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Dogs, But Not Wolves, Use Humans As Tools

Between fifteen and thirty thousand years ago, the protracted process of domestication began to alter the genetic code of the wolf, eventually leaving us with the animals we know as domestic dogs.

By Jason G. Goldman | April 30, 2012

Sometime between fifteen and thirty thousand years ago, probably in the Middle East, the long, protracted process of domestication began to alter the genetic code of the wolf, eventually leaving us with the animals we know and love as domestic dogs. While there are several different theories as to exactly how dog domestication began, what is clear is that there were some wolves who were less fearful of humans than others. Over time, those wolves were incorporated into early human settlements. Perhaps humans and early dogs learned to hunt cooperatively – both species hunt primarily by outrunning their prey – or perhaps early dogs instead learned that they could avoid hunting by scavenging on the leftovers of human hunting parties. Whatever the initial reason for the incorporation of wolves into human society, there their descendents still remain.

By sharing an environment with humans, dogs left behind their ancestral environment and found a place in a new one. No longer would they have to hunt to eat; humans would come to provide for their care and feeding. It is probably no accident that the relationship between dogs and their owners mirrors the attachment relationship between parents and their children, behaviorally and physiologically. Indeed, humans who have strong bonds with their dogs have higher levels of oxytocin in their urine than those with weaker bonds.

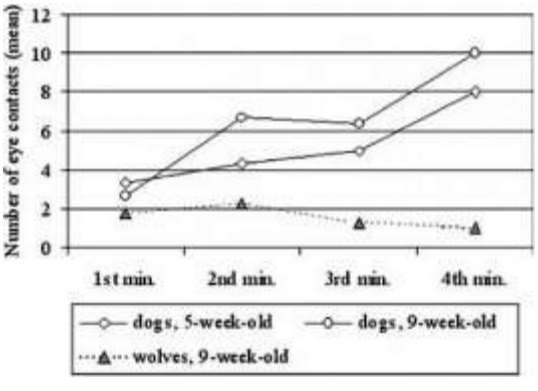
But it isn't only the source of their food that changed as wolves became dogs; their entire social ecology changed. Instead of sharing social space primarily with other wolves, dogs came to treat humans as social partners. This is one of the critical differences between a domesticate and a wild animal that is simply habituated to the presence of humans. Domestication is a genetic process; habituation is an experiential one. Domestication alters nature, habituation is nurture.

Several years ago, scientists at Eotvos University in Budapest wanted to determine whether the social-cognitive differences among dogs and wolves was primarily genetic or experiential. To do this, they hand-raised a group of dog puppies and a group of wolf pups from birth, resulting in roughly equivalent experiences. Any differences between the two groups' social cognitive skills, then, would be attributable to genetics.

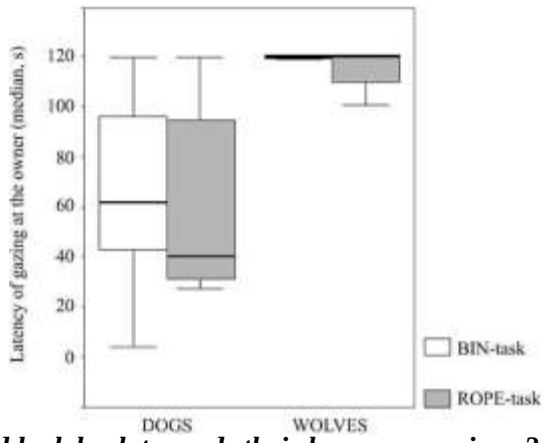
Wolf and dog pups were raised by humans starting four to six days after birth, before their eyes had fully opened. For the first months of their lives, the wolf and dog pups were in close contact with their human foster parents nearly twenty-four hours per day. They lived in the homes of their caregivers and slept with them at night. They were bottle-fed, and starting on the fourth or fifth week of life, hand fed with solid food. Their human caregivers carried them in a pouch so that the wolf pups and dog puppies could participate in as much of their daily activities as possible: traveling on public transportation, attending classes, visiting friends, and so on. Each of the pups had extensive experience meeting unfamiliar humans, and at least twice a week, they were socialized with each other as well as with unfamiliar adult dogs. The guiding principle for the hand-rearing paradigm, according to the researchers, was based not upon competition or aggressive interactions, but "to behave rather like a mother than a dominant conspecific."

Would wolves, having been raised by humans, demonstrate social-cognitive skills that approached the sophistication of dogs? Or is social-cognitive aptitude encoded in dogs' genes, a direct result of domestication?

In one simple task, a plate of food was presented to the wolf pups (at 9 weeks) or to the dog puppies (both at 5 weeks and at 9 weeks). However, the food was inaccessible to the animals; human help would be required to access it. The trick to getting the food was simple: all the animals had to do was make eye contact with the experimenter, and he or she would reward the dog with the food from the plate. Initially, all the animals attempted in vain to reach the food. However, by the second minute of testing, dogs began to look towards the humans. This increased over time and by the fourth minute there was a statistical difference. Dogs were more likely to initiate eye contact with the human experimenter than the wolves were. This is no small feat; initiating eye contact with the experimenter requires that the animal refocus its attention from the food to the human. Not only did the wolf pups not spontaneously initiate eye contact with the human experimenter, but they also failed to learn that eye contact was the key to solving their problem.



A second experiment, conducted when the wolves and puppies were between four and eleven months old, found similar results. Each animal was presented, in different testing sessions, with two different types of tasks. First, each of the wolves and dogs was trained to retrieve a food reward by opening a bin (in one task) or pulling a rope (in the second task). Then, after they had mastered the task, they were presented with an impossible version of the same problem. After attempting to retrieve the food, the dogs looked back towards the human caregivers. The wolves did no such thing. Dogs spontaneously initiated a communicative interaction with the humans earlier, and maintained it for longer periods of time, than did the human-reared wolves, who all but ignored their human caregivers.



How much time passed before the animals would look back towards their human caregivers?

Both dogs and wolves were equally adept at learning the two tasks, indicating that there were no group differences in terms of motivation or physical abilities, but large differences emerged when given impossible problems to solve. In both impossible tasks, as well as in the earlier eye contact experiment, dogs instinctively shifted their attention away from the food and towards the humans. Despite the fact that they had been fully socialized, the wolves treated each of the situations as physical problems rather than social ones. Only rarely did they ever attempt to engage in a communicative problem-solving interaction with a human. It's not that wolves are unintelligent; it's quite the opposite, in fact. Wolves are cooperative hunters, skilled at negotiating within their own social networks. It's just that even after being raised by humans, wolves simply do not see humans as potential social partners. The dogs, however, quite rapidly took a social approach to solving each problem they were given. In one sense, this is a remarkable example of tool use. Only in this case, the humans were the tools, and the dogs the tool-users.

ResearchBlogging.orgGácsi M, Gyori B, Miklósi A, Virányi Z, Kubinyi E, Topál J, & Csányi V (2005). Species-specific differences and similarities in the behavior of hand-raised dog and wolf pups in social situations with humans. Developmental psychobiology, 47 (2), 111-22 PMID: 16136572

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http://www.newscientist.com/blogs/culturelab/2012/04/the-prescience-of-edgar-allen-poe.html?

The medical prescience of Edgar Allan Poe

How Poe was able to describe so precisely the symptoms of what is now known as frontal lobe syndrome is doomed to remain a mystery.

Sara Reardon, San Francisco reporter

The macabre story of Phineas Gage, a US railroad worker who survived when an iron spike penetrated his skull in 1848, is truly stranger than fiction. Gage's impaled head became the darling of a budding medical profession who flocked to study his strange condition: fully functional, though his personality changed. But little did that profession realise that just such a fiction had already been created by the master of the macabre himself, Edgar Allan Poe.

Written eight years prior to Gage's accident, but published posthumously in 1850, Poe's story The Business Man, described a similar case. But how Poe was able to describe so precisely the symptoms of what is now known as frontal lobe syndrome is doomed to remain a mystery. When Eric Altschuler, a neurologist at New Jersey Medical School in Newark realised that the story describes the antisocial personality disorder and obsessions that are common to frontal lobe syndrome, he thought it was possible, although not likely, that the Gage case had inspired it. This conjecture was recently blown out of the water when he and reporter Seth Augustine, who were looking through Poe's stories, realised Poe had written an earlier version in 1840. "It's so exact that it's just weird, it's like he had a time machine," says Altschuler.

Like many of Poe's stories, ***The Business Man*** is told by an unnamed and unreliable narrator. He relates how he came to suffer a head trauma: a childhood nurse "took me up one day by the heels, when I was making more noise than was necessary, and swinging me round two or knocked my head into a cocked hat against the bedpost... a bump arose at once on my sinciput, and turned out to be as pretty an organ of order as one shall see on a summer's day. Hence that positive appetite for system and regularity which has made me the distinguished man of business that I am." That incident defines the man's life; he develops a slavish adherence to exactness and obsession with methods that are characteristic of a modern diagnosis of frontal lobe syndrome. After losing his job over a matter of two pennies, Poe's hero becomes an increasingly violent sociopath, going into the

"Assault and Battery trade" and is eventually thrown into prison. But he never loses his sense of order. "I am a businessman. I am a methodical man. Method is the thing, after all."

"There's a dozen symptoms and he knows every single one," Altschuler says. The only way Poe could have possibly described the disease so exactly, he believes, was if he had a childhood friend who'd been knocked on the head as a child and spent the rest of his life descending into orderly madness.

Poor Phineas Gage probably suffered a similar fate. His personality is described as having changed, although few specifics are known. By the end of his life, he was travelling with a freak show, a far cry from the respected railroad foreman he had been.

Even today, it's hard to describe the symptoms of frontal lobe syndrome, Altschuler says. But incredibly, Poe's narrator was injured as a child and shows symptoms specific to a paediatric case: paediatric frontal lobe syndrome wasn't formally described until 1999. (Nature Neuroscience, DOI:10.1038/14833). "There's everything in that story, We've hardly learned anything more," Altschuler says, putting the comprehensiveness down to Poe's incredible powers of observation.

This isn't the only strange case of Poe's prescient knowledge of modern medicine; his 1845 story, The Facts of the Case of M. Valdemar contains one of the first descriptions of informed consent, long before the concept was used in medicine (The Lancet, DOI:10.1016/S0140-6736(03)14710-1). The narrator of the story is a hypnotist who believes that mesmerism will preserve a dying person on a plane of consciousness and "the encroachments of death might be arrested by the process". He decides to test the technique on a dying patient, but first, interviews his patient to ensure he's willing to have the procedure performed, and has witnesses to confirm it. "It's like Poe's writing something for the internal review board," says Altschuler. (To find out if the procedure is a success, read the chilling story.)

Altschuler says he's still looking for other examples of medical mysteries from Poe. "The weird thing about Poe is that everything about him is a mystery. We've had 120 years to think about it and Poe's life has been researched but we still don't know... why his stories are so bizarre."

Journal reference: *Brain Injury, DOI: 10.3109/02699052.2012.676224*

http://arstechnica.com/science/news/2012/04/saturns-moon-phoebe-may-be-pluto-like.ars

Saturn may have snagged Pluto's cousin, turned it into a moon

Saturn's moon Phoebe might be a planetesimal - a remnant of the rocky building blocks of the planets in our Solar System.

By Matthew Francis | Published 5 days ago

A new study by Julie C. Castillo-Rogez et al. from Cassini spacecraft data indicates that Phoebe dates back to the very earliest days of the Solar System. Based on surface features and evidence that the moon is significantly more dense than the larger Saturnian satellites, the astronomers argue that Phoebe likely formed much farther from the Sun then fell inward, where it was snagged by Saturn's gravity.

Using detailed observations from Cassini and Earth-based telescopes, in combination with detailed computer simulations, Castillo-Rogez et al. determined that Phoebe began as a spherical body. Based upon the density and comparison with bodies of similar size, Phoebe may have a rocky core surrounded by a porous icy shell. The layered structure grants Phoebe kinship with the planets and the planet-like asteroid Vesta, as well as the larger Kuiper Belt objects such as Pluto. Phoebe's physical properties, as well as its odd orbital characteristics, led the authors to conclude that the moon formed in the Kuiper Belt region, making it a cousin to Pluto.

Phoebe's orbit is retrograde, meaning it circles in the opposite direction to Saturn's other moons, as well as the planet's rotation. It's also significantly non-circular. These orbital characteristics are in contrast to the so-called regular satellites: those with orbits the same direction as the planet's rotation and largely circular shape. Regular satellites likely formed along with Saturn, while irregular satellites were captured after formation, according to standard astronomical models.

