Exercise may lead to faster prostate tumor growth

DURHAM, N.C. -- Prostate tumors grew more quickly in mice who exercised than in those who did not, leading to speculation that exercise may increase blood flow to tumors, according to a new study by researchers in the Duke Comprehensive Cancer Center (DCCC) and the Duke Prostate Center.

"Our study showed that exercise led to significantly greater tumor growth than a more sedentary lifestyle did, in this mouse model," said Lee Jones, Ph.D., a researcher in the DCCC and senior investigator on this study. "Our thought is that we may, in the future, be able to use this finding to design better drug delivery models to more effectively treat prostate cancer patients, and those with other types of cancer as well."

The findings were presented in a poster session at the American Association for Cancer Research annual meeting on April 13 in San Diego, Calif. The study was funded by the United States Department of Defense, the Prostate Cancer Foundation and the American Urological Association Foundation, Rising Star in Urology Award, given to Stephen Freedland, one of the study's investigators.

The researchers implanted prostate tumors subcutaneously in the flanks of 50 mice and then put half of the mice in cages with exercise wheels and half in cages with no wheels. All mice were fed the same diet. On average, the exercising mice ran more than half a mile each day.

"We found that among the mice that had the opportunity to voluntarily exercise, tumors grew approximately twice as fast as they did among the mice that did not have the opportunity to exercise," Jones said.

Researchers and clinicians know that a challenge in delivering chemotherapy and radiation to tumors can be their poor blood flow, so these findings may hint at a way in which to improve blood flow to tumors, perhaps then allowing for better distribution of medicine, he said.

"We're wondering, can we combine exercise with treatments such as chemotherapy, hormone therapy or radiation, to maximize the results we achieve in prostate cancer patients," Jones said. "That question will be the subject of subsequent studies."

The researchers are currently conducting a validation study, in mice, in which tumors are injected directly into the prostate, thereby better simulating human prostate cancer, Jones said.

"Down the line, we will test this hypothesis in humans undergoing medical treatment for prostate cancer," he said.

The researchers want to caution men against interpreting these findings as an endorsement for not exercising for fear of getting or exacerbating cancer.

"These mice were not receiving treatment and we were allowing aggressive tumors to grow unchecked for the sake of the experiment," said study investigator Freedland, a urologist at Duke. "Patients would not find themselves in the same situation."

Concerns should also be overridden by the well-established benefits of exercise, including its positive effects on cardiovascular health, Type II diabetes, obesity, and many other chronic conditions, he said.

"This study gives us insight into which cellular pathways are affected by exercise, and starts to give us clues about how to harness the beneficial effects," said Michael Potter, a medical student at Duke and lead investigator on the study. "Ultimately, we hope that this knowledge will help us use exercise to both deliver medicines more effectively and protect the body from the harmful side effects of treatment, as we already know it can."

This is one of the first studies to look at the physiological effects of exercise on the tumor itself, rather than examining the quality-of-life or symptom-control effects of exercise in cancer patients, Jones said.

"The findings were a bit surprising, but provide a very important and exciting foundation upon which to build," he said.

Other researchers involved in this study include Susan Poulton and Mark Dewhirst.

Insects evolved radically different strategy to smell

Scientists find that insects use fast-acting ion channels to smell odors, a major break with the ideology of the field -- and evolution

Darwin's tree of life represents the path and estimates the time evolution took to get to the current diversity of life. Now, new findings suggest that this tree, an icon of evolution, may need to be redrawn. In research to be published in the April 13 advance online issue of Nature, researchers at Rockefeller University and the University of Tokyo have joined forces to reveal that insects have adopted a strategy to detect odors that is radically different from those of other organisms -- an unexpected and controversial finding that may dissolve a dominant ideology in the field.

Since 1991, researchers assumed that all vertebrates and invertebrates smell odors by using a complicated biological apparatus much like a Rube Goldberg device. For instance, someone pushing a doorbell would set off a series of elaborate, somewhat wacky, steps that culminate in the rather simple task of opening the door.

In the case of an insect's ability to smell, researchers believed that when molecules wafting in the air travel up the insect's nose, they latch onto a large protein (called a G-protein coupled odorant receptor) on the surface of the cell and set off a chain of similarly elaborate steps to open a molecular gate nearby, signaling the brain that an odor is present.

"It's that way in the nematode, it's that way in mammals, it's that way in every known vertebrate," says study co-author Leslie Vosshall, head of the Laboratory of Neurogenetics and Behavior at Rockefeller University. "So it's actually unreasonable to think that insects use a different strategy to detect odors. But here, we show that insects have gotten rid of all this stuff in the middle and activate the 'gate' directly."

The gate, a doughnut-shaped protein called an ion channel, provides a safe pathway for ions to flow into a cell. When molecules bind to the odor-sensitive ion channel, the protein changes its shape much like a gate or door changes its conformation as it is opened and closed. Opened, it allows millions of ions to surge into the cell. Closed, it prohibits the activity of the ions from sending a signal to the brain that an odor is present.

At the University of Tokyo, Vosshall's colleague Kazushige Touhara and his lab members puffed molecules onto cells engineered to make insect olfactory receptors. They then measured how long it took for the ion channel to open and recorded their electrical movement as they surged inside the cell via the channel. The rush of electrical activity occurred too fast for a series of steps to be involved, says Vosshall. In addition, poisoning several proteins involved in the G-protein pathway didn't affect the ions or the ion channel, suggesting that G-protein signaling isn't primarily involved in insect smell.

Experiment after experiment, "the most consistent interpretation is that these are ion channels directly gated by odors," says Vosshall. "But the dominant thinking in the field may have reflected an experimental bias that aimed at proving a more elaborate scheme."

The ion channels don't resemble any known ion channel on Earth, says Vosshall. They are composed of two proteins that work in tandem with one another: an olfactory receptor and its coreceptor, Or83b. While the coreceptor is common to every ion channel, the olfactory receptor is unique. Together, they form the olfactory receptor complex. Vosshall and Touhara specifically show that this complex forms nonselective cation channels, meaning that they allow any ion to pass through the gate as long as it has a positive charge.

Touhara and Vosshall developed their ion channel hypothesis in parallel with Vosshall's work on DEET, a widely used chemical in bug spray that jams the receptor complex. This research, which was published in Science last month, also showed that DEET jams other proteins that have nothing to do with smell, including several different types of ion channels that play important roles in the human nervous system. What these radically different proteins have in common, though, is that they all specifically inhibit the influx of positively charged ions into the cell. "Now the curious result in the DEET paper showing that this insect repellent blocks insect olfactory receptors and unrelated ion channels makes sense," says Vosshall. "I am optimistic that we can come up with blockers specific for this very strange family of insect olfactory ion channels."

