a nuclear accident or terrorist attack, say the researchers behind the new study.

High doses of radiation harm the body, partly by damaging rapidly dividing cells, such as those in the intestine. The damage leaves the intestine leaky, allowing harmful bacteria to escape into the bloodstream – consequently antibiotics may be used to treat individuals exposed to radiation.

Eva Guinan and Ofer Levy at Harvard Medical School and their colleagues have identified another approach to treatment involving a protein known as bactericidal/permeability-increasing protein (BPI), which plays a role in the immune response to the harmful bacteria from the intestine.

Guinan and Levy's team studied 48 people who were receiving radiation doses in preparation for a bone marrow transplant. Following radiation exposure, levels of BPI fell to an average of 71 times below normal levels. In 37 of the transplant patients the protein was undetectable. The team say this is probably due to damage to the bone marrow, which leaves it unable to produce enough of the white blood cells that normally encourage BPI production.

Survival boost

The team then used the information in the treatment of mice given a typically lethal dose of radiation. A day after exposure, some mice were given the oral antibiotic fluoroquinolone while some mice were given a combination of fluoroquinolone and injections of BPI. A third group had no treatment at all.

Most of the untreated mice died within 30 days. As expected, the antibiotic boosted the survival rate: around 40 per cent of the mice given the antibiotic were still alive after 30 days – but survival rates jumped to almost 80 per cent in the mice given the combination therapy.

The two drugs are already known to be safe in healthy and sick humans. A radiation treatment based on the two is likely to be practical because both drugs can be stored for long periods of time and the mouse study suggests they would be effective even if administered 24 hours after exposure, says Levy. "Maybe there needs to be a stockpile of BPI in case, God forbid, there was another Fukushima," he says.

Don Jones at the University of Leicester, UK, finds the study "very exciting". "The therapy looks to be very effective at mitigating the effects of total body irradiation," he says.

Journal reference: Science Translational Medicine, DOI: 10.1126/scitranslmed.3003126

http://www.physorg.com/news/2011-11-pluto-hidden-ocean.html

Pluto's hidden ocean

New research has not only concluded an ocean is likely, but also has highlighted features the spacecraft could identify that could help confirm an ocean's existence

November 24, 2011 by Nola Taylor Redd

When NASA's New Horizons cruises by Pluto in 2015, the images it captures could help astronomers determine if an ocean is hiding under the frigid surface, opening the door to new possibilities for liquid water to exist on other bodies in the solar system. New research has not only concluded such an ocean is likely, but also has highlighted features the spacecraft could identify that could help confirm an ocean's existence.

Pluto's outer surface is composed of a thin shell of nitrogen ice, covering a shell of water ice. Planetary scientists Guillaume Robuchon and Francis Nimmo, both of the University of California at Santa Cruz, wanted

to find out whether or not an ocean could exist underneath this icy shell, and what visible signs such an ocean might produce on the surface. The pair modeled the thermal evolution of the dwarf planet and studied the behavior of the shell to see how the surface would be affected by the presence of an ocean below.

Searching the surface

Ironically, the easiest feature to identify would appear if no ocean existed.

As spherical bodies spin, their angular momentum tends to push material towards the equator, forming a bulge. If Pluto boasts a liquid layer, the ice would flow, reducing such a protrusion. Thus, the appearance of a "frozen-in "primordial bulge, left over from when Pluto spun more rapidly, would signify a lack of ocean.

"If the bulge is present, it will be about 6 miles (10 km) high, so it should be readily detectable," Nimmo said.

New Horizons project scientist Hal Weaver agreed on the last point. "New Horizon imaging will measure the shape of Pluto very accurately."

Launched in 2006, the NASA mission should reach Pluto in April of 2015. In addition to determining the contours of Pluto, it will also study the temperature, the atmospheric makeup, and the solar wind around the distant planet. The surface features and composition also will be targets. These surface features could provide hints as to what lies beneath.

As Pluto cooled over its lifetime, the temperature changes resulted in a change in volume, creating surface stresses. Classifying these features should reveal whether or not they overlie an ocean.

Icy water beneath the shell would result in tensional stresses as the ice was stretched, while a solid layer would have meant compressional stresses as the material was squeezed.

Such fractures would likely span the globe, rather than being unique to specific areas.

This is ideal, since New Horizons will not map the entire surface of Pluto. Because of the complications involved in going into orbit, the craft will only fly past the icy dwarf planet. But imaging will begin around three months before its closest approach.

"New Horizons will map the entire sunlit surface of Pluto," Weaver explained, "but only the hemisphere facing the spacecraft near the time of the flyby will be mapped at the highest resolution."

The highest resolution will capture 62 meters per pixel when the craft is within 7,750 miles (12,500 km). However, the more distant images still will be approximately ten times more detailed than those captured by the Hubble Space Telescope.

Ridges and valleys with heights and depths of 260 feet (80 meters) should be distinguishable.

Other potential features include geysers similar to those found on Saturn's moon Enceladus and Neptune's moon Triton.