While Phoebe is obviously not a smooth sphere, it's also not as potato-like as many other moons of similar size. Castillo-Rogez and her collaborators showed that its shape is consistent with an oblate spheroid (meaning squashed at the poles and bulging at the equator, like Earth). Comparing the global shape and surface topology - craters, ridges, and so forth - they concluded that Phoebe began as as a spherical object, but battering by collisions during its early life changed its shape, creating the lumpier body we see today.

Additionally, the researchers modeled the interior, using the moon's density and shape. They determined that Phoebe likely has a differentiated interior, meaning that different materials have formed separate layers. The models suggest that Phoebe has a rocky core surrounded by a shell of water ice.

Many other moons, such as Enceladus have a greater water content in their core, while objects like comets and most asteroids are completely undifferentiated. In this sense, Phoebe more closely resembles planets, Pluto,

and the asteroid Vesta in that regard. An object structured like this also is likely to have formed in the early Solar System, since later bodies should not have become layered. This places Phoebe's formation no later than 3 million years after the beginning of the Solar System.

Based on its higher density and probable interior composition, Phoebe resembles objects in the Kuiper Belt, the region beyond Neptune's orbit where Pluto, Eris, and many comets reside. Its density is 1.63 times that of water, noticeably greater than the average for the inner Saturnian satellites (including Titan, Enceladus, and so forth), which is 1.24 times water's density. Pluto's density, by comparison, is approximately twice that of water.

Phoebe may have started out with Pluto's density, but the heavier bombardment it experienced may have disrupted it, stripping away some material and turning the outer layers into low-density fragments. Similar effects are seen in other bodies, to the extent where some have become piles of rubble held together by gravity; Phoebe occupies a middle ground between rubble piles and larger cratered spherical objects.

Finally, Phoebe's surface composition includes a lot of water ice mixed with carbon compounds, so it somewhat resembles the "dirty snowball" comets. While any of these details by themselves don't indicate a Kuiper Belt origin (for example, the carbon could have been deposited after formation), all together the picture suggests that Phoebe did originate beyond Neptune's orbit. The combination of surface characteristics (composition and cratering), shape, high density and probable differentiation in the interior, and orbital properties argue persuasively that Phoebe is a planetesimal that formed in the Kuiper Belt, more akin to Pluto than to Titan. *Icarus, 2012.* ***DOI: j.icarus.2012.02.002***

http://www.sciencedaily.com/releases/2012/04/120430152037.htm

Darwinian Selection Continues to Influence Human Evolution

New evidence proves humans are continuing to evolve and that significant natural and sexual selection is still taking place in our species in the modern world.

ScienceDaily - Despite advancements in medicine and technology, as well as an increased prevalence of monogamy, research reveals humans are continuing to evolve just like other species.

Scientists in an international collaboration, which includes the University of Sheffield, analysed church records of about 6,000 Finnish people born between 1760-1849 to determine whether the demographic, cultural and technological changes of the agricultural revolution affected natural and sexual selection in our species.

Project leader Dr Virpi Lummaa, of the University's Department of Animal and Plant Sciences, said: "We have shown advances have not challenged the fact that our species is still evolving, just like all the other species 'in the wild'. It is a common misunderstanding that evolution took place a long time ago, and that to understand ourselves we must look back to the hunter-gatherer days of humans."

Dr Lummaa added: "We have shown significant selection has been taking place in very recent populations, and likely still occurs, so humans continue to be affected by both natural and sexual selection. Although the specific pressures, the factors making some individuals able to survive better, or have better success at finding partners and produce more kids, have changed across time and differ in different populations." As for most animal species, the authors found that men and women are not equal concerning Darwinian selection.

Principal investigator Dr Alexandre Courtiol, of the Wissenschftskolleg zu Berlin, added: "Characteristics increasing the mating success of men are likely to evolve faster than those increasing the mating success of women. This is because mating with more partners was shown to increase reproductive success more in men than in women. Surprisingly, however, selection affected wealthy and poor people in the society to the same extent." The experts needed detailed information on large numbers of study subjects to be able to study selection over the entire life cycle of individuals: survival to adulthood, mate access, mating success, and fertility per mate.

Genealogy is very popular in Finland and the country has some of the best available data for such research thanks to detailed church records of births, deaths, marriages and wealth status which were kept for tax purposes. Movement in the country was also very limited until the 20th century. "Studying evolution requires large sample sizes with individual-based data covering the entire lifespan of each born person," said Dr Lummaa. "We need unbiased datasets that report the life events for everyone born. Because natural and sexual selection acts differently on different classes of individuals and across the life cycle, we needed to study selection with respect to these characteristics in order to understand how our species evolves."

The project was funded by the European Research Council and the Kone Foundation (Finland) and was carried out with Wissenschftskolleg zu Berlin and the Leibniz Institute for Zoo and Wildlife Research in Germany, University of Turku in Finland, University of Helsinki in Finland, and the Population Research Institute in Finland.

Alexandre Courtiol, Jenni E. Pettay, Markus Jokela, Anna Rotkirch, and Virpi Lummaa. Natural and sexual selection in a monogamous historical human population. PNAS, April 30, 2012 ***DOI: 10.1073/pnas.1118174109***

http://www.sciencedaily.com/releases/2012/04/120430152033.htm

Bilingualism Fine-Tunes Hearing, Enhances Attention

A new Northwestern University study provides the first biological evidence that bilinguals' rich experience with language "fine-tunes" their auditory nervous system and helps them juggle linguistic input in ways that enhance attention and working memory.

Wendy Leopold

ScienceDaily- Northwestern bilingualism expert Viorica Marian teamed up with auditory neuroscientist Nina Kraus to investigate how bilingualism affects the brain. In particular, they looked at subcortical auditory regions that are bathed with input from cognitive brain areas.

Kraus has already shown that lifelong music training enhances language processing, and looking at subcortical auditory regions helped to tell that tale. "For our joint study, we asked if bilingualism could also promote experience-dependent changes in the fundamental encoding of sound in the brainstem - an evolutionarily ancient part of the brain," said Marian, professor of communication sciences.

The answer is a resounding yes, according to the study in the April 30 issue of Proceedings of the National Academy of Sciences. The researchers found the experience of bilingualism changes how the nervous system responds to sound. "People do crossword puzzles and other activities to keep their minds sharp," Marian said. "But the advantages we've discovered in dual language speakers come automatically simply from knowing and using two languages. It seems that the benefits of bilingualism are particularly powerful and broad, and include attention, inhibition and encoding of sound." Co-authored by Kraus, Marian and researchers Jennifer Krizman, Anthony Shook and Erika Skoe, "Bilingualism and the Brain: Subcortical Indices of Enhanced Executive Function" underscores the pervasive impact of bilingualism on brain development.

"Bilingualism serves as enrichment for the brain and has real consequences when it comes to executive function, specifically attention and working memory," said Kraus, Hugh Knowles Professor at Northwestern's School of Communication. In future studies, she and Marian will investigate whether these advantages can be achieved by learning a language later in life.

In the study, the researchers recorded the brainstem responses to complex sounds (cABR) in 23 bilingual English-and-Spanish-speaking teenagers and 25 English-only-speaking teens as they heard speech sounds in two conditions. Under a quiet condition, the groups responded similarly. But against a backdrop of background noise, the bilingual brains were significantly better at encoding the fundamental frequency of speech sounds known to underlie pitch perception and grouping of auditory objects. This enhancement was linked with advantages in auditory attention.

"Through experience-related tuning of attention, the bilingual auditory system becomes highly efficient in automatically processing sound," Kraus explained. "Bilinguals are natural jugglers," said Marian. "The bilingual juggles linguistic input and, it appears, automatically pays greater attention to relevant versus irrelevant sounds. Rather than promoting linguistic confusion, bilingualism promotes improved 'inhibitory control,' or the ability to pick out relevant speech sounds and ignore others."

The study provides biological evidence for system-wide neural plasticity in auditory experts that facilitates a tight coupling of sensory and cognitive functions. "The bilingual's enhanced experience with sound results in an auditory system that is highly efficient, flexible and focused in its automatic sound processing, especially in challenging or novel listening conditions," Kraus added.

Jennifer Krizman, Viorica Marian, Anthony Shook, Erika Skoe, and Nina Kraus. Subcortical encoding of sound is enhanced in bilinguals and relates to executive function advantages. Proceedings of the National Academy of Sciences, 2012 DOI: 10.1073/pnas.1201575109

http://www.sciencenews.org/view/generic/id/340346/title/California_mad_cow_case_no_reason_for_panic

California mad cow case no reason for panic

Animal did not have foodborne form of disease

By Tina Hesman Saey

When a dairy cow in California was recently diagnosed with a rare form of mad cow disease, agriculture officials said the animal posed no danger to human health. The assurances are more than just platitudes, scientists and a new study in mice suggests.

On April 24, the U.S. Department of Agriculture announced that a 10-year-old dairy cow had been found to have bovine spongiform encephalopathy, or BSE, often called mad cow disease. The cow was the fourth animal ever diagnosed with the disease in the United States. One of those cows, an animal imported from Canada, had

the classical form of the disease caused by eating feed contaminated with infected brain and nervous system material from other cows.

But the new case does not appear to have been caused by contaminated feed. This case proved to be a spontaneous type of BSE. And a new study using mice suggests that it may be harder for this atypical BSE to cause disease in people compared with the more common form of BSE even if people are exposed to it.

All forms of BSE are prion diseases, which result when a normal brain protein called PrP twists into a different shape and then converts other normal copies of the protein into the disease-causing form. Such diseases strike many different animals, including sheep, deer, elk and people. In atypical forms of BSE, the PrP protein probably folds into slightly different shapes compared with the ones caused by eating contaminated feed. Scientists have found two atypical forms, the H-type and the L-type. The California dairy cow had the L-type.

About one in a million people contract the human form of prion disease called Creutzfeldt-Jakob disease. That disease strikes sporadically, meaning that it appears seemingly at random and doctors and scientists don't know why. The human disease that stems from eating beef infected with BSE, known as variant Creutzfeldt-Jakob disease, has been recorded in only 224 cases according to the World Health Organization.

So far, no humans are known to have contracted variant Creutzfeldt-Jakob disease from cattle infected with atypical BSE.

Whereas the classical form of BSE usually strikes cattle between 4 and 8 years old, the atypical form is found in cattle older than 8 years old. No one knows exactly how often the atypical form of the disease appears in cattle, but over a six-year period, French surveillance programs detected 13 cases of atypical BSE in 3.6 million cattle over 8 years old, says Thierry Baron, a neuroscientist at the French national food safety agency in Lyon.

Baron and his colleagues published a study in the January Emerging Infectious Diseases suggesting that mouse lemurs could contract the L-type of atypical BSE more easily than the classical version of the prion disease. The reason no humans have contracted variant Creutzfeldt-Jakob disease from cattle infected with L-type BSE may simply be a numbers game, he says: The disease occurs far too infrequently for people to get exposed to it.

But it may actually be harder for the L-type prion to corrupt human PrP than it is for the classical form of the prion, Rona Barron, a molecular biologist at the University of Edinburgh and colleagues, including Baron, report online April 11 in the Journal of General Virology. The researchers created mice that make the human version of PrP in their brains at normal levels. Atypical BSE, chronic wasting disease (a prion disease in deer and elk) and atypical forms of scrapie (a sheep prion disease) all failed to cause disease in the mice.

Her study is hardly the last word on the infectious potential of atypical BSE, Barron says. Other substances in the brain may have a hand in determining whether PrP will go rogue. Regardless of how infectious the atypical prion is, worldwide surveillance efforts and bans on including the brain and nervous system of cattle in food and feed are doing a good job of keeping all prions out of the food supply, she says. "I don't think there is a cause for mass hysteria."

http://www.eurekalert.org/pub_releases/2012-05/dumc-laf042612.php

Large-scale analysis finds majority of clinical trials don't provide meaningful evidence

The largest comprehensive analysis of ClinicalTrials.gov finds that clinical trials are falling short of producing high-quality evidence needed to guide medical decision-making.

DURHAM, N.C.- The analysis, published today in JAMA, found the majority of clinical trials is small, and there are significant differences among methodical approaches, including randomizing, blinding and the use of data monitoring committees.

"Our analysis raises questions about the best methods for generating evidence, as well as the capacity of the clinical trials enterprise to supply sufficient amounts of high quality evidence to ensure confidence in guideline recommendations," said Robert Califf, M.D., first author of the paper, vice chancellor for clinical research at Duke University Medical Center, and director of the Duke Translational Medicine Institute.

The analysis was conducted by the Clinical Trials Transformation Initiative (CTTI), a public private partnership founded by the Food and Drug Administration (FDA) and Duke. It extends the usability of the data in ClinicalTrials.gov for research by placing the data through September 27, 2010 into a database structured to facilitate aggregate analysis. This publically accessible database facilitates the assessment of the clinical trials enterprise in a more comprehensive manner than ever before and enables the identification of trends by study type.