This research was supported in part by the Foundation for the National Institutes of Health through the Grand Challenges in Global Health Initiative, the National Institutes of Health's U.S.-Japan Brain Research Collaborative Program and the Japan Society for the Promotion of Science's Japan-U.S. Cooperative Science Program.

Mouth may tell the tale of lung damage caused by smoking

M. D. Anderson scientists find same antitumor genes silenced in oral and lung tissue

SAN DIEGO - Cells lining the mouth reflect the molecular damage that smoking does to the lining of the lungs, researchers at The University of Texas M. D. Anderson Cancer Center report today at the annual meeting of the American Association for Cancer Research.

Examining oral tissue lining the mouth to gauge cancer-inducing molecular alterations in the lungs could spare patients and those at risk of lung cancer from more invasive, uncomfortable procedures used now, said senior researcher Li Mao, M.D., professor in M. D. Anderson's Department of Thoracic/Head and Neck Medical Oncology.

"We are talking about just a brushing inside of the cheek to get the same information we would from lung brushings obtained through bronchoscopy," said study presenter and first author Manisha Bhutani, M.D., a post-doctoral fellow in Thoracic/Head and Neck Medical Oncology.

The team examined the oral and lung lining tissue - called the epithelium - in 125 chronic smokers enrolled in a large, prospective lung cancer chemoprevention study.

The status of two crucial tumor-suppressing genes was analyzed. The genes, p16 and FHIT, are known to be damaged or silenced very early in the process of cancer development. "There is substantial damage long before there is cancer," Mao said.

Study participants gave both an oral and lung sample initially and then another at three months. The researchers tracked whether either p16, FHIT or both had been silenced by methylation - the attachment of a chemical methyl group to crucial spots in a gene that shut down its function. Patterns of methylation were compared between the tissues.

The baseline tissue comparison showed methylation of p16 in the lungs of 23 percent of study participants, of FHIT in 17 percent and of either of the two genes in 35 percent. The percentages were similar in oral tissue, with p16 methylated in 19 percent, FHIT in 15 percent and one of the two in 31 percent.

Strong correlations were observed between methylation patterns in both tissues. When methylation of either gene was considered positive, 37 of the 39 individuals (95 percent) with p16 and/or FHIT promoter methylation in the oral samples had promoter methylation in at least one matched bronchial sample. This compared with only 59 of the 86 (69 percent) individuals without the promoter methylation in the oral samples. Similar correlations were seen at the three-month analysis.

"Our study provides the first systematic evidence that accessible tissue, the oral epithelium, can be used to monitor molecular events in less accessible tissue," Bhutani said. "This provides a convenient biomonitoring method to provide insight into the molecular events that take place in the lungs of chronic smokers."

One follow-up area of study is to find additional biomarkers in oral tissue. "We hope that our findings encourage researchers to test an increasing compendium of biomarkers to confirm the reliability of oral epithelium not only in lung cancer chemoprevention but also in therapeutic settings" said Ashutosh Kumar Pathak, M.D., another key study author and a post-doctoral fellow in Surgical Oncology.

"Our study opens the door to enhancing our ability to predict who has higher probability of getting tobacco-related cancers," Mao said. "Not only lung cancer, but pancreatic, bladder and head-and-neck cancers, which also are associated with tobacco use."

The study was funded as part of a grant National Cancer Institute to evaluate celecoxib, known commercially as Celebrex, as a preventive agent against lung cancer.

Co-authors with Bhutani, Mao and Pathak, are You Hong Fan, Jonathan Kurie, Edward Kim, and M. D. Anderson Chair of the Division of Cancer Medicine Waun Ki Hong, all of the Department of Thoracic/Head and Neck Medical Oncology; Diane Liu, of M. D. Anderson's Division of Quantitative Sciences; J. Jack Lee, of the Department of Biostatistics; Hongli Tang, of the Department of Molecular Genetics; and Rodolfo Morice of the Department of Pulmonary Medicine.

Jefferson scientists' discovery may help explain smoking-pancreatic cancer link

(PHILADELPHIA) If lung cancer and heart disease aren't bad enough, cigarette smokers are also at higher risk for developing, among other things, pancreatic cancer. Now, researchers at the Kimmel Cancer Center at Jefferson in Philadelphia have preliminary evidence indicating one possible reason why. Data being presented April 13, 2008 during the Annual Meeting of the American Association for Cancer Research shows that they have found that nicotine in cigarettes increases the production of a protein that is known to promote cancer cell survival, invasion and spread.

According to Hwyda Arafat, M.D., Ph.D., associate professor of Surgery at Jefferson Medical College of Thomas Jefferson University, the protein, osteopontin, is found in a variety of fluids in the body, such as plasma, cerebrospinal fluid, synovial fluid and breast milk. Osteopontin is also present in different organs and plays an important role during embryonic development. Recent studies have demonstrated that osteopontin levels are significantly higher in the blood and pancreas tissue of pancreatic cancer patients. The protein, when over-produced, can make cancer cells more likely to become metastatic.

Dr. Arafat wanted to see if osteopontin might play a role in the cigarette smoking-pancreatic cancer connection. In collaboration with groups at the University of Nebraska and Rutgers University, Dr. Arafat and her co-workers looked at rats exposed to cigarette smoke and measured the amount of osteopontin in the rat pancreas and blood. They found that the more cigarette smoke to which the rats were exposed, the greater the amount of nicotine in the blood and osteopontin in the pancreas.

The researchers also looked at osteopontin expression in pancreatic cancer cell lines exposed to nicotine, finding that osteopontin expression went up when the cells were exposed to more nicotine. "We found that dose-dependently, nicotine increased osteopontin expression not only through transcriptional but also translational (protein secretion) levels in pancreatic cancer cells," Dr. Arafat explains. Pancreas tissue samples from pancreatic cancer patients also showed higher than normal levels of the protein.

Dr. Arafat believes that osteopontin could be a drug target. "We are now proposing that perhaps blocking osteopontin can interfere with the progression of pancreatic cancer and other cancers," she says, adding that her team would like to understand more about osteopontin's effects on pancreatic cancer cell behavior. Dr. Arafat's group now is comparing differences in osteopontin expression between smokers and non-smokers.

"For example, if you put the cells with nicotine and block osteopontin, will the cells still be migratory? Is it osteopontin or something else in combination that is at work here?"