Water on an icy planet

At an average of forty times the distance from the Sun to the Earth, Pluto seems an unlikely candidate for harboring an ocean, even underground. But the heat that might melt the ice would come from inside.

The main source of energy likely stems from the rocky interior, where isotopes undergo radioactive decay. Among these elements, the researchers found potassium to be key - enough potassium in Pluto's core would result in melted ice above it. And signs look good - the amount of potassium needed would be about a tenth of that found in meteorites from the early solar system.

"I think there is a good chance that Pluto has enough potassium to maintain an ocean," Nimmo said.

An important factor that would influence the formation of an ocean is the viscosity of the ice, or how much it resists flowing. A slushier ice shell would suck the heat from the water beneath it, causing the ocean to freeze, while a more solid, high-viscosity shell would not. According to the models, the planet-wide ocean would have an average depth of approximately 100 miles (165 km), beneath a crust of ice of the same thickness.

The growing habitable zone

Scientists regard water as necessary for life as we know it, so focus tends to fall on the habitable zone around stars, the region where temperatures allow for liquid water to exist on a rocky planet.

But in our solar system, liquid water is already anticipated to exist outside this region. Jupiter's moons Europa, Ganymede, and Callisto may each contain a sea beneath their icy surfaces, and Saturn's moon Titan also shows hints of an underground water ocean.

According to Nimmo, Pluto is unlikely to contain life because the organic nutrients considered necessary were probably leached away years ago. However, if a subsurface ocean exists on the dwarf planet, then other objects in the Kuiper belt are potentially more habitable than previously suspected.

"They almost certainly have oceans too, since some are about the size of Pluto," Nimmo said. Such objects could contain not only liquid water but the necessary ingredients for life that Pluto probably lacks.

Source: Astrobio.net (news : web)

http://medicalxpress.com/news/2011-11-scientist-drug-boosts-memory-syndrome.html

Scientist discovers why drug boosts memory in Down syndrome mice

A University of Colorado School of Medicine researcher who found a drug that improved memory in mice with Down syndrome has unlocked the mystery of how it works.

Medical Xpress - In a new study published in Learning & Memory, Alberto Costa, MD, Ph.D., Associate Professor of Medicine and Neuroscience, and Graduate Assistant Jonah Scott-McKean found the mechanism behind excessive levels of long-term synaptic depression, or LTD, in mice with Down syndrome. LTD makes transmission of messages along the brain's synapses more difficult and is frequently referred to as a mechanism for forgetting.

The study proposes that the excess LTD is likely caused by the overrepresentation of a limited subset of genes contained in the extra chromosome carried by these mouse models of Down syndrome. The investigators also found that when the drug memantine was administered to these mice at doses similar to those used to treat Alzheimer's disease, LTD levels fell significantly. Therefore, Costa and Scott-McKean hypothesize that similar phenomena might also occur in the brains of persons with Down syndrome.

"We found the mechanism by which LTD is exaggerated in a mouse model of Down syndrome," Costa said. "We wanted to see if memantine would normalize the brain function of these mice. We found that the drug brings this important physiological parameter associated to learning and memory ice to near normal levels."

Costa found that this exaggerated LTD in Down syndrome mice does not share the same cellular mechanism as a similar phenomenon seen in a mouse that mimics the human disorder known as fragile X syndrome, which is the second most common form of intellectual disability of genetic origin. Costa had earlier discovered that memantine, currently used to treat patients with Alzheimer's disease, improved memory in mice with Down syndrome but exactly how was unclear. He recently completed the data collection phase of a clinical trial using the drug on about 40 people with Down syndrome. The results have not yet been published.

"This will help us develop rational therapies for different intellectual disabilities. For example, based on these findings, it is probably unlikely that certain compounds that are currently being tested for the treatment of fragile X would work in persons with Down syndrome and, conversely, it is unlikely that a drug like memantine might be of any help in the improvement of cognition of young individuals with fragile X" he said. "It will also help us in the planning of clinical trials and represents another move toward more personalized therapies."

Provided by University of Colorado Denver

http://www.eurekalert.org/pub_releases/2011-11/hms-rtb112311.php

Rebuilding the brain's circuitry

Carefully selected young, healthy neurons can functionally integrate into diseased brain circuitry

David Cameron

BOSTON, MA - Neuron transplants have repaired brain circuitry and substantially normalized function in mice with a brain disorder, an advance indicating that key areas of the mammalian brain are more reparable than was widely believed.

Collaborators from Harvard University, Massachusetts General Hospital, Beth Israel Deaconess Medical Center (BIDMC) and Harvard Medical School (HMS) transplanted normally functioning embryonic neurons at a carefully selected stage of their development into the hypothalamus of mice unable to respond to leptin, a hormone that regulates metabolism and controls body weight. These mutant mice usually become morbidly obese, but the neuron transplants repaired defective brain circuits, enabling them to respond to leptin and thus experience substantially less weight gain.