The National Library of Medicine (NLM), a part of the National Institutes of Health, developed and manages ClinicalTrials.gov. This site maintains a registry of past, current, and planned clinical research studies.

"Since 2007, the Food and Drug Administration Amendment Act has required registration of clinical trials, and the expanded scope and rigor of trial registration policies internationally is producing more complete data from around the world," stated Deborah Zarin, MD, director, ClinicalTrials.gov, and assistant director for clinical research projects, NLM. "We have amassed over 120,000 registered clinical trials. This rich repository of data has a lot to say about the national and international research portfolio."

This CTTI project was a collaborative effort by informaticians, statisticians and project managers from NLM, FDA and Duke. CTTI comprises more than 60 member organizations with the goal of identifying practices that will improve the quality and efficiency of clinical trials.

"Since the ClinicalTrials.gov registry contains studies sponsored by multiple entities, including government, industry, foundations and universities, CTTI leaders recognized that it might be a valuable source for benchmarking the state of the clinical trials enterprise," stated Judith Kramer, MD, executive director of CTTI.

The project goal was to produce an easily accessible database incorporating advances in informatics to permit a detailed characterization of the body of clinical research and facilitate analysis of groups of studies by therapeutic areas, by type of sponsor, by number of participants and by many other parameters.

"Analysis of the entire portfolio will enable the many entities in the clinical trials enterprise to examine their practices in comparison with others," says Califf. "For example, 96% of clinical trials have ≤1000 participants, and 62% have ≤ 100. While there are many excellent small clinical trials, these studies will not be able to inform patients, doctors and consumers about the choices they must make to prevent and treat disease."

The analysis showed heterogeneity in median trial size, with cardiovascular trials tending to be twice as large as those in oncology and trials in mental health falling in the middle. It also showed major differences in the use of randomization, blinding, and data monitoring committees, critical issues often used to judge the quality of evidence for medical decisions in clinical practice guidelines and systematic overviews.

"These results reinforce the importance of exploration, analysis and inspection of our clinical trials enterprise," said Rachel Behrman Sherman, MD, associate director for the Office of Medical Policy at the FDA's Center for Drug Evaluation and Research. "Generation of this evidence will contribute to our understanding of the number of studies in different phases of research, the therapeutic areas, and ways we can improve data collection about clinical trials, eventually improving the quality of clinical trials."

An analysis-ready copy of the ClinicalTrials.gov database is now available at www.ctti-clinicaltrials.org. Specialists from numerous therapeutic areas are now scrutinizing the contents to better understand how the number and characteristics of clinical trials match the perceived needs of the research communities. This dataset will be useful for academic institutions and also for pharmaceutical and device companies to produce reports showing the completeness of their data entry compared to other institutions. Advocacy groups can chronicle the number and types of trials in their area of interest. Data quality is likely to improve as a function of the accountability fostered by this transparency.

The results of other projects conducted by CTTI can be found on the CTTI web site along with general information about the organization.

http://www.bbc.co.uk/news/health-17905601

Way to spot breast cancer years in advance

A genetic test could help predict breast cancer many years before the disease is diagnosed, experts hope.

By Michelle Roberts Health editor, BBC News website

Ultimately the findings, in the journal Cancer Research, could lead to a simple blood test to screen women, they say. The test looks for how genes are altered by environmental factors like alcohol and hormones - a process known as epigenetics.One in five women is thought to have such a genetic "switch" that doubles breast cancer risk. The scientists from Imperial College London analysed blood samples from 1,380 women of various ages, 640 of whom went on to develop breast cancer. And they found a strong link between breast cancer risk and molecular modification of a single gene called ATM, which is found on white blood cells.

Predicting cancer

They then looked for evidence of what was causing this change. Specifically, they looked for a chemical effect called methylation, which is known to act as a "gene switch". Women showing the highest methylation levels affecting the ATM gene were twice as likely to develop breast cancer compared with those with the lowest levels. In some cases the changes were evident up to 11 years before a breast tumour was diagnosed.

Dr James Flanagan, of Imperial College London, who led the new research, said: "We know that genetic variation contributes to a person's risk of disease. "With this new study we can now also say that epigenetic variation, or differences in how genes are modified, also has a role. "We hope that this research is just the beginning of our understanding about the epigenetic component of breast cancer risk and in the coming years we hope to find many more examples of genes that contribute to a person's risk.

"The challenge will be how to incorporate all of this new information into the computer models that are currently used for individual risk prediction."

It is not yet clear why breast cancer risk might be linked to changes in a white blood cell gene. But the team envisage that a blood test could be used in combination with other information about breast cancer risk, such as family history and the presence of other known breast cancer genes, to help identify those women at greatest risk of developing the disease in the future. These women could then be closely monitored and offered pre-emptive treatment, such as surgery.

Epigenetics
The focus is on targeting cancer-causing errors in the way the body reads DNA code, rather than errors in the genetic code itself
A series of chemical switches determine whether genes are turned on or off, and ultimately what the cell will look like and how it will function
Alterations in this "epigenetic" control can lead to cancer
Environmental factors like hormones can act as triggers for these errors
Scientists are working on new drugs that can regulate gene expression and effectively solve epigenetic problems

Baroness Delyth Morgan of the Breast Cancer Campaign, which funded the work, said: "By piecing together how this happens, we can look at ways of preventing the disease and detecting it earlier to give people the best possible chance of survival."

Laura Bell of Cancer Research UK said: "This study gives us a fascinating glimpse of the future and the promise that the emerging field of epigenetics holds. But it's too early to say exactly how these particular changes might affect our ability to detect who is likely to develop certain types of cancer. "With further studies, scientists will increase our knowledge of how genetic switches like this interplay together to affect breast cancer risk, with the hope that one day this could lead to a blood test that could help predict a woman's chance of getting the disease."

http://www.scientificamerican.com/article.cfm?id=this-is-your-brain-on-drugs

This Is Your Brain on Drugs

To the great surprise of many, psilocybin, a potent psychedelic, reduces brain activity

By Christof Koch | Tuesday, May 15, 2012 | 2

In the 1954 foundational text of the Age of Aquarius, The Doors of Perception, Aldous Huxley describes his encounters with mescaline, a psychoactive substance derived from the peyote cactus and traditionally used by Native Americans for religious purposes. Huxley's experiences include profound changes in the visual world, colors that induce sound, the telescoping of time and space, the loss of the notion of self, and feelings of oneness, peacefulness and bliss more commonly associated with religious visions or an exultant state: "A moment later a clump of Red Hot Pokers, in full bloom, had exploded into my field of vision. So passionately alive that they seemed to be standing on the very brink of utterance, the flowers strained upwards into the blue.... I looked down at the leaves and discovered a cavernous intricacy of the most delicate green lights and shadows, pulsing with undecipherable mystery." Yet remarkably these enhanced percepts are not grounded in larger but in reduced brain activity, as a recent experiment reports. More on that in a moment.

Mescaline, together with psilocybin, another natural psychoactive compound produced by "magic" mushrooms, and lysergic acid diethylamide (LSD or, simply, acid), a potent synthetic psychedelic drug, became widely popular in the 1960s counterculture. The striking similarities between the reports of LSD users and symptoms of acute psychosis led researchers to postulate that serotonin, a chemical-signaling compound or neurotransmitter released by certain groups of neurons in the brain stem, helped to mediate both types of experiences. Indeed, it is now quite certain that the characteristic subjective and behavioral effects of psychedelics are initiated via stimulation of serotonin 2A receptors (known as 5-HT2A) on cortical neurons.

All these hallucinogens were declared controlled drugs in the late 1960s and early 1970s for a variety of medical, political and cultural reasons. Their use moved underground, and research on their psychological, physiological and neuronal effects all but ceased. With the realization of possible therapeutic benefits of psychedelics to reduce anxiety and chronic pain, however, the societal taboos against scientific research on their neurobiology have somewhat relaxed. A number of well-controlled European studies have carefully explored the action of hallucinogens on the brains of normal volunteers [see "Psychedelic Healing?" by David Jay Brown; Scientific American Mind, December 2007/January 2008].

Functional brain-imaging experiments done at the end of the past century using positron-emission tomography (PET) found marked activation in the frontal lobe of volunteers who had taken hallucinogens, in particular in the prefrontal cortex (PFC), anterior cingulate cortex (ACC) and the insula cortex. This was in line with the expectation that the intensification of ordinary experiences and the consciousness-expanding aspects that are so widely associated with psychedelics would be reflected in higher than usual brain activity. Now

comes a study from David Nutt, a psychopharmacologist at Imperial College London, and his colleagues that completely upends this view.

Turn On, Tune In and Drop Out

The British scientists injected either a harmless saltwater concoction (a placebo) or two milligrams of psilocybin directly into the veins of 30 volunteers while they were lying inside a magnetic scanner. As expected, the subjects experienced within a minute or two the effects of the drug. During their short "trip," their brains were scanned with one of two different functional MRI techniques. Both gave consistent but very surprising results.

Brain activity was widely reduced! That is, these mind-altering drugs decreased hemodynamic activity, including blood flow, in selected regions, such as the thalamus, the medial prefrontal cortex (mPFC), the ACC and the posterior cingulate cortex (PCC). Activity in these regions dropped by up to 20 percent, relative to before the injection. Even more striking, the deeper the reduction in activity in the ACC and mPFC, the stronger the subject felt the effects of the hallucinogen. Nowhere did activity show an increase. Furthermore, the communication between the PFC and cortical regions in the back of the brain was also disrupted. The surprise is not that reduction of hemodynamic activity in specific sectors of the brain is unheard of. Nor was the activity completely turned off - that would lead within minutes to permanent damage and brain death.

Hemodynamic activity as registered by fMRI scanners is tightly linked to neuronal activity. A standard reading of Nutt's fMRI data seems to imply that expanding your mind by taking magic mushrooms turns many brain circuits down rather than up. Suddenly, Timothy Leary's famous admonition to hippies to "turn on, tune in and drop out" acquires a whole new meaning.

The ACC and parts of the mPFC inhibit limbic and other structures. Thus, their downregulation, or reduction in response, would allow the content of the limbic systems that process emotion and perhaps sensory cortices to play a relatively more dominant role. It is not that enhanced hemodynamic, or even neuronal, activity by itself gives rise to perception and thought. After all, epileptic seizures are hypersynchronized discharges that engulf the entire cortex in massive rhythmic activity that renders the patient unconscious. It is the pattern of spiking across heterogeneous populations of neurons that carries the specific information, the messages, that are represented in consciousness.

At this point, this is all pure speculation because the detailed biophysical mechanisms and the effects of psilocybin on different neurons remain to be worked out.

Any such remarkable finding needs to be replicated by other groups before it becomes part of textbook knowledge. Moreover, the discrepancy with the earlier PET experiments needs to be explained. Two major differences are the mode of taking the drug (intravenously versus orally) and the time of measurement (immediately versus an hour later).

What is intriguing is that the regions that show the strongest reduction in activity are among the most heavily interconnected in the brain. They act like traffic circles or hubs that link disparate regions. Thus, the brain on psilocybin becomes more disconnected, more fragmented, which might explain some of the dissociative aspects of acid trips. Yet why this state should cause the mind-expanding effects that are the prime reason these drugs are treasured is utterly unclear. The study once again highlights how elusive our knowledge of the mind-brain hinge remains.

http://the-scientist.com/2012/04/19/synthetic-genetic-evolution/

Synthetic Genetic Evolution

Scientists show that manmade nucleic acids can replicate and evolve, ushering in a new era in synthetic biology.

By Ruth Williams | April 19, 2012

Synthetic genetic polymers, broadly referred to as XNAs, can replicate and evolve just like their naturally occurring counterparts, DNA and RNA, according to a new study published today (April 19) in Science. The results of the research have implications not only for the fields of biotechnology and drug design, but also for research into the origins of life - on this planet and beyond.

"It's a breakthrough," said Gerald Joyce of The Scripps Research Institute in La Jolla, California, who was not involved in the study - "a beautiful paper in the realm of synthetic biology."

"It shows that you don't have to stick with the ribose and deoxyribose backbones of RNA and DNA in order to have transmittable, heritable, and evolvable information," added Eric Kool of Stanford University, California, who also did not participate in the research.

Over the years, scientists have created a range of XNAs, in which the ribose or deoxyribose portions of RNA and DNA are replaced with alternative molecules. For example, threose is used to make TNA, and

anhydrohexitol is used to make HNA. These polymers, which do not exist naturally, are generally studied with various biotechnological and therapeutic aims in mind. But some researchers, like Philipp Holliger of the MRC Laboratory of Molecular Biology in Cambridge, UK, think XNAs might also provide insights into the origins of life. They might help to answer questions such as, "why is life based on DNA and RNA, and, if we ever find life beyond earth, is it likely to be based on the same molecule or could there be other possibilities?" Holliger said.