Pancreatic cancer, the fourth-leading cause of cancer death in this country, takes some 34,000 lives a year. The disease is difficult to treat; it frequently is detected after it has spread. Only 4 percent of individuals with pancreatic cancer live for five years after diagnosis, and about 25 percent of those who undergo successful surgical removal of their disease live at least that long.

Idea Lab

Total Recall

By GARY MARCUS

How much would you pay to have a small memory chip implanted in your brain if that chip would double the capacity of your short-term memory? Or guarantee that you would never again forget a face or a name?

There's good reason to consider such offers. Although our memories are sometimes spectacular — we are very good at recognizing photos, for example — our memory capacities are often disappointing. Faulty memories have been known to lead to erroneous eyewitness testimony (and false imprisonment), to marital friction (in the form of overlooked anniversaries) and even death (sky divers have been known to forget to pull their ripcords — accounting, by one estimate, for approximately 6 percent of sky-diving fatalities). The dubious dynamics of memory leave us vulnerable to the predations of spin doctors (because a phrase like "death tax" automatically brings to mind a different set of associations than "estate tax"), the pitfalls of stereotyping (in which easily accessible memories wash out less common counterexamples) and what the psychologist Timothy Wilson calls "mental contamination." To the extent that we frequently can't separate relevant information from irrelevant information, memory is often the culprit.

All this becomes even more poignant when you compare our memories to those of the average laptop. Whereas it takes the average human child weeks or even months or years to memorize something as simple as a multiplication table, any modern computer can memorize any table in an instant — and never forget it. Why can't we do the same?

Much of the difference lies in the basic organization of memory. Computers organize everything they store according to physical or logical locations, with each bit stored in a specific place according to some sort of master map, but we have no idea where anything in our brains is stored. We retrieve information not by knowing where it is but by using cues or clues that hint at what we are looking for.

In the best-case situation, this process works well: the particular memory we need just "pops" into our minds, automatically and effortlessly. The catch, however, is that our memories can easily get confused, especially when a given set of cues points to more than one memory. What we remember at any given moment depends heavily on the accidents of which bits of mental flotsam and jetsam happen to be active at that instant. Our mood, our environment, even our posture can all influence our delicate memories. To take but one example, studies suggest that if you learn a word while you happen to be slouching, you'll be better able to remember that word at a later time if you are slouching than if you happen to be standing upright.

And it's not just humans. Cue-driven memory with all its idiosyncrasies has been found in just about every creature ever studied, from snails to flies, spiders, rats and monkeys. As a product of evolution, it is what engineers might call a kluge, a system that is clumsy and inelegant but a lot better than nothing.

If we dared, could we use the resources of modern science to improve human memory? Quite possibly, yes. A team of Toronto researchers, for example, has shown how a technique known as deep-brain stimulation can make small but measurable improvements by using electrical stimulation to drive the cue-driven circuits we already have.

But techniques like that can only take us so far. They can make memories more accessible but not necessarily more reliable, and the improvements are most likely to be only incremental. Making our memories both more accessible and more reliable would require something else, perhaps a system modeled on Google, which combines cue-driven promptings similar to human memory with the location-addressability of computers.

However difficult the practicalities, there's no reason in principle why a future generation of neural prostheticists couldn't pick up where nature left off, incorporating Google-like master maps into neural implants. This in turn would allow us to search our own memories — not just those on the Web — with something like the efficiency and reliability of a computer search engine.

Would this turn us into computers? Not at all. A neural implant equipped with a master memory map wouldn't impair our capacity to think, or to feel, to love or to laugh; it wouldn't change the nature of what we chose to remember; and it wouldn't necessarily even expand the sheer size of our memory banks. But then again our problem has never been how much information we could store in our memories; it's always been in getting that information back out — which is precisely where taking a clue from computer memory could help.

Gary Marcus, professor of psychology at New York University, is the author of "Kluge: The Haphazard Construction of the Human Mind."

Celebrex-Lipitor combo may halt prostate cancer

Anti-inflammatory and statin used in tandem can stop progression of disease

NEW BRUNSWICK, N.J. – Researchers at Rutgers' Ernest Mario School of Pharmacy have shown that administering a combination of the widely used drugs Celebrex (celecoxib, a nonsteroidal anti-inflammatory drug) and Lipitor (atorvastatin, a cholesterol lowering drug) stops the transition of early prostate cancer to its more aggressive and potentially fatal stage.

Prostate cancer is the second leading cause of cancer death in men in the United States, with more than a quarter-million new cases appearing each year, according to the American Cancer Society. The findings are being presented by Rutgers Professor Xi Zheng at the annual meeting of the American Association for Cancer Research in San Diego, April 14th.

In the early stage of the disease, when it is typically diagnosed, prostate cancer cells depend on androgen hormones, such as testosterone, to grow. Treatment at this stage involves either decreasing the production of the hormone or blocking its actions on the cancer cells.

"Anti-androgen therapy slows the prostate cancer but eventually the cancer becomes androgen-independent, the therapy becomes ineffective and the cancer cells become more aggressive," said Xi Zheng, assistant research professor at Rutgers, The State University of New Jersey, who conducted the study.

"Treatments available for the later stage cancers are not very good," said Allan Conney, director of Rutgers' Susan Lehman Cullman Laboratory for Cancer Research, another researcher on the project. "Oncologists employ classical chemotherapy drugs which are very toxic and don't work all that well."

Zheng and Conney's research objective was to find a way to indefinitely delay the transition to androgen-independence, prolonging the time during which the cancer would be responsive to effective, low-toxicity, anti-hormone therapy.

Zheng explained that their experiments were first conducted on cell cultures in the laboratory, where the researchers tested the effects of the drugs on the growth of prostate cancer cells from four different cell lines. They then moved on to test the drugs on specially bred mice in which prostate cancer tumors were introduced under the skin. Celebrex alone, Lipitor alone, and the two in combination were tested at the lab bench and on the mice.

"A combination of low doses of Lipitor and Celebrex had a more potent inhibiting effect on the formation of later stage tumors than a higher dose of either agent alone," Zheng reported. "The results from our study indicate that a combination of Lipitor and Celebrex may be an effective strategy for the prevention of prostate cancer progression from the first to the second stage."

Zheng also noted that the team is exploring the underlying molecular mechanisms to understand how Lipitor and Celebrex work on prostate cancer, perhaps identifying an important signaling pathway for tumor cell growth that the drugs inhibit.

Conney pointed out that previous experiments reported in the Sept. 15, 2007, issue of Clinical Cancer Research had demonstrated that the Lipitor-Celebrex combination also inhibited the growth of prostate cancer cells in the later androgen-independent stage.