Repair at the cellular-level of the hypothalamus - a critical and complex region of the brain that regulates phenomena such as hunger, metabolism, body temperature, and basic behaviors such as sex and aggression - indicates the possibility of new therapeutic approaches to even higher level conditions such as spinal cord injury, autism, epilepsy, ALS (Lou Gehrig's disease), Parkinson's disease, and Huntington's disease.

"There are only two areas of the brain that are known to normally undergo ongoing large-scale neuronal replacement during adulthood on a cellular level - so-called 'neurogenesis,' or the birth of new neurons - the olfactory bulb and the subregion of the hippocampus called the dentate gyrus, with emerging evidence of lower level ongoing neurogenesis in the hypothalamus," said Jeffrey Macklis, Harvard University professor of stem cell and regenerative biology and HMS professor of neurology at Massachusetts General Hospital, and one of three corresponding authors on the paper. "The neurons that are added during adulthood in both regions are generally smallish and are thought to act a bit like volume controls over specific signaling. Here we've rewired a high-level system of brain circuitry that does not naturally experience neurogenesis, and this restored substantially normal function."

The two other senior authors on the paper are Jeffrey Flier, dean of Harvard Medical School, and Matthew Anderson, HMS professor of pathology at BIDMC. The findings are to appear Nov. 25 in Science.

In 2005, Jeffrey Flier, then the George C. Reisman professor of medicine at BIDMC, published a landmark study, also in Science, showing that an experimental drug spurred the addition of new neurons in the hypothalamus and offered a potential treatment for obesity. But while the finding was striking, the researchers were unsure whether the new cells functioned like natural neurons.

Macklis's laboratory had for several years developed approaches to successfully transplanting developing neurons into circuitry of the cerebral cortex of mice with neurodegeneration or neuronal injury. In a landmark 2000 Nature study, the researchers demonstrated induction of neurogenesis in the cerebral cortex of adult mice, where it does not normally occur. While these and follow-up experiments appeared to rebuild brain circuitry anatomically, the new neurons' level of function remained uncertain.

To learn more, Flier, an expert in the biology of obesity, teamed up with Macklis, an expert in central nervous system development and repair, and Anderson, an expert in neuronal circuitries and mouse neurological disease models. The groups used a mouse model in which the brain lacks the ability to respond to leptin. Flier and his lab have long studied this hormone, which is mediated by the hypothalamus. Deaf to leptin's signaling, these mice become dangerously overweight.

Prior research had suggested that four main classes of neurons enabled the brain to process leptin signaling. Postdocs Artur Czupryn and Maggie Chen, from Macklis's and Flier's labs, respectively, transplanted and studied the cellular development and integration of progenitor cells and very immature neurons from normal embryos into the hypothalamus of the mutant mice using multiple types of cellular and molecular analysis. To place the transplanted cells in exactly the correct and microscopic region of the recipient hypothalamus, they used a technique called high-resolution ultrasound microscopy, creating what Macklis called a "chimeric hypothalamus" -- like the animals with mixed features from Greek mythology.

Postdoc Yu-Dong Zhou, from Anderson's lab, performed in-depth electrophysiological analysis of the transplanted neurons and their function in the recipient circuitry, taking advantage of the neurons' glowing green from a fluorescent jellyfish protein carried as a marker. These nascent neurons survived the transplantation process and developed structurally, molecularly, and electrophysiologically into the four cardinal types of neurons central to leptin signaling. The new neurons integrated functionally into the circuitry, responding to leptin, insulin, and glucose. Treated mice matured and weighed approximately 30 percent less than their untreated siblings or siblings treated in multiple alternate ways.

The researchers then investigated the precise extent to which these new neurons had become wired into the brain's circuitry using molecular assays, electron microscopy for visualizing the finest details of circuits, and patch-clamp electrophysiology, a technique in which researchers use small electrodes to investigate the characteristics of individual neurons and pairs of neurons in fine detail. Because the new cells were labeled with fluorescent tags, postdocs Czupryn, Zhou, and Chen could easily locate them.

The Zhou and Anderson team found that the newly developed neurons communicated to recipient neurons through normal synaptic contacts, and that the brain, in turn, signaled back. Responding to leptin, insulin and glucose, these neurons had effectively joined the brain's network and rewired the damaged circuitry.

"It's interesting to note that these embryonic neurons were wired in with less precision than one might think," Flier said. "But that didn't seem to matter. In a sense, these neurons are like antennas that were immediately able to pick up the leptin signal. From an energy-balance perspective, I'm struck that a relatively small number of genetically normal neurons can so efficiently repair the circuitry."

"The finding that these embryonic cells are so efficient at integrating with the native neuronal circuitry makes us quite excited about the possibility of applying similar techniques to other neurological and psychiatric diseases of particular interest to our laboratory," said Anderson.

The researchers call their findings a proof of concept for the broader idea that new neurons can integrate specifically to modify complex circuits that are defective in a mammalian brain.

The researchers are interested in further investigating controlled neurogenesis - directing growth of new neurons in the brain from within - the subject of much of Macklis's research as well as Flier's 2005 paper, and a potential route to new therapies. "The next step for us is to ask parallel questions of other parts of the brain and spinal cord, those involved in ALS and with spinal cord injuries," Macklis said. "In these cases, can we rebuild circuitry in the mammalian brain? I suspect that we can."