To get at some of these questions, Holliger and his colleagues had to first create enzymes that could replicate XNAs, a necessary first step to evolution. They did this both by randomly mutating and screening existing DNA polymerases for their ability to read XNA, and by an iterative process of selecting polymerase variants with capacities for XNA synthesis. In the end, they had several polymerases that could synthesize six different types of XNA.

To see whether XNAs could evolve, they generated random HNA sequences, then selected for those that could bind to two target molecules. After selection, the HNAs were amplified by the newly designed polymerases and again selected for their ability to bind the targets. Eight rounds of selection later, the HNA sequences were no longer random, as those with a particular target-binding motif became more abundant. Through selection and replication, the HNAs had evolved.

The finding in itself is not surprising, said Kool. "Chemists have been working for 20 years to find new backbones for DNA and the feeling always was that it would be interesting and quite possible that some of them might be replicated one day." It was, nevertheless, impressive, he added. "The hard part was finding the enzymes that could do it. So the big leap ahead for this paper was finding those enzymes."

The new polymerases synthesized XNA through rounds of DNA-to-XNA and XNA-to-DNA synthesis. Generating polymerases that can make XNA direct from XNA will be the next step, Holliger said, but it will be a lot harder "because both strands would be foreign to the polymerase."

Holliger also explained that there was actually a benefit to having a DNA intermediate. "It allowed us to access the whole gamut of technologies that are available for analyzing DNA sequences." Working with XNAs uniquely, he said, "is like being thrown back to the way molecular biology was in the early 1970s, in that we have to develop all our tools afresh."

Holliger's polymerases maybe the first addition to the XNA toolbox but, as more tools are created the potential for XNA biology will grow, said Jack Szostak of Harvard Medical School, who was not involved in the study. "In the longer run, it may be possible to design and build new forms of life that are based on one or more of these non-natural genetic polymers," he said. That said, "I think it's too early to say whether such novel life-forms would have any practical applications," he added.

Regardless of what the future holds, the new polymerases could have applications right away. "We hope to be able to evolve XNA aptamers" - molecules that bind specific targets - "against medically interesting targets," Holliger said. Scientists are already creating DNA and RNA aptamers, but their use in the body is severely hampered by their susceptibility to naturally occurring nucleases that degrade DNA and RNA. "XNAs are not natural and so are not susceptible to nucleases," explained Joyce. "These things are bullet-proof."

Beyond the medical applications of the work, Holliger is finally getting some answers about the basis of life. "The exciting finding of our work is that there really seems to be many possibilities," he said. "There isn't anything Goldilocks about DNA or RNA." Does this mean that life elsewhere in the cosmos is more likely than previously thought? "I would say a cautious yes," said Holliger.

V.B. Pinheiro et al., "Synthetic Genetic Polymers Capable of Heredity and Evolution," Science, 336: 341-44, 2012.

http://www.sciencedaily.com/releases/2012/05/120501134119.htm

Risks of Mixing Drugs and Herbal Supplements: What Doctors and Patients Need to Know

Herbal, dietary, and energy or nutritional supplements may offer specific health benefits, but they can also have harmful and even life-threatening effects when combined with commonly used medications.

ScienceDaily - Clinicians need to be aware of and educate their patients about the potential risks of mixing supplements and therapeutic agents, since their interaction can diminish or increase drug levels. This timely topic is explored in a provocative article in Alternative and Complementary Therapies, published by Mary Ann Liebert, Inc. The article is available free on the Alternative and Complementary Therapies.

"'Natural' does not equal 'safe,'" and the effects and interactions of herbal or dietary supplements and functional foods such as energy drinks or nutritional bars can be difficult to predict, says Catherine Ulbricht, PharmD, co-founder of Natural Standard Research Collaboration and Senior Attending Pharmacist at

Massachusetts General Hospital (Boston, MA). "If something has a therapeutic action in a human body, this substance can also cause a reaction or an interaction."

The risk for interactions is greatest in younger and older people and in individuals with multiple health conditions or who take multiple medications, explains Dr. Ulbricht in the article "What Every Clinician Should Know About Herb–Supplement–Drug Interactions." She describes in detail some of the most common side effects that result from interactions between herbal supplements and therapeutic drugs, and provides guidance to clinicians on how to decrease the risk of harmful interactions in their patients and what resources are available for obtaining accurate information and reporting patient reactions.

Common examples include an increased risk of significant bleeding associated with garlic, ginkgo, ginger, and saw palmetto supplements; decreased blood sugar as a result of chromium, cinnamon, whey protein, and others; hormonal effects of dong quai, black cohosh, kudzu, and saw palmetto; and elevated blood pressure caused by bloodroot, green tea, hawthorn, and maté.

Catherine Ulbricht. What Every Clinician Should Know About Herb–Supplement–Drug Interactions. Alternative and Complementary Therapies, 2012; 18 (2): 67 ***DOI: 10.1089/act.2012.18202***

http://nyti.ms/IQlvra

Simple Device Helps Delay Birth to Lift Babies' Chances of Survival

In wealthy countries, some very premature babies are saved in intensive care units. In poor countries, they often die or develop blindness, retardation, lung problems or cerebral palsy.

By DONALD G. McNEIL Jr.

Now a new study has found that in women at high risk of premature birth, a pessary - a small silicon collar placed around the neck of the cervix (as seen on ultrasound, above) - may delay birth until a newborn has a greater chance of survival.

It also appears affordable, at least in middle-income countries, since pessaries cost less than $50 each and could be made cheaply if demand was greater. Placing one normally requires an ultrasound scan, but ultrasound machines are fairly common in hospitals and clinics in all but the poorest countries.

The study, published in The Lancet last month, was the first randomized trial of pessaries for this purpose.

Various pessary designs have been around for centuries, usually to prevent the uterus from prolapsing into the vagina or causing stress incontinence.

For this trial, doctors at five Spanish hospitals divided in half a group of 385 women, all of whom had cervixes less than an inch long, which put them at high risk for early labor. Only 6 percent of the women who got pessaries give birth prematurely, compared with 27 percent of those who did not get them. Exactly why pessaries delay labor is unclear. In an editorial, The Lancet said the study raises the "novel and exciting possibility" that the load-bearing capacities of pelvic organs are important in pregnancy and starting labor.

http://nyti.ms/IpCzKE

Life in the Sea Found Its Fate in a Paroxysm of Extinction

It may never be as well known as the Cretaceous extinction, the one that killed off the dinosaurs. Yet the much earlier Permian extinction - 252 million years ago - was by far the most catastrophic of the planet's five known paroxysms of species loss.

By ALANNA MITCHELL

No wonder it is called the Great Dying: Scientists calculate that about 95 percent of marine species, and an uncountable but probably comparable percentage of land species, went extinct in a geological heartbeat.

The cause or causes of the Permian extinction remain a mystery. Among the hypotheses are a devastating asteroid strike, as in the Cretaceous extinction; a catastrophic volcanic eruption; and a welling-up of oxygen-depleted water from the depths of the oceans.

Now, painstaking analyses of fossils from the period point to a different way to think about the problem. And at the same time, they are providing startling new clues to the behavior of modern marine life and its future.

In two recent papers, scientists from Stanford and the University of California, Santa Cruz, adopted a cellular approach to what they called the "killing mechanism": not what might have happened to the entire planet, but what happened within the cells of the animals to finish them off.

Their study of nearly 50,000 marine invertebrate fossils in 8,900 collections from the Permian period has allowed them to peer into the inner workings of the ancient creatures, giving them the ability to describe precisely how some died while others lived. "Before, scientists were all over the map," said one of the authors, Matthew E. Clapham, an earth scientist at Santa Cruz. "We thought maybe lots of things were going on."

Dr. Clapham and his co-author, Jonathan L. Payne, a Stanford geochemist, concluded that animals with skeletons or shells made of calcium carbonate, or limestone, were more likely to die than those with skeletons

of other substances. And animals that had few ways of protecting their internal chemistry were more apt to disappear.

Being widely dispersed across the planet was little protection against extinction, and neither was being numerous. The deaths happened throughout the ocean. Nor was there any correlation between extinction and how a creature moved or what it ate.

Instead, the authors concluded, the animals died from a lack of dissolved oxygen in the water, an excess of carbon dioxide, a reduced ability to make shells from calcium carbonate, altered ocean acidity and higher water temperatures. They also concluded that all these stresses happened rapidly and that each one amplified the effects of the others. That led to a wholesale change in the ocean's dominant animals within just 200,000 years, or perhaps much less, Dr. Clapham said.

Among the hardest hit were corals; many types, including the horn-shaped bottom-dwellers known as rugose corals, disappeared altogether. Sea sponges were also devastated, along with the shelled creatures that commanded the Permian reefs and sea. Every single species of the once common trilobites, with their helmetlike front shells, vanished for good.

No major group of marine invertebrates or protists, a group of mainly one-celled microorganisms, went unscathed. Instead, gastropods like snails and bivalves like clams and scallops became the dominant creatures after the Permian. And that shift led directly to the assemblage of life in today's oceans. "Modern marine ecology is shaped by the extinction spasms of the past," Dr. Clapham said.

So what happened 252 million years ago to cause those physiological stresses in marine animals? Additional clues from carbon, calcium and nitrogen isotopes of the period, as well as from organic geochemistry, suggest a "perturbation of the global carbon cycle," the scientists' second paper concluded - a huge infusion of carbon into the atmosphere and the ocean. But neither an asteroid strike nor an upwelling of oxygen-deprived deep-ocean water would explain the selective pattern of death.

Instead, the scientists suspect that the answer lies in the biggest volcanic event of the past 500 million years - the eruptions that formed the Siberian Traps, the stairlike hilly region in northern Russia. The eruptions sent catastrophic amounts of carbon gas into the atmosphere and, ultimately, the oceans; that led to long-term ocean acidification, ocean warming and vast areas of oxygen-poor ocean water.

The surprise to Dr. Clapham was how closely the findings from the Great Dying matched today's trends in ocean chemistry. High concentrations of carbon-based gases in the atmosphere are leading to warming, rapid acidification and low-oxygen dead zones in the oceans.

The idea that changes in ocean chemistry, particularly acidification, could be a factor in a mass extinction is a relatively new idea, said Andrew H. Knoll, a Harvard geologist who wrote a seminal paper in 1996 exploring the consequences of a rapid increase in carbon dioxide in the atmosphere on the physiology of organisms.

"In terms of the overall pattern of change, what we're seeing now and what is predicted in the next two centuries is riding a parallel track to what we think happened in the past," he said.

Dr. Clapham noted that Permian and modern similarities are not exact. The Permian ocean was easier to acidify than today's ocean because it had less deep-water calcium carbonate, which offsets the acid. But he said that corals are the most vulnerable creatures in the modern ocean for the same reason they were during the Permian extinction. They have little ability to govern their internal chemistry and they rely on calcium carbonate to build their reefs.

Chris Langdon, a University of Miami biologist who is a pioneer in ocean acidification research, said corals are undoubtedly in danger across the globe. "Corals, I think, are going to take it on the chin," he said.

In a recent study, Dr. Langdon examined the effects of naturally high acidification on coral reefs in Papua New Guinea. They showed drastic declines in coral cover at acidity levels likely to be present in the ocean by the end of this century, especially among branching corals that shelter fish.

Hans Pörtner, an animal ecophysiologist at the Alfred Wegener Institute in Bremerhaven, Germany, said his work showed that a warmer ocean with less dissolved oxygen and greater acidity had an array of negative physiological effects on modern marine animals. The Permian extinction provides an archive of effects suggesting how modern marine creatures will fare as the carbon load in the atmosphere increases, he said.

Like Dr. Clapham, he cautioned that the trends between the two periods were not exactly comparable. Back in the Permian, the planet had a single supercontinent, Pangea, and ocean currents were different.

And he and Dr. Langdon noted that carbon was being injected into the atmosphere today far faster than during the Permian extinction. As Dr. Knoll put it, "Today, humans turn out to be every bit as good as volcanoes at putting carbon dioxide into the atmosphere."

http://www.sciencedaily.com/releases/2012/05/120501182755.htm

Dopamine Impacts Your Willingness to Work

Slacker or go-getter? Everyone knows that people vary substantially in how hard they are willing to work, but the origin of these individual differences in the brain remained a mystery. Until now.

ScienceDaily - Slacker or go-getter? Everyone knows that people vary substantially in how hard they are willing to work, but the origin of these individual differences in the brain remains a mystery.