"So if you can affect the early stage and prevent it from becoming the more severe form, that's a good thing. If you can also inhibit the growth of the more severe form, that's also a good thing," Conney said.

Human clinical trials are being planned at the Robert Wood Johnson Medical School of the University of Medicine and Dentistry of New Jersey in New Brunswick.

"If the clinical trials go well, we could have something available in five years, but it would be nice to speed that up," Conney said. "If the trials show that the drug therapy does a good job of preventing the cancer from advancing, we won't need to worry about how to handle the more aggressive later stage cancer.

"This is something we hope is going to save lives," he added.

High blood pressure may protect against migraine

ST. PAUL, Minn. – People with high blood pressure appear to be less likely to have migraine than those with low blood pressure. Researchers say stiff arteries associated with high blood pressure may play a role in protecting against migraine. The research is published in the April 15, 2008, issue of Neurology®, the medical journal of the American Academy of Neurology.

Researchers tested the blood pressure of 51,353 men and women over the age 20 in Norway, including the systolic, diastolic and pulse pressure rates. Pulse pressure is the change in blood pressure when the heart contracts. The rate is determined by subtracting the diastolic blood pressure, the bottom number, from the systolic blood pressure, or the top number.

The participants also completed a survey on the presence and frequency of headaches and their use of blood pressure medications.

The study found people with higher systolic blood pressure were up to 40 percent less likely to have a headache or migraine compared to people with healthier blood pressure rates.

"Higher pulse pressure was linked to up to a 50-percent reduction in the amount of headache and migraine for both men and women," said study author Erling Tronvik, MD, with the Norwegian National Headache Center at Trondheim University Hospital in Trondheim, Norway. "The finding was not as strong, however, for people who were taking blood pressure medications, which are sometimes used to treat migraine."

Tronvik says both high systolic blood pressure and pulse pressure are related to stiff arteries and that may decrease the risk of headaches by affecting the baroreflex arch. "The baroreflex arch helps maintain blood pressure, but when it is affected, it can cause hypoalgesia, a condition that makes a person less sensitive to pain," said Tronvik.

Tronvik says these results confirm previous studies which have found that increasing blood pressure is linked to decreasing amounts of chronic pain in all parts of the body.

Testosterone levels predict city traders' profitability

Research provides insight into irrational decision making during crashes and bubbles

When City traders have high morning testosterone levels they make more than average profits for the rest of that day, researchers at the University of Cambridge have discovered.

The scientists hypothesize that this may be because testosterone has been found to increase confidence and appetite for risk – qualities that would augment the performance of any trader who had a positive expected return.

The influence of steroids naturally produced in the body (specifically testosterone and cortisol) may also provide insight into why people caught up in bubbles and crashes often find it difficult to make rational choices, unintentionally exacerbating financial crises.

Testosterone is a steroid hormone which controls competitive encounters as well as sexual behaviour. Testosterone in male athletes, for example, will rise prior to a competition and rise even further in a winning athlete (but decrease in a losing one). This increase of testosterone in the winner can increase confidence and risk taking and improve chances of winning yet again, leading to a positive-feedback loop termed the 'winner effect'. However, too much testosterone can have a detrimental affect on the ability to assess risk rationally.

In order to determine how hormone levels affect those working in the financial sector, the researchers followed 17 City of London male traders for eight consecutive business days. To measure the traders' hormones, they took saliva samples twice per day at 11:00 a.m. and 4:00 p.m., times that fell before and after the bulk of the day's trading. At each sampling time, traders recorded their profit and loss (P&L).

Using the trader's previous trading history, the scientists determined a daily-average to which they could compare the test results. They found that daily testosterone levels were significantly higher on days when traders made more than their one-month daily average than on other days.

The researchers also speculated that if testosterone continued to rise or became chronically elevated, it could begin to have the opposite effect on a trader's profitability by increasing risk-taking to unprofitable levels. Previous studies have shown that administered testosterone can lead to irrational decision-making. They believe that this is because testosterone has also been found to lead to impulsivity and sensation seeking, to harmful risk taking, and in extreme cases (among users of anabolic steroids) to euphoria and mania.

Testosterone may therefore underlie a secondary consequence of the 'winner effect' in which a previous win in the markets leads to increased, and eventually irrational, risk taking in the next round of trading.

Professor Joe Herbert, Cambridge Centre for Brain Repair, said: "Market traders, like some other occupations (such as air traffic controllers), work under extreme pressure and the consequences of the rapid decisions they have to make can have profound consequences for them, and for the market as a whole. Our work suggests that these decisions may be biased by emotional and hormonal factors that have not so far been considered in any detail.

"Any theory of financial decision-making in the highly demanding environment of market trading now needs to take these hormonal changes into account. Inappropriate risk-taking may be disastrous. Hormones may also be important for determining how well an individual trader performs in the highly stressful and competitive world of the market. We are now exploring this in much more detail."

The researchers also examined the effects of increased levels of cortisol, a hormone which plays a role in our response to stress, on traders. They found that it rose when the variance of the market and traders P&L rose. The results suggested that cortisol responds to economic uncertainty.

During the study, traders experienced acutely raised cortisol in association with higher volatility in the markets and the increased chances of making money that higher volatility brings. The researchers suggest, however, that rising cortisol levels can reduce appetite for risk: that is, affect a trader's risk taking in the opposite direction to testosterone. Cortisol is known to have powerful cognitive and emotional effects. Amongst these effects are heightened memory for adverse events, and alteration in mood.

Together, these effects would tend to decrease a trader's risk taking. A situation of persistently elevated cortisol might occur if financial market volatility were to rise for an extended period, something that normally happens when the economy receives an unwelcome shock or enters a depression.

Cortisol is likely, therefore, to rise in a market crash and, by increasing risk aversion, to exaggerate the market's downward movement. Testosterone, however, is likely to rise in a bubble and, by increasing risk taking, to exaggerate the market's upward movement. These steroid feedback loops may help explain why people caught up in bubbles and crashes often find it difficult to make rational choices.

Dr. John Coates, lead author, said, "Rising levels of testosterone and cortisol prepare traders for taking risk. However, if testosterone reaches physiological limits, as it might during a market bubble, it can turn risk-taking into a form of addiction, while extreme cortisol during a crash can make traders shun risk altogether."

Coates, himself a former trader, continued, "In the present credit crisis traders may feel the noxious effects of chronic cortisol exposure and end up in a psychological state known as 'learned helplessness'. If this happens central banks may lower interest rates only to find that traders still refuse to buy risky assets. At times like these economics has to consider the physiology of investors, not just their rationality."