This study was funded by the National Institutes of Health, the Jane and Lee Seidman Fund for Central Nervous System Research, the Emily and Robert Pearlstein Fund for Nervous System Repair, the Picower Foundation, the National Institute of Neurological Disorders and Stroke, Autism Speaks, and the Nancy Lurie Marks Family Foundation.

Citation: *Science, Vol. 334 (6059), November 25, 2011 "Transplanted Hypothalamic Neurons Restore Leptin Signaling and Ameliorate Obesity in db/db Mice" by Czupryn et al.*

http://bit.ly/rwiZMt

CO2 may not warm the planet as much as thought

The climate may be less sensitive to carbon dioxide than we thought – and temperature rises this century could be smaller than expected.

19:00 24 November 2011 by Michael Marshall

That's the surprise result of a new analysis of the last ice age. However, the finding comes from considering just one climate model, and unless it can be replicated using other models, researchers are dubious that it is genuine.

As more greenhouse gases enter the atmosphere, more heat is trapped and temperatures go up – but by how much? The best estimates say that if the amount of carbon dioxide in the atmosphere doubles, temperatures will rise by 3 °C. This is the "climate sensitivity". But the 3 °C figure is only an estimate. In 2007, the Intergovernmental Panel on Climate Change (IPCC) said the climate sensitivity could be anywhere between 2 and 4.5 °C. That means the temperature rise from a given release of carbon dioxide is still uncertain.

To pin down the sensitivity, Andreas Schmittner of Oregon State University, Corvallis, and colleagues took a close look at the Last Glacial Maximum around 20,000 years ago, when the last ice age was at its height.

Icy cold

They used previously published data to put together a detailed global map of surface temperatures. This showed that the planet was, on average, 2.2 °C cooler than today. We already know from ice cores that greenhouse gas levels in the atmosphere at the time were much lower than they are now.

Schmittner plugged the atmospheric greenhouse gas concentrations that existed during the Last Glacial Maximum into a climate model and tried to recreate the global temperature patterns. He found that he had to assume a relatively small climate sensitivity of 2.4 °C if the model was to give the best fit.

If climate sensitivity really is so low, global warming this century will be at the lower end of the IPCC's estimates. Assuming we keep burning fossil fuels heavily, the IPCC estimates that temperatures will rise about 4 °C by 2100, compared with 1980 to 1999. Schmittner's study suggests the warming would be closer to their minimum estimate for the "heavy burning" scenario, which is 2.4 °C.

Sensitive models

Past climates can help us work out the true climate sensitivity, says Gavin Schmidt of the NASA Goddard Institute of Space Studies in New York City. But he says the results of Schmittner's study aren't strong enough to change his mind about the climate sensitivity. "I don't expect this to impact consensus estimates," he says.

In particular, the model that Schmittner used in his analysis underestimates the cooling in Antarctica and the mid-latitudes. "The model estimate of the cooling during the Last Glacial Maximum is a clear underestimate," Schmidt says. "A different model would give a cooler Last Glacial Maximum, and thus a larger sensitivity."

Schmittner agrees it is too early to draw firm conclusions. Individual climate models all have their own quirks, so he wants to try the experiment with several models to find out if others repeat the result.

Even if the climate sensitivity really is as low as 2.4 °C, Schmittner says that doesn't mean we are safe from climate change. The Last Glacial Maximum was only 2.2 °C cooler than today, yet there were huge ice sheets, plant life was different, and sea levels were 120 metres lower.

"Very small changes in temperature cause huge changes in certain regions," Schmittner says. So even if we get a smaller temperature rise than we expected, the knock-on effects would still be severe.

Journal reference: Science, DOI: 10.1126/science.1203513

http://bit.ly/vds3zS

Deep sea fishing for tuna began 42,000 years ago

Tuna has been on the menu for a lot longer than we thought. Even 42,000 years ago, the deep-sea dweller wasn't safe from fishing tackle according to new finds in southeast Asia.

19:00 24 November 2011 by Wendy Zukerman

We know that open water was no barrier to travel in the Pleistocene - humans must have crossed hundreds of kilometres of ocean to reach Australia by 50,000 years ago. But while humans had already been pulling shellfish out of the shallows for 100,000 years by that point, the first good evidence of fishing with hooks or spears comes much later - around 12,000 years ago.

The new finds blow that record out of the water. Sue O'Connor at the Australian National University in Canberra and colleagues dug through deposits at the Jerimalai shelter in East Timor. They discovered 38,000 fish bones from 23 different taxa, including tuna and parrotfish that are found only in deep water. Radiocarbon dating revealed the earliest bones were 42,000 years old.

Amidst the fishy debris was a broken fish hook fashioned from shell, which the team dated to between 16,000 and 23,000 years. "This is the earliest known example of a fish hook," says O'Connor. Another hook, made around 11,000 years ago, was also found.