Now the veil has been pushed back by a new brain imaging study that has found an individual's willingness to work hard to earn money is strongly influenced by the chemistry in three specific areas of the brain. In addition to shedding new light on how the brain works, the research could have important implications for the treatment of attention-deficit disorder, depression, schizophrenia and other forms of mental illness characterized by decreased motivation.

The study was published May 2 in the Journal of Neuroscience and was performed by a team of Vanderbilt scientists including post-doctoral student Michael Treadway and Professor of Psychology David Zald.

Using a brain mapping technique called positron emission tomography (PETscan), the researchers found that "go-getters" who are willing to work hard for rewards had higher release of the neurotransmitter dopamine in areas of the brain known to play an important role in reward and motivation, the striatum and ventromedial prefrontal cortex. On the other hand, "slackers" who are less willing to work hard for a reward had high dopamine levels in another brain area that plays a role in emotion and risk perception, the anterior insula.

"Past studies in rats have shown that dopamine is crucial for reward motivation," said Treadway, "but this study provides new information about how dopamine determines individual differences in the behavior of human reward-seekers."

The role of dopamine in the anterior insula came as a complete surprise to the researchers. The finding was unexpected because it suggests that more dopamine in the insula is associated with a reduced desire to work, even when it means earning less money. The fact that dopamine can have opposing effects in different parts of the brain complicates the picture regarding the use of psychotropic medications that affect dopamine levels for the treatment of attention-deficit disorder, depression and schizophrenia because it calls into question the general assumption that these dopaminergic drugs have the same effect throughout the brain.

The study was conducted with 25 healthy volunteers (52 percent female) ranging in age from 18 to 29. To determine their willingness to work for a monetary reward, the participants were asked to perform a button-pushing task. First, they were asked to select either an easy or a hard button-pushing task. Easy tasks earned $1 while the reward for hard tasks ranged up to $4. Once they made their selection, they were told they had a high, medium or low probability of getting the reward. Individual tasks lasted for about 30 seconds and participants were asked to perform them repeatedly for about 20 minutes.

"At this point, we don't have any data proving that this 20-minute snippet of behavior corresponds to an individual's long-term achievement," said Zald, "but if it does measure a trait variable such as an individual's willingness to expend effort to obtain long-term goals, it will be extremely valuable."

The research is part of a larger project designed to search for objective measures for depression and other psychological disorders where motivation is reduced. "Right now our diagnoses for these disorders is often fuzzy and based on subjective self-report of symptoms," said Zald. "Imagine how valuable it would be if we had an objective test that could tell whether a patient was suffering from a deficit or abnormality in an underlying neural system. With objective measures we could treat the underlying conditions instead of the symptoms."

Further research is needed to examine whether similar individual differences in dopamine levels help explain the altered motivation seen in forms of mental illness such as depression and addiction. Additional research is under way to examine how medications specifically impact these motivational systems.

Robert Kessler, professor of radiology and radiological sciences, Ronald Cowan, associate professor of psychiatry, Joshua Buckholtz, assistant professor of psychology at Harvard, Neil Woodward, assistant professor of psychology, Rui Li, senior research specialist of radiology and radiological sciences, Sib Ansari, associate of radiology and radiological sciences, Ronald Baldwin, research associate professor of radiology and radiological sciences, and research assistant Ashley Schwartzman also contributed to the study. The National Institute of Drug Abuse funded the research..

*The above story is reprinted from materials provided by Vanderbilt University, via **Newswise**. The original article was written by David Salisbury.*

http://www.scientificamerican.com/podcast/episode.cfm?id=garlic-compound-fights-food-borne-b-12-05-01

Garlic Compound Fights Food-Borne Bacteria

Diallyl sulfide, a compound found in garlic, was much more effective than two standard antibiotics at wiping out bacteria responsible for digestive system infections. Sophie Bushwick reports

It's more bad news for vampires, but good news for the fight against food-borne illness: a compound in garlic is extremely effective at fighting Campylobacter, bacteria that frequently cause intestinal infections. The work is in the Journal of Antimicrobial Chemotherapy. [Xiaonan Lu et al., *"Antimicrobial effect of diallyl sulphide on Campylobacter jejuni biofilms"]*

Campylobacter causes problems in part because its cells produce a slime that holds them together in a biofilm. This biofilm sticks to food and food preparation surfaces, helping contamination spread. And it protects the bacteria from antibiotics.

Researchers tried treating Campylobacter jejuni with two common antibiotics, as well as with diallyl sulfide, the compound derived from garlic. The antibiotics did some damage. But the garlic compound worked faster and was a hundred times as effective. It quickly infiltrated the biofilm, and killed the bacteria, apparently by inhibiting the functions of enzymes.

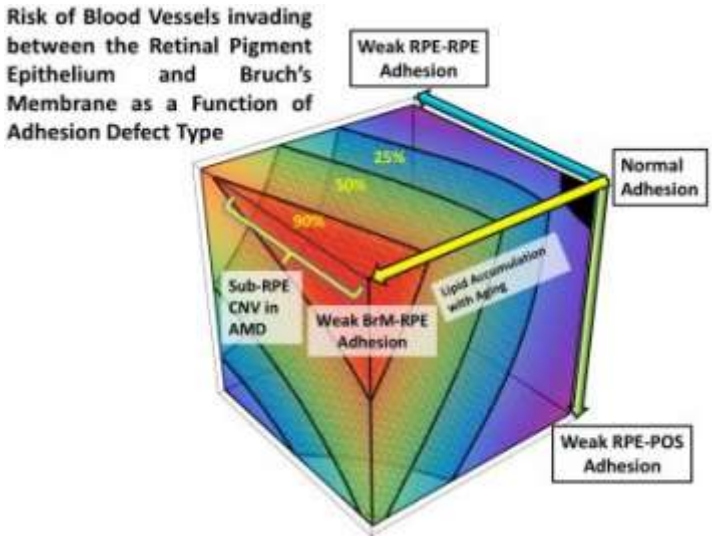
Eating garlic won't slay Campylobacter. But diallyl sulfide could one day be used to clean surfaces used for food preparation, and to stop bacteria from colonizing packaged foods, like salads and deli meats. Which may annoy any vampires getting by on rare roast beef. - ***Sophie Bushwick***

http://www.eurekalert.org/pub_releases/2012-05/iu-sso050312.php

Sloppy shipping of human retina leads IU researchers to discover new treatment path for eye disease

After 9,000 research papers on disease in 10 years, new underlying mechanism uncovered

BLOOMINGTON, Ind. - Sloppy shipping of a donated human retina to an Indiana University researcher studying a leading cause of vision loss has inadvertently helped uncover a previously undetected mechanism causing the disease. The discovery has led researchers to urge review of how millions of dollars are spent investigating the cause of a type of age-related macular degeneration called choroidal neovascularization.



Working at IU's Biocomplexity Institute, postdoctoral researcher Abbas Shirinifard had hit a brick wall trying to develop detailed computer simulations of the behaviors and interactions of the cells and membranes composing the rear of the retina and its supporting vasculature. In choroidal neovascularization (CNV), blood vessels that supply the eye with oxygen and nutrients and originate in the choroid just behind the eye abruptly break into the retina and disrupt it. Blindness can follow in a matter of months.

The black region shows normal adhesion, with each black axis an independent type of adhesion failure. The red region shows adhesion defects making invasion most likely, as the yellow arrow denotes increasing risk of blood vessel invasion in the retinal pigment epithelium (RPE) lining. The blue arrow follows reduced adhesion but with no increased risk of sub-RPE invasion; green arrow shows reduced adhesion between RPE and photoreceptors (POS) from impaired retina, reducing risk of sub-RPE invasion but increasing risk of other types of invasion. **Indiana University Biocomplexity Institute**

Two current treatments for CNV either kill the invading blood vessels with drugs injected into the eye (also damaging the retina and killing needed blood vessels as well) or laser-heat the blood vessels, which can cause damaging retinal scars. Yet with 9,000 research papers published on CNV over the past 10 years, neither treatment still addresses the underlying problems that cause the blood vessels to invade, so relapses are common and many patients still lose vision within a year or two.

A serendipitous accident in which a donated human retina from an eye bank was severely shaken during shipping inspired Shirinifard to try again with a series of new simulations. Upon examination of the eye,

Shirinifard and Biocomplexity Institute senior microscopist Sherry Clendenon found that regions of the retina with invading blood vessels had separated from their underlying membrane, while regions that had stayed attached showed much less invasion, suggesting that adhesion might be an essential but overlooked mechanism in maintaining the retina's structure.

Using an open-source modeling software program called CompuCell3D developed by the Biocomplexity Institute in collaboration with the University of Washington and the University of Wisconsin under National Institutes of Health funding, the team quickly began extending existing simulations to study the effects of adhesion defects.

"The simulations showed that reduced adhesion in the retina could indeed lead to its invasion by blood vessels," Shirinifard said. "But the complex structure of the retina meant that many types of adhesion could be important -- the three most prominent being between the pigmented retinal cells (the black lining of the eye) and Bruch's membrane (the substrate that supports the retina), between adjacent pigmented retinal cells, and between pigmented retinal cells and the overlying photoreceptors."

Those variables, the team realized, could be independent of one another or interact in complex ways, and knowing that the rate and type of progression of the disease varies greatly from patient to patient, they needed to examine many examples of each adhesion combination.

That's when Quarry, the IU computer cluster operated by the Office of the Vice President for Information Technology, was called in to push out 32,000 hours of calculations.

"We were able to model the interactions of different degrees of impairment of each type of adhesion and the variation from case to case," Shirinifard said. "Amazingly, these simulations were able to replicate the complex spectrum of CNV seen in the clinic."

Simulations of adhesion defects caused by reduced adhesion between pigmented retinal cells and Bruch's membrane -- the type of CNV typical of aging -- produced a pattern and frequency of invasion agreeing with that in the clinic. Similarly, reduced adhesion between neighboring pigmented retinal cells, typical of inflammation due to severe infection, produced a pattern of invasion agreeing with that seen in young adults.

By combining thousands of simulations, Shirinifard was able to produce maps that related defects in each type of adhesion to the risk of each type of invasion. In turn, he could show that cell adhesion is key to keeping blood vessels out of the retina and that combination defects in the different types of adhesion are sufficient to determine the probability, pattern and rate of progression of CNV.

The full results of one of the most complex tissue evolution models ever deployed were published today in PLoS Computational Biology, and while the team has yet to move toward developing new CNV therapies, the work should have great significance in the search for better therapies, according to Biocomplexity Institute Director James Alexander Glazier, a co-author on the paper and professor in the IU Bloomington College of Arts and Sciences' Department of Physics.

"Hundreds of millions of dollars are spent annually to develop drugs and treatment approaches based on the two commonly hypothesized CNV initiation and progression mechanisms," he said. "Because the current work shows that neither hypothesized mechanism is an important cause of CNV, that money and effort are extremely unlikely to improve outcomes for patients.

Scientists have been barking up the wrong tree. Instead, a search for therapies which restore normal adhesion in the eye is much more likely to produce effective treatments. In addition, the detailed agreement between simulation and clinical observations suggests that new approaches to measuring adhesion in patients would allow much more accurate predictions of the prognosis for individual patients."

The researchers believe these results will also have a much broader impact, as they apply to any tissue -- like the gut and the lung -- in which a basement membrane separates a capillary network from a nearby epithelium.

"The relationships between specific classes of adhesion failures and the types and dynamics of CNV in the eye simulations should carry over to the neovascularization-dependent pathologies of those tissues and to invasion of those tissues in cancer progression," Shirinifard said.

Co-authors on the paper, "Adhesion Failures Determine the Pattern of Choroidal Neovascularization in the Eye: A Computer Simulation Study," with Shirinifard and Glazier were associate scientists Maciej Swat and J. Scott Gens, both of the Biocomplexity Institute and the Department of Physics; Fereydoon Family and Hans E. Grossniklaus, M.D., of Emory University; and Yi Jiang of Georgia State University and Los Alamos National Laboratory.

http://www.eurekalert.org/pub_releases/2012-05/fhcr-pof050312.php

Presence of fetal cells in women lowers risk of breast cancer but raises risk of colon cancer

Study is first to find possible causative link but biological reasons are unknown

SEATTLE – For the first time, scientists have found what could be a causative link between the concentration of circulating Y-chromosome fetal cells in women who gave birth to children of either sex and their risk of later developing breast cancer and colon cancer. The findings show that the presence of fetal cells is a double-edged sword: Women with the lowest concentration of fetal cells were 70 percent less likely to have breast cancer, while women with the highest concentration of fetal cells had a four-fold increased risk for colon cancer when compared with healthy controls.