Excess pneumonia deaths linked to engine exhaust

Atmospheric pollutants and mortalities in English local authority areas

Engine exhaust fumes are linked to excess deaths from pneumonia across England, suggests research published in the Journal of Epidemiology and Community Health.

The annual death toll is comparable to that caused by the London smog in 1952, suggests the author.

Data on atmospheric emissions, published causes of death, and expected causes of death for 352 local authority jurisdictions in England were combined to calculate the impact of pollution on death rates between 1996 and 2004.

Levels of air pollution varied substantially among the local authorities.

Calculations revealed that pneumonia, peptic ulcer, coronary and rheumatic heart diseases, lung and stomach cancers, and other diseases, were all associated with a range of emissions, as well as deprivation, smoking, binge drinking and a northern location.

Further analysis, allowing for the effects of the social factors, showed that pneumonia deaths were strongly and independently linked to emissions, with the exception of sulphur dioxide from coal burning.

The primary culprits were emissions associated with oil combustion, including vehicle exhaust fumes.

During the eight years of the study there were almost 390.000 deaths from pneumonia.

And 35 local authorities accounted for almost 54,000 of these deaths, or around15,,000 more than would be expected.

"Total annual losses as a result of air pollution probably approach those of the 1952 London smog," writes the author.

Because the links were so strong across all categories of exposure and deaths were so much higher than would be expected, this suggests that these pollutants directly damage lung tissue, he says.

Excess deaths from the progressive lung disease COPD (Chronic Obstructive Pulmonary Disease) and rheumatic heart disease, both of which are characterised by failing lung function, could also be precipitated by engine exhaust, he adds.

Calorie restriction inhibits, obesity fuels development of epithelial cancers

M.D. Anderson-led team connects dietary balance to common cancer pathways

SAN DIEGO - A restricted-calorie diet inhibited the development of precancerous growths in a two-step model of skin cancer, reducing the activation of two signaling pathways known to contribute to cancer growth and development, researchers at The University of Texas M. D. Anderson Cancer Center report today at the American Association for Cancer Research annual meeting.

An obesity-inducing diet, by contrast, activated those pathways, said first author Tricia Moore, a graduate student in M. D. Anderson's Department of Carcinogenesis.

"These results, while tested in a mouse model of skin cancer, are broadly applicable to epithelial cancers in other tissues," said senior author John DiGiovanni, Ph.D., director of the Department of Carcinogenesis and of M.D. Anderson's Science Park - Research Division in Smithville, Texas.

Epithelial cancers arise in the epithelium - the tissue that lines the surfaces and cavities of the body's organs. They comprise 80 percent of all cancers.

"Calorie restriction and obesity directly affect activation of the cell surface receptors epidermal growth factor (EGFR) and insulin-like growth factor (IGF-1R)," Moore said. "These receptors then affect signaling in downstream molecular pathways such as Akt and mTOR."

"Calorie restriction, which we refer to as negative energy balance, inhibits this signaling, and obesity, or positive energy balance, enhances signaling through these pathways, leading to cell growth, proliferation and survival," Moore said.

Dietary energy balance refers to the relationship between caloric intake and energy expenditure. Previous research, both experimental and epidemiological, suggests that chronic positive energy balance, which can lead to obesity, increases the risk of developing a variety of cancers, DiGiovanni said, while negative balance often decreases risk.

This study employed four diets, two representing calorie reductions of 30 percent and 15 percent, a control diet including 10 percent kilocalories from fat, and an obesity-inducing diet consisting of 60 percent kilocalories from fat. Agents were then given to the mice to induce premalignant lesions called papillomas, which are precursors to cancer.

Those on the calorie restricted diets had statistically significant inhibition of papilloma formation compared with the other two diets.

In a separate experiment the development of carcinomas and the effect of dietary energy balance on conversion of papillomas to carcinomas was evaluated. This study demonstrated that dietary energy balance determines the number of carcinomas found through its effects on the number of premalignant lesions but does not affect the rate of malignant conversion.

Akt and mTOR pathways are known to be important for skin tumor development in this model system. In addition, increased Akt and mTOR signaling are linked to the growth, proliferation and survival of many human cancers.

"These findings provide the basis for future translational studies targeting Akt/mTOR pathways through combinations of lifestyle and pharmacologic approaches to prevent and control obesity-related epithelial cancers in humans," DiGiovanni said.

The research was funded by grants from both the National Cancer Institute and National Institute of Environmental Health Sciences.

Co-authors with Moore and DiGiovanni are Steve Carbajal, Anna Jiang, Linda Beltran, and Steve Hursting of M. D. Anderson's Science Park-Research Division. Moore, DiGiovanni and Hursting are also affiliated with the University of Texas at Austin Division of Nutritional Sciences.

Unconscious decisions in the brain

A team of scientists has unravelled how the brain unconsciously prepares our decisions

Already several seconds before we consciously make a decision its outcome can be predicted from unconscious activity in the brain. This is shown in a study by scientists from the Max Planck Institute for Human Cognitive and Brain Sciences in Leipzig, in collaboration with the Charité University Hospital and the Bernstein Center for Computational Neuroscience in Berlin. The researchers from the group of Professor John-Dylan Haynes used a brain scanner to investigate what happens in the human brain just before a decision is made. "Many processes in the brain occur automatically and without involvement of our consciousness. This prevents our mind from being overloaded by simple routine tasks. But when it comes to decisions we tend to assume they are made by our conscious mind. This is questioned by our current findings." (Nature Neuroscience, April 13th 2008)

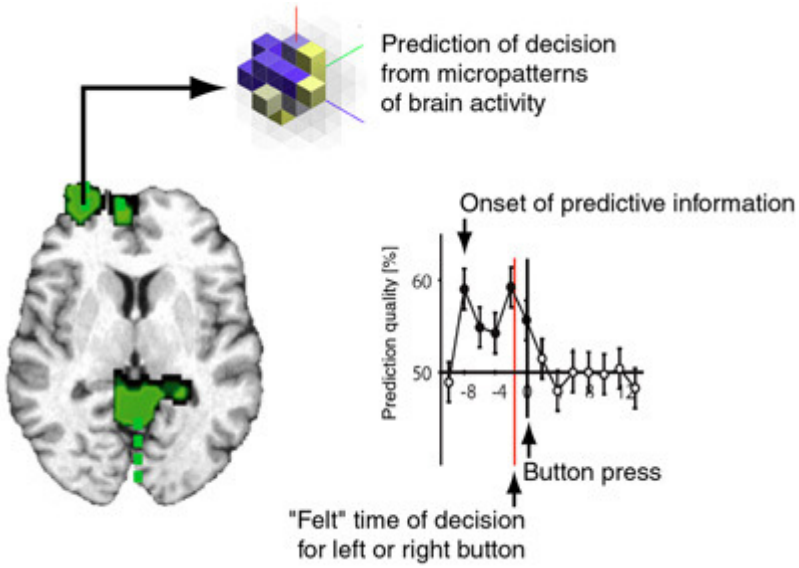

***Fig.: Brain regions (shown in green) from which the outcome of a participant's decision can be predicted before it is made. The top shows an enlarged 3D view of a pattern of brain activity in one informative brain region. Computer-based pattern classifiers can be trained to recognize which of these micropatterns typically occur just before either left or right decisions. These classifiers can then be used to predict the outcome of a decision up to 7 seconds before a person thinks he is consciously making the decision*. Image: John-Dylan Haynes**