Sandra Bowdler at the University of Western Australia in Perth, who was not involved in the study, is convinced that those colonising East Timor 42,000 years ago had "fully formed" fishing skills. "By this time, modern humans are assumed to have the same mental capacities as today," she says.

"There is nothing like this anywhere else in the world," says Ian McNiven of Monash University in Melbourne, who was not a member of O'Connor's team. "Maybe this is the crucible for fishing."

East Timor hosts few large land animals, so early occupants would have needed highly developed fishing skills to survive. "Necessity is the mother of invention," says O'Connor. "Apart from bats and rats, there's nothing to eat here." But that doesn't necessarily mean that fishing began in the region. At the time, sea-levels were around 60 to 70 metres lower than today. Any sites of former human occupation that were located on the Pleistocene shore – rather than in coastal cliffs like the Jerimalai shelter – are now submerged.

Broader patterns of human migration suggest that more evidence of fishing would be found through examining those submerged sites. After leaving Africa around 70,000 years ago, it took modern humans only 20,000 years to skirt around Asia and reach Australia. The journey over land into Europe, although much shorter, took 30,000 years. "Humans appeared to move quite quickly along the coasts," says McNiven. "Developed fishing skills could have kept them moving." *Journal Reference: Science DOI: 10.1126/science.1207703*

http://www.bbc.co.uk/news/science-environment-15876145

New state of matter seen on cheap

Students and enthusiasts attending a recording for BBC Radio 4 have probably seen a new state of matter only recently discovered, an expert says.

By Roland Pease BBC Radio Science Unit

The state of matter is a plasma like those in conventional nuclear fusion tests, but at higher densities. And far from needing hundred-million-pound apparatus, the conditions can be achieved in a simple glass tube containing a routine liquid. The professor behind the demonstration says it can be achieved for a mere £10.

The audience were attending a demonstration lecture by chemist Professor Andrea Sella being recorded at University College London for Spooklights on Radio 4. During the lecture, Professor Sella demonstrated a phenomenon called sonoluminescence - flashes of light created by collapsing bubbles in a fluid. The flashes are extraordinarily faint, but in the darkened auditorium, those attending could see the evanescent sparks quite clearly.

As the name suggests, sonoluminescence is traditionally created by intense sound waves - rapid pressure oscillations - focused into a liquid. In the low-pressure regions of the sound waves, fluid is ripped apart to create tiny bubbles, the source of the light.

Professor Sella's demonstration is far simpler, involving a simple sealed glass tube part filled with phosphoric acid and traces of the inert gas xenon. Then all that's needed is a gentle shaking of the tube. As the acid hits the tube's bottom, there's a distinct metallic clink, as if a heavy ball bearing is striking the glass wall.

Hotter than the Sun

In fact, it's just a water-hammer effect, an impact that shatters the liquid column, creating a trail of bubbles that are clearly visible in daylight. With the lights off, what's seen is a trail of blue sparks - the sonoluminescence.

"When the bubbles collapse," Professor Sella explains, "they generate incredibly high temperatures - 10 thousand degrees. That's twice the temperature of the surface of the Sun."

Seeking more information on what goes on inside that bubble, Professor Sella contacted a world authority on the effect, physicist Seth Putterman of the University of California, Los Angeles (UCLA). And he learned far more than he bargained for.

Professor Putterman has also long been trying to understand the precise source of the light. Judging from its intensity and characteristics, the light demands a source containing billions upon billions of free electrons.

But although ten thousand degrees sounds extreme by human experience, it's nowhere near enough to strip the electrons from the molecules and atoms in the sonoluminescence.

Dense plasma

What Professor Putterman realised earlier this year is that under these peculiar circumstances a kind of electrical cascade can take place. If a few electrons escape the embrace of their home atoms, their field makes it easier for further electrons to escape, and so on until the entire bubble interior has become ionised.

"Not only is it creating a plasma," Professor Putterman explains, "we believe it's an new state of matter because it's an extremely dense plasma - the density is hundreds to ten thousand times the density they achieve inside nuclear fusion experiments."

According to Professor Putterman's experiments, the plasma goes through a phase transition - analogous the melting of ice to water. Which is why he feels justified in describing the plasma as an entirely new state.

He also confirmed that the conditions in Andrea Sella's "plink tube" demonstration are precisely those needed to create this new state. Not that that means nuclear fusion is occurring inside the tubes. Claims of nuclear fusion inside fluid bubbles have been extremely controversial.

Professor Putterman is emphatic: "We have not yet succeeded - no-one has yet succeeded - in generating nuclear fusion inside these bubbles. However, we're looking around for that trick that could boost our parameters by a factor of 10, to get it to the region of fusion."

Professor Sella, meanwhile, is delighted that his simple demonstration should reveal to onlookers a state of matter that has only just been discovered. "I can't wait to tell my nuclear physicist friends, that for a cost of around £10, I'm up in the region that they do for the cost of hundreds of millions of pounds. It's very exciting."

http://www.physorg.com/news/2011-11-debut-chromium-signatures-clocks-great.html

Debut of chromium signatures clocks great oxidation event

Banded ironstone core samples from the Pilbara have aided in dating the first appearance of atmospheric oxygen at 2.48 billion years ago.