The how and why of this contradictory role of fetal microchimerism is not known and requires more study, according to Vijayakrishna K. (V.K.) Gadi, M.D., Ph.D, an assistant member of the Clinical Research Division at Fred Hutchinson Cancer Research Center and senior author of a study that appears online in the European Journal of Cancer.

Scientists at the University of Copenhagen, Denmark, led the research, which was based on data from 428 Danish women whose blood was drawn in the mid-1990s when they were cancer free. Ten years later, the cancer status of these women was determined based on an examination of Danish breast and colon cancer registries. Molecular analysis of the blood samples was done at the Hutchinson Center to measure how much microchimerism they had. Male fetal microchimerism was detected in 40 percent of 89 women who had developed breast cancer, and 90 percent of the 67 women who had developed colon cancer. Residual male fetal cells were also found in 70 percent of the 272 women who remained cancer free.

The colon cancer finding was unexpected; no prior studies had ever associated that cancer with fetal microchimerism, Gadi said. The researchers chose to measure microchimerism in women who later developed colon cancer to determine whether the possible beneficial effect of microchimerism is specific to breast cancer, as past studies have shown.

Previous studies, including research by Gadi and colleagues, found associative links between concentrations of fetal microchimerism and a decreased risk of breast cancer as well as a heightened risk of some autoimmune diseases. However, those studies were based on blood drawn from women after the onset of their disease.

"Fetal microchimerism may be highly relevant to later cancer development. However, the study does not allow us to identify the underlying biological mechanisms," Gadi said.

Gadi has a hypothesis (not contained in the study) that the fetal cells could be producing a naturally occurring graft-versus-tumor effect but the effect may be having different impacts based on the cancer type. "There are diseases of the GI tract that are associated with chronic inflammation and it is entirely possible that fetal cells are driving, seeding or initiating that inflammation or are involved in the process," he said regarding the link to colon cancer.

Detection of Y-chromosome fetal cells, thought to originate from previous pregnancies with a male fetus, is common in women. During pregnancy, fetal cells naturally pass into the mother where they can persist in small numbers in the blood and tissues for decades after childbirth. Interestingly, this latest study also found no obvious association between the number of live-born sons and testing positive for male microchimerism. Overall, 65 percent of women with no live-born sons tested positive for Y-chromosome fetal cells, according to the study. "A source of Y chromosomes in women with no sons could be unrecognized pregnancies with a male fetus that terminated early," Gadi said regarding a possible explanation.

Mads Kamper-Jorgensen of the University of Copenhagen's Institute of Public Health is the study's corresponding author. Colleagues from the Danish Statens Serum Institute, the Danish Cancer Society, Copenhagen University Hospital and the University of Washington contributed to the research. The study was funded by the Danish Cancer Society.

http://www.eurekalert.org/pub_releases/2012-05/f-sf-jae050312.php

Jealousy and envy at work are different in men and women

A study carried out by researchers from Spain, the Netherlands and Argentina suggests that in a work environment, sexual competition affects women more than men.

However, a rival's social skills provoke jealousy and professional envy equally in both sexes.

A group of researchers from the universities of Valencia, Groningen (the Netherlands) and Palermo (Argentina) have analysed the differences between men and women in their way of feeling envious and jealous at work. "Women with a high level of intrasexual competition are more jealous if the rival is more attractive and more envious if the rival is more powerful and dominating. They did not get any results in men, as no rival characteristics that provoke jealousy or envy predicted intrasexual competition" Rosario Zurriaga, researcher at

the University of Valencia and one of the authors of the study which has been published in the journal Revista de Psicología Social, told SINC.

Intrasexual rivalry is competition with other people of the same sex caused by the desire to obtain and keep access to the opposite sex. Zurriaga, together with researchers at the universities of Groningen (the Netherlands) and Palermo (Argentina) analysed this type of rivalry using questionnaires distributed directly to 200 subjects in their workstations. From those, they finally chose 114 "a large enough sample as it is an exploratory study" the expert from the University of Valencia explained.

They distinguished between two emotions: jealousy and envy. Jealousy is a threat or loss of success in a relationship due to interference from a rival and implies a loss or threat of loss of what they had. Envy is a response to another person who has success, skills or qualities that they desire and involves a lack in comparison to the envied person. According to their results, sexual competition generally causes more jealousy and envy in women. However, rivals' social skills provoke both emotions, both in men and women. "This result shows the importance of social skills in work environments" Zurriaga stated.

Preventing the negative effects of these emotions

"Our research intends to clarify the role of emotions like envy and jealousy at work. These feelings have not been studied in working contexts and can cause stress in workers and negatively affect the quality of working life" the researcher added.

The main implication derived from this study is that in order to prevent the negative effects of these feelings, they should modify aspects such as the perception of threat, loss or comparison with others at work.

"This is one of the first studies that examines rivals' characteristics in this environment and contributes to a better understanding of conflicts and problems that can occur in working relationships" they concluded.

Some 26% of employees that participated worked in administration, 21% in services sector, 30% in education and the rest in health and other professions. Regarding sex, the sample was 50% men and 50% women, with an average age of 36 years, and having spent 11 years in their current company.

References: *Abraham P. Buunk, Rosario Zurriaga, Pilar González, Alejandro Castro Solano. "Intra-sexual competition at work: Sex differences in jealousy and envy in the workplace". Revista de Psicología Social 27 (1): 85-96, 2012.*

http://bit.ly/IpWfZs

Why Jupiter's moon Ganymede is an exciting destination

Ganymede, here we come. A €1 billion mission to place spacecraft in orbit around Jupiter's largest moon - also the largest in the solar system - has received the green light from the European Space Agency.

Called the Jupiter Icy Moon Explorer, or Juice, the spacecraft will fly past two other Jovian moons - Callisto and Europa - and end its journey in orbit around a third, Ganymede.

While Europa, a water world with the potential to support life, has grabbed more of the limelight over the years, Ganymede,with its own ocean, auroras and oxygen, may have even more to offer, says Emma Bunce, a physicist at the University of Leicester, UK, and a member of the science team behind Juice.

Europa caught the public imagination in the 1980s when images from the Voyager spacecraft suggested water from a liquid ocean might lie beneath a relatively thin, icy crust. The Galileo spacecraft later confirmed the presence of such an ocean.

NASA has tentative plans to visit Europa and at one stage planned to send a Europa orbiter along with Juice. But the agency's financial woes have intervened and ESA will now go to Jupiter's moons alone. What will it find?

A little bigger than Mercury, Ganymede is, like Europa, a large, ice-covered moon. Ganymede too has a subsurface ocean, which could potentially also host life. Just how deep this ocean is, and whether it exists in pockets or as a continuous band around the moon, are questions the Juice team hopes to answer.

Ganymede is also more complex. It is the only moon in the solar system with its own magnetic field, probably generated by a liquid-iron core like Earth's. This field is even powerful enough to generate an aurora, like Earth's. Understanding the origin of this field and how it interacts with Jupiter's field is one of the key goals of the mission.

If all that isn't convincing enough, Ganymede also has a tenuous oxygen atmosphere formed by the breakdown of water ice on the surface.

"Ganymede appeals to geologists, astrobiologists, magnetophysicists and atmospheric scientists," says Bunce. "It's clearly a very rich environment, which is why we're so excited to be going."

The plan is to launch Juice in 2022 and for it to enter Ganymede orbit in 2032.

http://bit.ly/IFLCUH

One gene helped human brains become complex

A single ancestral human gene that made two copies of itself may have helped the evolution of our large brains 2.5 million years ago

17:00 03 May 2012 by Sara Reardon

When it comes to brain development, slow and steady wins the race. A single ancestral human gene that made two copies of itself may have helped the evolution of our large brains 2.5 million years ago, as our ancestors were diverging from australopithecines.

Paradoxically, it seems the effect of the extra copies was to slow down individual brain development. This allowed time for neurons to develop more and better connections with one another.

Gene duplications are rare in human history: only about 30 genes have copied themselves since we split from chimps 6 million years ago. Few have been studied, but those that have encode genes that are very exciting, says human geneticist Evan Eichler of the University of Washington in Seattle. Many are involved in brain development.

Photograph of a photograph

Eichler and Franck Polleux of the Scripps Institute in La Jolla, California, chose to look at a duplicated gene called SRGAP2. It helps drive development of the neocortex, which controls higher-order brain functions such as language and conscious thought. Humans with mutations in this gene are prone to epileptic seizures, as are mice that have been engineered to lack it.

Eichler's group discovered that SRGAP2 duplicated itself 3.5 million years ago, well after humans and chimps diverged. One million years later, this "daughter" of the original gene underwent its own duplication and created a "granddaughter" copy. All three coexist in modern humans.

But just like a photograph of a photograph, as the duplications took place, each copy decreased in quality. The daughter and granddaughter genes were shorter than the original and weren't able to help the brain mature the way the original gene does.

In fact, they did just the opposite: when Polleux and colleagues put human copies of the daughter and granddaughter genes into mice, the proteins they made bound to the original SRGAP2 and hindered its ability to do its job.

The effect of this genetic sabotage, however, was that the brain had more time to develop. Although the mouse's brain itself didn't grow larger, the neurons in the neocortex changed to look like human brain cells, growing thick spines to exchange information with other cells. The neurons also formed 50 to 60 per cent more of these spines than normal mouse neurons do, which would likely increase the brain's processing power.

Smarter mice?

Although Polleux and his colleagues have not yet figured out whether the mice were smarter, he says those experiments are in the works. They also plan to put the human genes into a much closer human relative, a marmoset, and see if its behaviour is altered.

The timing of the second duplication 2.5 million years ago, the researchers point out, coincides with when our genus, Homo, began separating from the now-extinct Australopithecus.

We know that the cognitive abilities of Homo must have increased tremendously to enable our ancestors to develop complex social structures and tools that australopithecines didn't have. The rare double gene duplication may have been instrumental in this.

What's interesting about the duplication, Eichler says, is that it would have changed brain development immediately and dramatically. Human ancestors with two, three, or even more copies of SRGAP2 – and consequently stark differences in their cognitive abilities – could have been running around together at one point. "That's fun to think about," he says.

Journal references: Cell, DOI: 10.1016/j.cell.2012.03.033 and 10.1016/j.cell.2012.03.034

http://bit.ly/KxMb0E

Blonde hair evolved independently in Pacific islands

Science can't yet tell us whether they have more fun – but it has uncovered a new genetic change that makes people blonde.

19:00 03 May 2012 by Lisa Raffensperger

And contrary to long held belief, it seems golden hair hasn't simply been introduced across the globe by travelling tow heads, but instead evolved separately in different human populations.

Indigenous people of the Solomon Islands in the South Pacific have some of the darkest skin pigmentation outside of Africa. But unlike most other tropical populations, they also have a high prevalence of blonde hair.

Up to 10 per cent of the population is fair haired, the highest proportion outside of Europe. Until now, this odd trait had generally been attributed to the introduction of blonde genes by European explorers and traders in preceding centuries. "We originally thought, well that must be a Captain Cook allele," says Carlos Bustamante at Stanford University.

Yet a closer look revealed that the genetics behind blonde hair in Brussels are distinct from those leading to flaxen locks in the South Pacific.

Bustamante, Sean Myles and colleagues at Stanford discovered this after analysing saliva samples from 43 blondes and 42 dark-haired Solomon Islanders. A genome-wide scan pointed to a single strong difference between the groups at a gene called TYRP1. Further analysis revealed that a single-letter change in the gene accounted for 46 per cent of the population's hair colour variation, with the blonde allele being recessive to the dark hair allele. The blonde mutation wasn't found in any of the 900 other individuals sampled from outside the South Pacific (Science, DOI: 10.1126/science.1217849).

TYRP1 is known to be involved in skin and hair pigmentation in several species. In normally black mice, for example, a mutation in the gene produces light brown coats. A rare kind of human albinism is also caused by mutations in TYRP1, which produces reddish skin colour and ginger hair. TYRP1 isn't, however, one of the genes that produces blonde hair in Europeans. The novel blonde mutation in Solomon Islanders is likely to have cropped up around 10,000 years ago, and it appears to be the same one behind blondness in Fiji and other regions of the South Pacific.