In the study, participants could freely decide if they wanted to press a button with their left or right hand. They were free to make this decision whenever they wanted, but had to remember at which time they felt they had made up their mind. The aim of the experiment was to find out what happens in the brain in the period just before the person felt the decision was made. The researchers found that it was possible to predict from brain signals which option participants would take already seven seconds before they consciously made their decision. Normally researchers look at what happens when the decision is made, but not at what

happens several seconds before. The fact that decisions can be predicted so long before they are made is a astonishing finding.

This unprecedented prediction of a free decision was made possible by sophisticated computer programs that were trained to recognize typical brain activity patterns preceding each of the two choices. Micropatterns of activity in the frontopolar cortex were predictive of the choices even before participants knew which option they were going to choose. The decision could not be predicted perfectly, but prediction was clearly above chance. This suggests that the decision is unconsciously prepared ahead of time but the final decision might still be reversible.

"Most researchers investigate what happens when people have to decide immediately, typically as a rapid response to an event in our environment. Here we were focusing on the more interesting decisions that are made in a more natural, self-paced manner", Haynes explains.

More than 20 years ago the American brain scientist Benjamin Libet found a brain signal, the so-called "readiness-potential" that occurred a fraction of a second before a conscious decision. Libet's experiments were highly controversial and sparked a huge debate. Many scientists argued that if our decisions are prepared unconsciously by the brain, then our feeling of "free will" must be an illusion. In this view, it is the brain that makes the decision, not a person's conscious mind. Libet's experiments were particularly controversial because he found only a brief time delay between brain activity and the conscious decision.

In contrast, Haynes and colleagues now show that brain activity predicts even up to 7 seconds ahead of time how a person is going to decide. But they also warn that the study does not finally rule out free will: "Our study shows that decisions are unconsciously prepared much longer ahead than previously thought. But we do not know yet where the final decision is made. We need to investigate whether a decision prepared by these brain areas can still be reversed."

Original work: *Chun Siong Soon, Marcel Brass, Hans-Jochen Heinze & John-Dylan Haynes Unconscious determinants of free decisions in the human brain. Nature Neuroscience April 13th, 2008.*

Clues to ancestral origin of placenta emerge in Stanford study

STANFORD, Calif. - Researchers at the Stanford University School of Medicine have uncovered the first clues about the ancient origins of a mother's intricate lifeline to her unborn baby, the placenta, which delivers oxygen and nutrients critical to the baby's health.

The evidence suggests the placenta of humans and other mammals evolved from the much simpler tissue that attached to the inside of eggshells and enabled the embryos of our distant ancestors, the birds and reptiles, to get oxygen.

"The placenta is this amazing, complex structure and it's unique to mammals, but we've had no idea what its evolutionary origins are," said Julie Baker, PhD, assistant professor of genetics. Baker is senior author of the study, which will be published in the May issue of Genome Research.

The placenta grows inside the mother's uterus and serves as a way of exchanging gas and nutrients between mother and fetus; it is expelled from the mother's body after the birth of a baby. It is the only organ to develop in adulthood and is the only one with a defined end date, Baker said, making the placenta of interest to people curious about how tissues and organs develop.

Beyond being a biological curiosity, the placenta also plays a role in the health of both the mother and the baby. Some recent research also suggests that the placenta could be a key barrier in preventing or allowing molecules to pass to the unborn baby that influence the baby's disease risk well into adulthood.

"The placenta seems to be critical for fetal health and maternal heath," Baker said. Despite its major impact, almost nothing was known about how the placenta evolved or how it functions.

Baker and Kirstin Knox, graduate student and the study's first author, began addressing the question of the placenta's evolution by determining which genes are active in cells of the placenta throughout pregnancy in mice.

They found that the placenta develops in two distinct stages. In the first stage, which runs from the beginning of pregnancy through mid-gestation, the placental cells primarily activate genes that mammals have in common with birds and reptiles. This suggests that the placenta initially evolved through repurposing genes the early mammals inherited from their immediate ancestors when they arose more than 120 million years ago.

In the second stage, cells of the mammalian placenta switch to a new wave of species-specific genes. Mice activate newly evolved mouse genes and humans activate human genes.

It makes sense that each animal would need a different set of genes, Baker said. "A pregnant orca has different needs than a mouse and so they had to come up with different hormonal solutions to solve their problems," she said. For example, an elephant's placenta nourishes a single animal for 660 days. A pregnant mouse gestates an average of 12 offspring for 20 days. Clearly, those two pregnancies would require very different placentas.

Baker said these findings are particularly interesting given that cloned mice are at high risk of dying soon after the placenta's genetic transition takes place. "There's obviously a huge regulatory change that takes place," she said. What's surprising is that despite the dramatic shift taking place in the placenta, the tissue doesn't change in appearance.

Understanding the placenta's origins and function could prove useful. Previous studies suggest the placenta may contribute to triggering the onset of maternal labor, and is suspected to be involved in a maternal condition called pre-eclampsia, which is a leading cause of premature births.

Baker intends to follow up on this work by collaborating with Theo Palmer, PhD, associate professor of neurosurgery; Gill Bejerano, PhD, assistant professor of developmental biology, and Anna Penn, MD, PhD, assistant professor of pediatrics. Together, the group hopes to learn how the placenta protects the growing brain of the unborn baby, a protection that seems to extend into adulthood.

The work was funded by the National Institutes of Health, the March of Dimes and Stanford's Medical Scientist Training Program.