UWA Associate Professor Mark Barley says the theory - published in the journal Nature by Prof Barley and his colleagues -- rested on the reliability of the rock samples they used as evidence. Prof Barley is one of a group of geobiologists that date the Great Oxidation Event, when earth's atmospheric oxygen formed, at between 2.48 and 2.32 billion years ago. He says the groups' argument depended on pinpointing the time that chromium - previously bonded in igneous rocks - began to appear in the ocean's waters.

"This was evidence for the most primitive form of aerobic respiring life, aerobic respiring bacteria which oxidise pyrite that released acid that dissolved rocks and soils on land, including chromium, that was then carried to the oceans by the flow of water," Prof Barley says. "The aerobic respiring chemolitho-autorobic bacteria require coexistence with cyanobacteria producing oxygen to do this."

The advent of breathable oxygen had been previously dated at 2.7 billion years BP - at date Prof Barley said comes from unreliable data. He says rocks of that age are often "overprinted" by data from later metamorphic processes. "The banded iron formations have good representation of the geochemistry in the earth's early ocean, but also a lot of [the formations] were later altered," he says. "The later changing of banded iron formations into iron ores happened after the main event of oxidation.

Prof Barley says geobiologists are working towards a better database, for more evidence of when the types of bacteria linked to the rise of oxygen were really functioning. "We got a good group of samples from banded iron formations and analysed the chromium isotopes and other elements because that gives the strongest evidence of oxidation," he says. "If you have a good deep drill hole that's not close to a big iron ore deposit, you have got the appropriate chemistry record."

Dr Barley says he contributed core samples of banded ironstone that he obtained from the Pilbara. "I added some key samples to gaps in the global database," he says.

Dr Barley says this analysis provided no evidence of dissolved chromium in the oceans older than 2.48 billion years, and therefore no evidence of atmospheric oxygen. *Provided by ScienceNetwork Western Australia*

http://bit.ly/vRu5Of

Life began with a planetary mega-organism

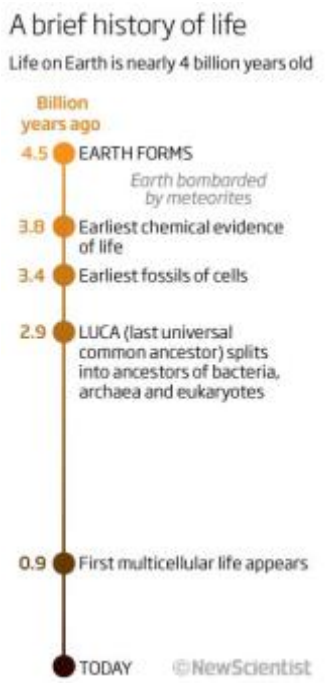
An enormous mega-organism filled the planet's oceans before splitting into three and giving birth to the ancestors of all living things on Earth today

25 November 2011 by Michael Marshall

ONCE upon a time, 3 billion years ago, there lived a single organism called LUCA. It was enormous: a mega-organism like none seen since, it filled the planet's oceans before splitting into three and giving birth to the ancestors of all living things on Earth today. This strange picture is emerging from efforts to pin down the last universal common ancestor - not the first life that emerged on Earth but the life form that gave rise to all others.

The latest results suggest LUCA was the result of early life's fight to survive, attempts at which turned the ocean into a global genetic swap shop for hundreds of millions of years. Cells struggling to survive on their own exchanged useful parts with each other without competition - effectively creating a global mega-organism.

It was around 2.9 billion years ago that LUCA split into the three domains of life: the single-celled bacteria and archaea, and the more complex eukaryotes that gave rise to animals and plants (see timeline). It's hard to know what happened before the split. Hardly any fossil evidence remains from this time, and any genes that date that far back are likely to have mutated beyond recognition.



That isn't an insuperable obstacle to painting LUCA's portrait, says Gustavo Caetano-Anollés of the University of Illinois at Urbana-Champaign. While the sequence of genes changes quickly, the three-dimensional structure of the proteins they code for is more resistant to the test of time. So if all organisms today make a protein with the same overall structure, he says, it's a good bet that the structure was present in LUCA. He calls such structures living fossils, and points out that since the function of a protein is highly dependent on its structure, they could tell us what LUCA could do.

"Structure is known to be conserved when sequences aren't," agrees Anthony Poole of the University of Canterbury in Christchurch, New Zealand, though he cautions that two very similar structures could conceivably have evolved independently after LUCA.

To reconstruct the set of proteins LUCA could make, Caetano-Anollés searched a database of proteins from 420 modern organisms, looking for structures that were common to all. Of the structures he found, just 5 to 11 per cent were universal, meaning they were conserved enough to have originated in LUCA (BMC Evolutionary Biology, DOI: 10.1186/1471-2148-11-140).