"Before this, everybody would have thought, blonde hair evolved once in humans," says Bustamante. "This tells us we can't really assume that even these common mutations are common across different human populations. Non-European populations are critical to study to find mutations that may be underlying the vast phenotypic variation of humans."

http://bit.ly/KYC3D8

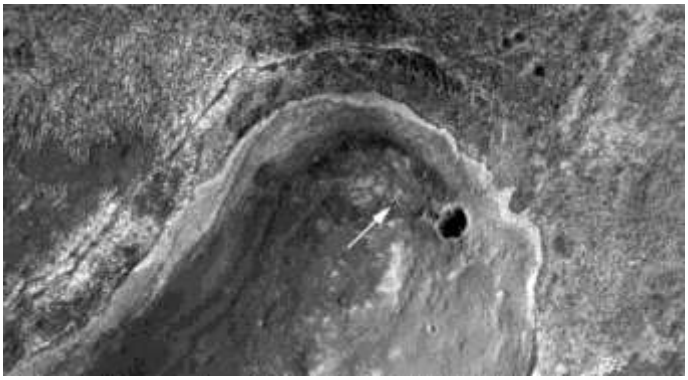
Mars Opportunity rover reaches Endeavour crater, finds signs of ancient Martian water

Over seven years into its (originally) 90-day mission, the Mars rover Opportunity arrived at the rim of Endeavour Crater

By Matthew Francis | Published 2 days ago

While the crater itself was formed from an ancient meteorite impact, the rocks at its rim show signs of a watery past. Chemical analysis found deposits typical of hydrothermal vents on Earth, along with features usually associated with evaporation. Together, these pieces of evidence suggest warm, shallow water formerly existed in the region of Endeavour.

In a new Science paper, S. W. Squyres and colleagues describe the process Opportunity used to obtain and analyze the rock samples. The landscape around Endeavour is very old, dating back to the era when Mars was under constant bombardment by meteorites, which is why it was chosen as a site for exploration by rover. If Mars' history parallels Earth's in any way, the early cataclysmic period gave way to calmer times, and water—possibly life—may have been present. Based both on the sedimentary and evaporative characteristics of the rocks around the crater, the researchers conclude the region may have been habitable for at least a short period of time.



The Opportunity rover at Chester Lake, as seen by the HiRISE Mars orbiter. (North is at the bottom of this image.)

As on Earth, Mars has regions where the rocks date back to early times, shortly after the planets cooled sufficiently to allow the surface to solidify. On Mars, this era is known as the Noachian period (in reference to the biblical figure Noah), as the now-dry planet probably had a lot of surface water. This period was also characterized by heavy meteorite bombardment: Noachian landscape is heavily cratered, and bears some resemblance to the highland regions on Earth's Moon.

Endeavour Crater is the site of one such meteorite impact. The crater is about 22 kilometers across, and the layers of rock exposed by the impact resemble similar structures on Earth. Thus, Endeavour provides a good laboratory for understanding early Martian history, so scientists selected it for exploration by the Opportunity rover during its extended

While Cape York is named for a place on Earth Shoemaker Ridge and Greeley Haven are named in memory of planetary scientists Eugene Shoemaker and Ronald Greeley. Greeley helped design some of the instruments used on the Opportunity rover known as the Athena payload.

mission.

Opportunity approached Endeavour along a relatively low rise known as Shoemaker Ridge at the lip of the crater, which itself is part of a region known as Cape York. For the current study, the rover analyzed rocks at two locations, known as Chester Lake and Greeley Haven, respectively at the southern and northern ends of Cape York. Since these rocks are separated by about 700 meters, Squyres et al. assume they are representative of the entire Shoemaker formation.

In both locations, Opportunity examined rock within outcrops (the matrix) and broken off fragments (clasts), some of which were ejected from the impact that formed Endeavour. Grinding small amounts off rocks allowed Opportunity to test their chemical composition and the hardness of the minerals, both of which reveal information about formation and history.

One type of rock known as breccias (which are well known from Earth) consists of solid fragments embedded in fine-grained stone. Analysis of breccias in near Chester Lake revealed the presence of a lot of zinc in high concentrations. On Earth, such features are produced in hydrothermal vents, when volcanic heating sends water through fissures, allowing it to pick up minerals.

In addition, when Opportunity studied rocks in the Greeley Haven region, it found veins of material threading the matrix. Based on the chemical analysis and modeling, Squyres et al. concluded this material is gypsum, a soft white calcium sulfide compound containing water ($CaSO4•2H2O$). On Earth, gypsum is most commonly found when water has evaporated, leaving previously dissolved minerals behind. Based on the temperature at which gypsum forms, the researchers postulated a warm shallow body of water, perhaps transient—and possibly habitable.

Both the presence of zinc deposits and veins of gypsum are very suggestive—water was likely once present in the Endeavour Crater region. Comparison with sandstone found elsewhere on Mars hints that Cape York's water was transitional. The hydrothermal deposits mark the early period, when volcanic activity was more common, while the evaporative deposits show a later period, when seas covered much of the Martian surface. The warm water required to form and precipitate gypsum hints that perhaps transient pools may have been habitable. *Science, 2012. DOI: 10.1126/science.1220476*

http://www.bbc.co.uk/news/health-17942181

Massive rise in Asian eye damage

Up to 90% of school leavers in major Asian cities are suffering from myopia - short-sightedness - a study suggests.

By Matt McGrath Science reporter, BBC World Service

Researchers say the "extraordinary rise" in the problem is being caused by students working very hard in school and missing out on outdoor light. The scientists told the Lancet that up to one in five of these students could experience severe visual impairment and even blindness. In the UK, the average level of myopia is between 20% and 30%. According to Professor Ian Morgan, who led this study and is from the Australian National University, 20-30% was once the average among people in South East Asia as well.

"What we've done is written a review of all the evidence which suggests that something extraordinary has happened in east Asia in the last two generations," he told BBC News. "They've gone from something like 20% myopia in the population to well over 80%, heading for 90% in young adults, and as they get adult it will just spread through the population. It certainly poses a major health problem."

Eye experts say that you are myopic if your vision is blurred beyond 2m (6.6ft). It is often caused by an elongation of the eyeball that happens when people are young. According to the research, the problem is being caused by a combination of factors - a commitment to education and lack of outdoor light.

Professor Morgan argues that many children in South East Asia spend long hours studying at school and doing their homework. This in itself puts pressure on the eyes, but exposure to between two and three hours of daylight acts as a counterbalance and helps maintain healthy eyes.

The scientists believe that a chemical called dopamine could be playing a significant part. Exposure to light increases the levels of dopamine in the eye and this seems to prevent elongation of the eyeball.

"We're talking about the need for two to three hours a day of outdoor light - it doesn't have to be massively sunny, we think the operating range is 10-20,000 lux, we're not sure about that - but that's perfectly achievable on a cloudy day in the UK."

'Massive pressures'

Cultural factors also seem to play a part. Across many parts of South East Asia, children often have a lunchtime nap. According to Professor Morgan they are missing out on prime light to prevent myopia.

"Children suffer from a double whammy in South East Asia," says Professor Morgan. "As a result of massive educational pressures and the construction of a child's day, the amount of time they spend outside in bright light is minimised."

A big concern is the numbers of students suffering from "high" myopia. According to Professor Morgan, this affects between 10% and 20% of students in Asian cities. It can lead to vision loss, visual impairment and even blindness. "These people are at considerable risk - sometimes people are not told about it and are just given more powerful glasses - they need to be warned about the risk and given some self-testing measures so they can get to an ophthalmologist and get some help."

For decades, researchers believed there was a strong genetic component to the condition. It was believed that people from China, Japan, Korea and other countries were particularly susceptible to developing myopia. But this study strongly suggests an alternative view. In Singapore, where there are large numbers of people from Chinese, Malay and Indian backgrounds, all three ethnic groups have seen a dramatic rise in short-sightedness.

Professor Morgan says you cannot rule out genetics completely, but for him it's not the major factor.

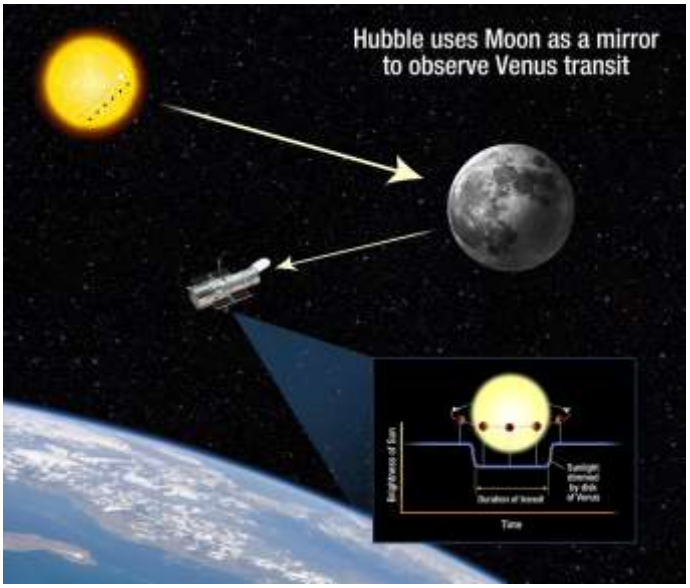
"Any type of simple genetic explanation just doesn't fit with that speed of change; gene pools just don't change in two generations. "Whether it's a purely environmental effect or an environmental effect playing a sensitive genome, it really doesn't matter, the thing that's changed is not the gene pool - it's the environment."

Further evidence on the impact of light is provided by UK researchers. Kathryn Saunders from the University of Ulster was part of a team which compared short-sightedness in children in Australia and Northern Ireland. "White UK kids are much more likely to be myopic than white Australian children," Dr Saunders told BBC News. "We've proposed that this might be due to the protective effect in Australia of increased exposure to bright sunlight. "This requires further exploration and research, but I guess we might want to encourage children to spend more time outside when the sun is shining. It's unlikely to do them any harm."

http://www.eurekalert.org/pub_releases/2012-05/nsfc-htu050412.php

Hubble to use moon as mirror to see Venus transit

Hubble cannot look at the sun directly, so astronomers are planning to point the telescope at the Earth's moon, using it as a mirror to capture reflected sunlight



Hubble cannot look at the sun directly, so astronomers are planning to point the telescope at the Earth's moon, using it as a mirror to capture reflected sunlight and isolate the small fraction of the light that passes through Venus's atmosphere. Imprinted on that small amount of light are the fingerprints of the planet's atmospheric makeup.

These observations will mimic a technique that is already being used to sample the atmospheres of giant planets outside our solar system passing in front of their stars. In the case of the Venus transit observations, astronomers already know the chemical makeup of Venus's atmosphere, and that it does not show signs of life on the planet. But the Venus transit will be used to test whether this technique will have a chance of detecting the very faint fingerprints of an Earth-like planet, even one that might be habitable for life, outside our solar system that similarly transits its own star. , Venus is an excellent proxy because it is similar in size and mass to our planet.

The astronomers will use an arsenal of Hubble instruments, the Advanced Camera for Surveys, Wide Field Camera 3, and Space Telescope Imaging Spectrograph, to view the transit in a range of wavelengths, from ultraviolet to near-infrared light. During the transit, Hubble will snap images and perform spectroscopy, dividing the sunlight into its constituent colors, which could yield information about the makeup of Venus's atmosphere.

Hubble will observe the moon for seven hours, before, during, and after the transit so the astronomers can compare the data. Astronomers need the long observation because they are looking for extremely faint spectral signatures. Only 1/100,000th of the sunlight will filter through Venus's atmosphere and be reflected off the moon.

This image, taken with Hubble's Advanced Camera for Surveys, reveals lunar features as small as roughly 560 feet (170 meters) across. The large "bulls-eye" near the top of the picture is the impact crater, caused by an asteroid strike about 100 million years ago. The bright trails radiating from the crater were formed by material ejected from the impact area during the asteroid collision. Tycho is about 50 miles (80 kilometers) wide and is circled by a rim of material rising almost 3 miles (5 kilometers) above the crater floor. The image measures 430 miles (700 kilometers) across, which is slightly larger than New Mexico.

Because the astronomers only have one shot at observing the transit, they had to carefully plan how the study would be carried out. Part of their planning included the test observations of the moon, made on Jan. 11, 2012, as shown in the release image.

Hubble will need to be locked onto the same location on the moon for more than seven hours, the transit's duration. For roughly 40 minutes of each 96-minute orbit of Hubble around the Earth, the Earth occults Hubble's view of the moon. So, during the test observations, the astronomers wanted to make sure they could point Hubble to precisely the same target area.

This is the last time this century sky watchers can view Venus passing in front of the sun. The next transit won't happen until 2117. Venus transits occur in pairs, separated by eight years. The last event was witnessed in 2004.

The Hubble Space Telescope is a project of international cooperation between NASA and the European Space Agency. NASA's Goddard Space Flight Center in Greenbelt, Md., manages the telescope. The Space Telescope Science Institute (STScI) in Baltimore, Md., conducts Hubble science operations. STScI is operated by the Association of Universities for Research in Astronomy, Inc., in Washington, D.C.

http://bit.ly/KkQGBT

New electrode material could lead to powerful rechargeable sodium batteries

A new electrode material could help make lightweight, powerful rechargeable sodium batteries to replace lithium-ion batteries used in electronics and some electric vehicles.