Too many choices -- good or bad -- can be mentally exhausting

Researchers show that people have less stamina, are less productive when they have more choices

WASHINGTON – Each day, we are bombarded with options -- at the local coffee shop, at work, in stores or on the TV at home. Do you want a double-shot soy latte, a caramel macchiato or simply a tall house coffee for your morning pick-me-up" Having choices is typically thought of as a good thing. Maybe not, say researchers who found we are more fatigued and less productive when faced with a plethora of choices.

Researchers from several universities have determined that even though humans' ability to weigh choices is remarkably advantageous, it can also come with some serious liabilities. People faced with numerous choices, whether good or bad, find it difficult to stay focused enough to complete projects, handle daily tasks or even take their medicine.

These findings appear in the May issue of Journal of Personality and Social Psychology, which is published by the American Psychological Association.

Researchers conducted seven experiments involving 328 participants and 58 consumers at a shopping mall. In the laboratory experiments, some participants were asked to make choices about consumer products, college courses or class materials. Other participants did not have to make decisions but simply had to consider the options in front of them.

The scientists then asked each group to participate in one of two unpleasant tasks. Some were told to finish a healthy but ill-tasting drink (akin to taking ones medicine). Other participants were told to put their hands in ice water. The tasks were designed to test how the previous act of choosing, or not choosing, affected peoples' ability to stay on task and maintain behaviors aimed at reaching a goal.

Researchers found that the participants who earlier had made choices had more trouble staying focused and finishing the disagreeable but goal-focused tasks compared to the participants who initially did not have to make choices.

In other experiments, participants were given math problems to practice for an upcoming test. The participants who had to make important choices involving coursework spent less time solving the math problems and more time engaging in other distractions such as playing video games or reading magazines, compared to participants who were not asked to make choices prior to that point. The participants who made choices also got more math problems wrong than participants not faced with decisions.

To further buttress their laboratory findings, the researchers conducted a field test at a shopping mall. The shoppers reported how much decision-making they had done while shopping that day and then were asked to solve simple arithmetic problems. The researchers found that the more choices the shoppers had made earlier in the day, the worse they performed on the math problems. The authors note they controlled for how long the participants had been shopping, and for several demographic categories such as age, race, ethnicity and gender.

Kathleen D. Vohs, PhD, the study's lead author and a member of the University of Minnesota's marketing department, concluded that making choices apparently depletes a precious resource within the human mind. "Maintaining one's focus while trying to solve problems or completing an unpleasant task was much harder for those who had made choices compared to those who had not," says Vohs. "This pattern was found in the laboratory, classroom and shopping mall. Having to make the choice was the key. It did not matter if the researchers told them to make choices, or if it was a spontaneously made choice, or if making the choice had consequences or not."

But what about making fun choices" How does that affect our mental acuity" In their last experiment, researchers determined that making a few enjoyable decisions, such as spending four minutes selecting items for a gift registry, was shown to be less mentally draining than when participants spent 12 minutes doing the

same task. In other words, even if people are having fun making decisions, their cognitive functions are still being depleted with every choice they make.

Vohs says these experiments provide evidence that making choices, as opposed to just thinking about options, is what is especially taxing. "There is a significant shift in the mental programming that is made at the time of choosing, whether the person acts on it at that time or sometime in the future. Therefore, simply the act of choosing can cause mental fatigue," says Vohs. "Making choices can be difficult and taxing, and there is a personal price to choosing."

Article: "Making Choices Impairs Subsequent Self-Control: A Limited-Resource Account of Decision Making, Self-Regulation, and Active Initiative," Kathleen D. Vohs, PhD, and Noelle M. Nelson, PhD, University of Minnesota; Roy Baumeister, PhD, Florida State University; Brandon J. Schmeichel, PhD, Texas A&M University; Jean M. Twenge, PhD, San Diego State University; Dianne M. Tice, PhD, Florida State University; Journal of Personality and Social Psychology, Vol. 94, No. 5

Full text of the article is available from the APA Public Affairs Office and at
http://www.apa.org/journals/releases/psp945883.pdf

Hayabusa asteroid probe may never return to Earth

* Updated 21:06 14 April 2008
* NewScientist.com news service
*** Elise Kleeman**

Even though Japan's problem-plagued Hayabusa spacecraft is now on its return trip to Earth, it might never complete the journey. A catastrophic failure of its last remaining reaction wheel, which helps point the craft, might prevent it from reaching the Earth to drop a capsule into the atmosphere, mission members say.

Hayabusa was meant to collect samples from the asteroid Itokawa by firing pellets into the surface of the 535-metre-long rock and scooping up the resulting debris. But data from two landings in November 2005 suggest the pellets never fired because the craft's onboard computer sent conflicting signals to its collection instruments.

***Hayabusa was meant to collect samples by firing pellets into the surface of the asteroid Itokawa and scooping up the resulting debris* (Image: JAXA)**

Still, mission officials hoped to bring the spacecraft back to Earth in case some asteroid dust had slipped into its collection chamber by chance. If it completes the trip, it is expected to drop a capsule in the Australian outback in June 2010.

But Hayabusa's project manager, Jun'ichiro Kawaguchi, told New Scientist that if any other systems break down, it could be fatal to the mission. He is particularly concerned about the spacecraft's last remaining reaction wheel. "We are eager to make it return with our best efforts, but the situation is not optimistic," he says.

Weak thrusters

Mission managers are now pointing Hayabusa using jets of xenon gas from the craft's ion propulsion system. The relatively weak thrusters, which use electric fields to accelerate a beam of xenon ions, were originally designed only to propel the craft forwards on its 2-billion-kilometre round trip to Itokawa.

Without the ability to aim the spacecraft, mission engineers could not maintain communication with Hayabusa or keep it on the right trajectory to return to Earth. The team lost contact once before, in late 2005, and regained it only three months later. A glitch this time would probably be permanent.

Despite these worries, mission planners could still pull off a safe landing, according to Hayabusa team member Don Yeomans of NASA's Jet Propulsion Laboratory in Pasadena, California, US. "I wouldn't bet against them – they're doing pretty well," he says.

Indeed, the team from the Japanese Aerospace Exploration Agency has managed to keep Hayabusa flying despite a long list of near-catastrophic failures, including the leaks of critical fuel and a temporary loss of contact with the spacecraft that caused its return to Earth to be delayed by three years.

Plucky spacecraft

"Yeah, the spacecraft is hurting," Yeomans says. "It's a credit to the Japanese that they've had some work-arounds. It's the little spacecraft that could."

During the mission, engineers also suffered the disappearance of the miniature robot Minerva, which was supposed to hop across the surface of asteroid surface but instead was accidentally released to drift off into space.