By looking at their function, he concludes that LUCA had enzymes to break down and extract energy from nutrients, and some protein-making equipment, but it lacked the enzymes for making and reading DNA molecules. This is in line with unpublished work by Wolfgang Nitschke of the Mediterranean Institute of Microbiology in Marseille, France. He reconstructed the history of enzymes crucial to metabolism and found that LUCA could use both nitrate and carbon as energy sources. Nitschke presented his work at the UCL Symposium on the Origin of Life in London on 11 November.

If LUCA was made of cells it must have had membranes, and Armen Mulkidjanian of the University of Osnabrück in Germany thinks he knows what kind. He traced the history of membrane proteins and concluded that LUCA could only make simple isoprenoid membranes, which were leaky compared with more modern designs (Proceedings of the International Moscow Conference on Computational Molecular Biology, 2011, p 92).

LUCA probably also had an organelle, a cell compartment with a specific function. Organelles were thought to be the preserve of eukaryotes, but in 2003 researchers found an organelle called the acidocalcisome in bacteria. Caetano-Anollés has now found that tiny granules in some archaea are also acidocalcisomes, or at least their precursors. That means acidocalcisomes are found in all three domains of life, and date back to LUCA (Biology Direct, DOI: 10.1186/1745-6150-6-50).

So LUCA had a rich metabolism that used different food sources, and it had internal organelles. So far, so familiar. But its genetics are a different story altogether. For starters, LUCA may not have used DNA. Poole has studied the history of enzymes called ribonucleotide reductases, which create the building blocks of DNA, and found no evidence that LUCA had them (BMC Evolutionary Biology, DOI: 10.1186/1471-2148-10-383). Instead, it may have used RNA: many biologists think RNA came first because it can store information and control chemical reactions (New Scientist, 13 August, p 32).

The crucial point is that LUCA was a "progenote", with poor control over the proteins that it made, says Massimo Di Giulio of the Institute of Genetics and Biophysics in Naples, Italy. Progenotes can make proteins using genes as a template, but the process is so error-prone that the proteins can be quite unlike what the gene specified. Both Di Giulio and Caetano-Anollés have found evidence that systems that make protein synthesis accurate appear long after LUCA. "LUCA was a clumsy guy trying to solve the complexities of living on primitive Earth," says Caetano-Anollés.

He thinks that in order to cope, the early cells must have shared their genes and proteins with each other. New and useful molecules would have been passed from cell to cell without competition, and eventually gone global. Any cells that dropped out of the swap shop were doomed. "It was more important to keep the living system in place than to compete with other systems," says Caetano-Anollés. He says the free exchange and lack of competition mean this living primordial ocean essentially functioned as a single mega-organism.

"There is a solid argument in favour of sharing genes, enzymes and metabolites," says Mulkidjanian. Remnants of this gene-swapping system are seen in communities of microorganisms that can only survive in mixed communities. And LUCA's leaky membranes would have made it easier for cells to share.

"It's a plausible idea," agrees Eric Alm of the Massachusetts Institute of Technology. But he says he "honestly can't tell" if it is true.

Only when some of the cells evolved ways of producing everything they needed could the mega-organism have broken apart. We don't know why this happened, but it appears to have coincided with the appearance of oxygen in the atmosphere, around 2.9 billion years ago. Regardless of the cause, life on Earth was never the same again.

http://www.bbc.co.uk/news/health-15890749

Alzheimer's: Deep brain stimulation 'reverses' disease

Scientists in Canada have raised a tantalising prospect - reversing Alzheimer's disease.

By James Gallagher Health reporter, BBC News

Brain shrinkage, declining function and memory loss had been thought to be irreversible.

They used a technique known as deep brain stimulation - applying electricity directly to regions of the brain. In two patients, the brain's memory hub reversed its expected decline and actually grew.

Deep brain stimulation has been used in tens of thousands of patients with Parkinson's as well as having an emerging role in Tourette's Syndrome and depression.

Yet precisely how it works is still unknown.

The procedure is all done under a local anaesthetic. An MRI scan identifies the target within the brain. The head is held in a fixed position, a small region of the brain is exposed and thin electrodes are positioned next to the region of the brain to be stimulated.

The electrodes are hooked up to a battery which is implanted under the skin next to the collar bone.

Prof John Stein, from the University of Oxford, said: "Most people would say we do not know why this works."

His theory is that in Parkinson's, brain cells become trapped in a pattern of electrical bursts, followed by silences, then bursts and silences and so on. Continuous high frequency stimulation then disrupts the rhythm. However, he accepts that "not everyone will accept this account".

Mystery

How deep brain stimulation could have a role in Alzheimer's is even more of an unknown.

In Alzheimer's, the hippocampus is one of the first regions to shrink. It is the memory hub converting short-term memory to long-term memory. Damage leads to some of the early symptoms of Alzheimer's - memory loss and disorientation.

By late stage Alzheimer's brain cells are dead or dying across the whole of the brain.

The study at the University of Toronto took six patients with the condition. Deep brain stimulation was applied to the fornix - a part of the brain which passes messages onto the hippocampus.

Lead researcher Prof Andres Lozano said you would expect the hippocampus to shrink by five per cent on average in a year in patients with Alzheimer's.