By Melissae Fellet | Published a day ago

The material contains widely available iron, instead of the nickel and cobalt commonly used in these electrodes, and enables a similar energy density to electrodes in lithium batteries.

Sodium is an attractive candidate to replace lithium in batteries because it’s cheaper and widely available around the world. But building a sodium battery requires redesigning battery technology to accommodate the chemical reactivity and larger size of sodium atoms.

A rechargeable battery, whether lithium or sodium, contains two electrodes, the anode and the cathode. When a battery with an anode made from sodium metal discharges, electrons flow from that electrode to the other. The anode sloughs off positively charged sodium ions, which travel over to the cathode and wiggle inside the material to balance the extra negative charges coming in through the circuit.

When the battery is charged, this process is reversed: electrons flow out of the cathode, releasing the sodium ions inside. These ions float over to the other electrode, gain an electron, and replace the atoms lost during discharging. The energy density of a battery depends on the amount of charged ions that the electrode can hold as well as the amount of energy released by each electron. The greater the energy density, the smaller a powerful battery can be.

Lithium batteries pack more of an electrical punch than sodium batteries because lithium atoms naturally release more energy when losing an electron than sodium does. So, for sodium batteries to reach energy densities similar to lithium ones, the positive electrode in the sodium battery has to hold more ions. And ideally, the ion-sized spaces in the electrode do not change size during the electron exchange, so that sodium ions can easily squeeze in and out as the battery charges and discharges.

To make this new electrode material, Shinichi Komaba, of Tokyo University of Science and his colleagues ground together iron oxide, sodium oxide, and manganese oxide. They squished the powder into a pellet and heated it to 900°C for 12 hours. This created a material with the formula Na2/3[Fe1/2Mn1/2]O2.

Then the researchers made a battery using this new material as the positive electrode and sodium metal as the negative electrode. The capacity of the new material, which reflects how much charge one gram of electrode material can store, was 190 milliAmp-hours/gram, with an average voltage of 2.75 V. The capacity decreases over 30 charging cycles, meaning that the battery held less energy each time it was recharged.

The energy density of this material was estimated to be about 520 mWhr/g, similar to the energy density of LiFePO4 and about 80 mWhr/g higher than LiMn2O4 cathodes. Using carbon or titanium dioxide for negative

electrode, instead of sodium, might allow the researchers to build a rechargeable battery that puts out three volts of power (the amount in two AA batteries).

Another recently published material using layered vanadium pentoxide as the positive electrode in a rechargeable sodium battery has a higher capacity and energy density than this material. It also maintains its capacity for 200 charging cycles. The new material is unique because it contains cheap iron, says chemist Christopher Johnson, of Argonne National Laboratory in Illinois, who helped develop the vanadium-containing material. Since sodium battery technology is still new, it's encouraging to see materials with energy densities similar to current lithium batteries, he says. "Who knows where we'll be in 10 years?"

But using a cheaper material for the positive electrode does not necessarily reduce the overall cost of a battery, says Jay Whitacre, of Carnegie Mellon University. Dropping the total cost requires considering the other components, like electrolyte and anode, in the battery too. And a battery made with this new material does not use anything different than a standard lithium-ion battery, he says.

Nature Materials, 2012. ***DOI: 10.1038/NMAT3309***.

http://www.sciencedaily.com/releases/2012/05/120504110504.htm

What Is Your Dog Thinking? Brain Scans Unleash Canine Secrets

Many dog lovers make all kinds of inferences about how their pets feel about them, but no one has captured images of actual canine thought processes -- until now

ScienceDaily - When your dog gazes up at you adoringly, what does it see? A best friend? A pack leader? A can opener? Many dog lovers make all kinds of inferences about how their pets feel about them, but no one has captured images of actual canine thought processes -- until now.

Emory University researchers have developed a new methodology to scan the brains of alert dogs and explore the minds of the oldest domesticated species. The technique uses harmless functional Magnetic Resonance Imaging (fMRI), the same tool that is unlocking secrets of the human brain.

The Public Library of Science (PLoS ONE) is publishing the results of their first experiment, showing how the brains of dogs reacted to hand signals given by their owners.

"It was amazing to see the first brain images of a fully awake, unrestrained dog," says Gregory Berns, director of the Emory Center for Neuropolicy and lead researcher of the dog project. "As far as we know, no one has been able to do this previously. We hope this opens up a whole new door for understanding canine cognition and inter-species communication. We want to understand the dog-human relationship, from the dog's perspective."

Key members of the research team include Andrew Brooks, a graduate student at the Center for Neuropolicy, and Mark Spivak, a professional dog trainer and owner of Comprehensive Pet Therapy in Atlanta.

Two dogs are involved in the first phase of the project. Callie is a two-year-old Feist, or southern squirrel-hunting dog. Berns adopted her at nine months from a shelter. McKenzie is a three-year-old Border Collie, who was already well-trained in agility competition by her owner, Melissa Cate. Both dogs were trained over several months to walk into an fMRI scanner and hold completely still while researchers measured their neural activity.

The researchers aim to decode the mental processes of dogs by recording which areas of their brains are activated by various stimuli. Ultimately, they hope to get at questions like: Do dogs have empathy? Do they know when their owners are happy or sad? How much language do they really understand?

In the first experiment, the dogs were trained to respond to hand signals. One signal meant the dog would receive a hot dog treat, and another signal meant it would not receive one. The caudate region of the brain, associated with rewards in humans, showed activation in both dogs when they saw the signal for the treat, but not for the no-treat signal. "These results indicate that dogs pay very close attention to human signals," Berns says. "And these signals may have a direct line to the dog's reward system."

Berns is a neuroeconomist, who normally uses fMRI technology to study how the human mind works. His human brain-imaging studies have looked at everything from why teens engage in risky behavior to how adults decide to follow, or break, established rules of society.

Dog lovers may not need convincing on the merits of researching the minds of our canine companions. "To the skeptics out there, and the cat people, I would say that dogs are the first domesticated species, going back at least 10,000 years, and by some estimates 30,000 years," Berns says. "The dog's brain represents something special about how humans and animals came together. It's possible that dogs have even affected human evolution. People who took dogs into their homes and villages may have had certain advantages. As much as we made dogs, I think dogs probably made some part of us, too."

The idea for the dog project came to Berns about a year ago, when he learned that a U.S. Navy dog had been a member of the SEAL team that killed Osama bin Laden. "I was amazed when I saw the pictures of what

military dogs can do," Berns says. "I realized that if dogs can be trained to jump out of helicopters and airplanes, we could certainly train them to go into an fMRI to see what they're thinking."

All procedures for the dog project were approved by the Institutional Animal Care and Use Committee of Emory. "From the outset, we wanted to ensure the safety and comfort of the dogs," Berns says. "We wanted them to be unrestrained and go into the scanner willingly." The dogs were trained to wear earmuffs, to protect them from the noise of the scanner. They were also taught to hold their heads perfectly still on a chin rest during the scanning process, to prevent blurring of the images.

"We know the dogs are happy by their body language," says Mark Spivak, the professional trainer involved in the project. Callie, in particular, seems to revel in the attention of breaking new ground in science.

"She enters the scanner on her own, without a command, sometimes when it's not her turn," Spivak says. "She's eager to participate."

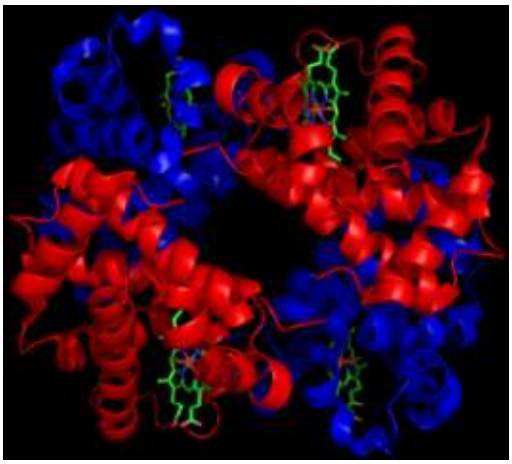
Gregory Berns, Andrew Brooks, Mark Spivak. ***Functional MRI in Awake Unrestrained Dogs****. SSRN, April 27, 2012*

http://blogs.scientificamerican.com/lab-rat/2012/05/05/pathogens-that-feed-off-human-blood/

Pathogens that feed off human blood

For bacteria that live within the human body, there is one incredibly iron-rich molecule that circulates throughout the human body and can be found permeating the tissues.

By S.E. Gould | May 5, 2012



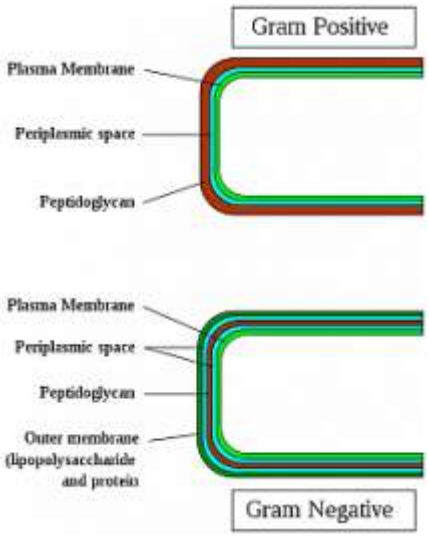
Bacteria may be tiny little micro-organisms but like any other living creature there are certain molecules that they need for survival. No matter what niche a bacterial colony occupies, it eventually requires a source of iron. For bacteria that live within the human body, there is one incredibly iron-rich molecule that circulates throughout the human body and can be found permeating the tissues.

The image above (credit link) shows the structure of the haemoglobin molecule. It consists of four sub-chains (shown in red and blue) each of which carries an iron containing "haem co-factor" which you can just about see in the diagram as the spikey green things. These haemoglobin molecules are packed tight into red blood cells, so tightly that the red blood cells don't even have a nucleus but are just haemoglobin carrying machines.

Haemoglobin – the molecule that gives blood its red colour and is used to tran sport oxgyen through the body. **Richard Wheeler (Zephyris) 2007.**

The lack of nucleus means that they can't grown or divide (or do anything much), so after being put together in the bone marrow and circulating the blood for around three months red blood cells are discreetly removed and replaced.

All of this circulating iron is a great opportunity for pathogenic bacteria, who have developed varies systems to get hold of it. Firstly they have to break down the red blood cells, usually by secreting various chemicals that break up the cell membrane, releasing the haemoglobin. Then they have to bind to the haemoglobin via specialised receptors on their cell surface. Once bound, the haemoglobin passes through the bacterial cell wall and into the interior of the cell. For bacteria with two cell membranes (Gram negative bacteria) this is a complex task involving various different proteins, transporters, and use of the proton-motive force. For bacteria with one large thick cell membrane (Gram positive bacteria) some sort of protein relay process seems to be involved, which uses far less energy. Greater detail on both these processes can be found in the references below.



A very simply schematic of the difference between Gram positive bacteria (top) and Gram negative (bottom). **Original uploader was Graevemoore at en.wikipedia.**

Once inside the bacterium, the haemoglobin is broken down to release the precious iron that it carries. This is more dangerous than it sounds, because the iron in haemoglobin is carrying oxygen, which means that there is potential for reactive oxgyen species to be released and cause havoc inside the cell. Not only that but in some bacteria the "haem co-factor" itself can be toxic. Some bacteria contain special enzymes called "Haem oxygenases" which deal with the oxgyen species, while others sequester the haem in vacuoles away from the

rest of the cell, or turn on exporter molecules. It's not quite clear whether the exporters are taking away the haem or some other toxic product, but they are vital for preventing the toxic effects of haemoglobin within the bacteria.

The whole process of extracting iron from haemoglobin is actually fraught with dangers for the bacteria. The process requires all sorts of special molecules and transporters which don't feature in human cells, which makes them a prime target for the immune system to recognise an invading element. In particular the haemoglobin binding proteins, which are a bit like a large red flag labelled "invader" sticking out of the bacterial cell surface. Not only that, but they are quite energy expensive to run, particularly for the Gram negative cells. In consequence, the bacteria tend to only activate this system when they are running particularly low on iron, and there are no other available sources around.

Ref 1: Pishchany G, & Skaar EP (2012). Taste for blood: hemoglobin as a nutrient source for pathogens. PLoS pathogens, 8 (3) PMID: 22412370

Ref 2: Pishchany, G., McCoy, A., Torres, V., Krause, J., Crowe, J., Fabry, M., & Skaar, E. (2010). Specificity for Human Hemoglobin Enhances Staphylococcus aureus Infection Cell Host & Microbe, 8 (6), 544-550 DOI: 10.1016/j.chom.2010.11.002

Haemoglobin – the molecule that gives blood its red colour and is used to tran sport oxgyen through the body.

Richard Wheeler (Zephyris) 2007.