After 12 months of stimulation, he said one patient had a five per cent increase and another had an eight per cent increase.

"How big a deal is 8%? It is huge. We've never seen the hippocampus grow in Alzheimer's under any circumstance. It was an amazing finding for us," he told the BBC.

"This is the first time that brain stimulation in a human being has been shown to grow an area of your brain.

When it came to the symptoms he said: "In one of the patients, he is better after a year's stimulation than when he started, so his Alzheimer's has reversed if you like."

Early days

The findings were presented at the Society for Neuroscience conference in November but they have yet to be published in an academic journal.

Prof Lozano said experiments in animals showed that this kind of stimulation could create new nerve cells.

Prof Stein said he was "very encouraged" by the early findings, but the key would be showing "whether their memory improved". "It is not unexpected that there might be some saviour of the brain which is dying if you can keep it going," he added.

Dr Marie Janson, from Alzheimer's Research UK, said "it would be very significant" if you could reverse brain shrinkage and that "if you could delay the onset of Alzheimer's for five years you would halve the number of people affected."

To test whether this is really working, rather than being a fluke result, the researchers are going to perform a larger trial.

Prof Lozano says that for now: "a word of caution is appropriate, these are very early days and a very small number of patients are involved."

Starting in April they are aiming to enrol around 50 patients with mild Alzheimer's. All will be implanted with electrodes, but they will be turned on in only half of them. The researchers will then see if there is any difference in the hippocampus between the two groups.

They are specifically looking at patients with mild Alzheimer's because of the six patients with the condition, it was only the two with the mildest symptoms that improved.

One theory they are considering is that after a certain level of damage patients reach a point of no return.

http://www.eurekalert.org/pub_releases/2011-11/rson-rcd111611.php

Restricted calorie diet improves heart function in obese patients with diabetes

A low-calorie diet eliminates insulin dependence and leads to improved heart function in obese patients with type 2 diabetes

CHICAGO – A low-calorie diet eliminates insulin dependence and leads to improved heart function in obese patients with type 2 diabetes, according to a study presented today at the annual meeting of the Radiological Society of North America (RSNA).

"Lifestyle interventions may have more powerful beneficial cardiac effects than medication in these patients," said the study's lead author, Sebastiaan Hammer, M.D., Ph.D., from the Department of Radiology at Leiden University Medical Center in the Netherlands. "It is striking to see how a relatively simple intervention of a very low calorie diet effectively cures type 2 diabetes mellitus. Moreover, these effects are long term, illustrating the potential of this method."

Diabetes is a chronic illness in which there are high levels of glucose in the blood. According to the Centers for Disease Control and Prevention (CDC), diabetes affects 25.8 million people in the U.S., with 18.8 million diagnosed cases and an estimated seven million undiagnosed cases. Type 2 is the most common form of diabetes, representing 90 to 95 percent of diagnosed cases among adults.

Pericardial fat is a visceral fat compartment around the heart that can be detrimental to cardiac function, especially in people with metabolic disease. Dr. Hammer and colleagues set out to determine the long-term effects of initial weight loss induced by caloric restriction on pericardial fat and cardiac function in obese patients with type 2 diabetes.

Using cardiac MRI, the researchers analyzed cardiac function and pericardial fat in 15 patients—including seven men and eight women—with type 2 diabetes before and after four months of a diet consisting of 500 calories daily. Changes in body mass index (BMI) were also measured.

The results showed that caloric restriction resulted in a decrease in BMI from 35.3 to 27.5 over four months. Pericardial fat decreased from 39 milliliters (ml) to 31 ml, and E/A ratio, a measure of diastolic heart function, improved from 0.96 to 1.2.

After an additional 14 months of follow-up on a regular diet, BMI increased to 31.7, but pericardial fat only increased slightly to 32 ml. E/A ratio after follow-up was 1.06.

"Our results show that 16 weeks of caloric restriction improved heart function in these patients," Dr. Hammer said. "More importantly, despite regain of weight, these beneficial cardiovascular effects were persistent over the long term."

Dr. Hammer pointed out that these findings stress the importance of including imaging strategies in these types of therapy regimens.

"MRI clearly showed all the changes in fat compartments, structural changes in the heart and improvements in diastolic function, making it a very effective method of quantifying the effects of metabolic interventions," he said.

While these results are promising, not all patients are eligible for this type of therapy. Patients should consult with their doctors before embarking on any type of reduced calorie diet.

"It is of utmost importance to follow such a complicated intervention under strict medical supervision," Dr. Hammer said, "especially as patients may be able to stop all anti-diabetic therapy from Day 1."

Coauthors are Jan W. Smit, M.D., Ph.D., Johannes A. Romijn, M.D., Ph.D., Jacqueline Jonker, M.D., Marieke Snel, M.D., Albert De Roos, M.D., Hildo Lamb, M.D., and Rutger W. Van Der Meer, M.D.

Note: *Copies of RSNA 2011 news releases and electronic images will be available online at RSNA.org/press11 beginning Monday, Nov. 28.*