Despite these setbacks, Hayabusa was successful in returning "stunning images" of Itokawa, Yeomans says. The pictures and other data collected by the craft revealed an unexpectedly crater-free surface and loosely compacted body.

"It seems to be what we call a rubble pile, an object that was blasted apart and is held together by not much more than its own gravity," he says.

"Mostly we're just marking time until the sample capsule gets back," Yeomans adds. "Hopefully the sample will get back."

Dumbo didn't fly – he swam

* 22:00 14 April 2008
* NewScientist.com news service
*** Jeff Hecht**

Did elephants' trunks evolve to function as snorkels? This suggestion might be outlandish but new fossils make a strong case that extinct relatives of elephants were aquatic.

Speculation about a watery stage in the evolution of the world's largest land mammal has continued on and off for years, but now palaeontologists have solid evidence that relatives of elephants lived in freshwater swamps or rivers near the coast of what is now Egypt.

Elwyn Simons of Duke University in North Carolina and colleagues analysed the teeth of ***Moeritherium***, an elephant ancestor the size of a large hog that lived 37 million years ago. The teeth have uniformly low levels of oxygen-18, a distinctive signature of organisms that live in fresh water. And their carbon-13 levels indicate that the animal ate freshwater plants.

Oxygen and carbon isotope levels are similar in the teeth of Barytherium, a much larger but poorly known beast more closely related to modern elephants.

No connection

Simons says that the results suggest that the ancestors of modern elephants went through an aquatic or semi-aquatic stage before going back to the land.

William Sanders of the University of Michigan agrees that both Moeritherium and Barytherium were aquatic but says neither was on the direct line to elephants.

He also dismissed the "trunk-as-snorkel" hypothesis, arguing that trunks grew long to reach beyond the elephants' tusks. He doubts that purely aquatic traits would have remained long after ancestral forms left the water.

Paleomastodons, which are direct ancestors of elephants, were fully terrestrial when they appeared around 30 million years ago, but no one knows what their ancestors were or what they were doing. Simons hopes that isotopic studies of other fossils might provide the answer.

Journal reference: Proceedings of the National Academy of Sciences (DOI: 10.1073/pnas.0800884105)

Sexually transmitted bug is the strongest organism

* 22:00 14 April 2008
* NewScientist.com news service
*** Debora MacKenzie**

Pound-for-pound, it's the strongest organism ever. This mighty beast is the gonorrhea bacterium – the strongest creature alive.

These tiny creatures can pull with a force equal to 100,000 times their body weight – as though a human could drag 10 million kilos.

Many bacteria produce filaments called pili. These are a hundred times as long as they are wide and up to ten times longer than the bacterium itself. They can also contract. Scientists knew that Neisseria gonorhoeae bacteria use "type four" pili to crawl along a surface and to attach to cells and infect them.

What they didn't know was that these bacteria can bundle pili together to exert long, strong pulls. Michael Sheetz and colleagues at Columbia University in New York put the bacteria in a field of tiny gel "pillars" and measured the amount the bacteria could bend them as a way of measuring the force of their pull.

Short and long

They mostly saw a lot of short grabs. But one pull in a hundred started out at the same strength as these short pulls, then increased in increments about equal to the force of the original pull, as if the bacteria were calling in more individual pili to help out the first.

This eventually resulted in a pull that was up to ten times stronger than the initial short grab, and it could last for several hours.

See video of the bacteria pulling the pillars here and here.

Electron microscopic images confirmed the bundles. They also revealed that the reason scientists have not seen this before is because a protein usually added to bacterial culture medium happens to block it.

Great motor

The actual force the bacteria exerted was around a nanoNewton, or one billionth of a Newton, the force you would need to accelerate a kilogram by a metre per second squared.

Not a lot – but it means the bacteria can pull with a force equivalent to 100,000 times its bodyweight, and hold it. This, say the authors, makes the retraction protein in the pili "the strongest biological motor known to date".

"This constitutes a new paradigm for the generation of forces in the biological realm," Sheetz and colleagues say, and could completely change our understanding of the way gonorrhea bacteria muscle up to cells and infect them.

Journal reference: PLoS Biology (DOI: 10.1371/journal.pbio.0060087)

JCSM: A single subjective question can be an effective sleepiness screening tool

WESTCHESTER, Ill. – A single subjective (SS) question may be an effective screening tool for excessive daytime sleepiness, according to a study published in the April 15 issue of the Journal of Clinical Sleep Medicine (JCSM).

Sarah Nath Zallek, MD, of the Illinois Neurological Institute Sleep Center in Peoria, Ill., sought to determine whether the following single question about sleepiness can measure subjective sleepiness comparably to the Epworth Sleepiness Scale (ESS):

"Please measure your sleepiness on a typical day: (0 = none, 10 is highest)."

The study focused on 303 subjects between 18-78 years of age, who had been diagnosed with a variety of sleep disorders, including obstructive or central sleep apnea, narcolepsy, periodic limb movement disorder, restless legs syndrome, psychophysiological insomnia, inadequate sleep hygiene, and idiopathic hypersomnia. ESS scores ranged from 0-24, while SS scores ranged from 0-10.

According to Dr. Zallek, the finding that the single question used in this study had significant associations with the ESS in all subject groups and was able to distinguish between "subjectively sleepy" and "subjectively not sleepy" groups suggests the SS is a good measure of subjective sleepiness.

"Excessive sleepiness is an important and widespread symptom of insufficient sleep and a variety of sleep disorders," said Dr. Zallek. "It increases the risk of accidents and injuries, and leads to lost work productivity. Recognition of sleepiness is the first step to finding a cause and treating it. Most physicians don't use the existing questionnaires to determine if someone is excessively sleepy. Sleepiness often goes unrecognized."

By using a single question to detect excessive sleepiness, one can quickly determine who might need further evaluation, noted Dr. Zallek.

"This scale can also assess change in an individual's sleepiness over time. This study provides individuals, physicians, and employers a simple, single question to initiate an evaluation of this important symptom," added Dr. Zallek.

On average, most adults need seven to eight hours of nightly sleep to feel alert and well-rested.

The American Academy of Sleep Medicine (AASM) offers the following tips on how to get a good night's sleep:

* Follow a consistent bedtime routine.
* Establish a relaxing setting at bedtime.
* Get a full night's sleep every night.
* Avoid foods or drinks that contain caffeine, as well as any medicine that has a stimulant, prior to bedtime.
* Do not bring your worries to bed with you.
* Do not go to bed hungry, but don't eat a big meal before bedtime either.
* Avoid any rigorous exercise within six hours of your bedtime.
* Make your bedroom quiet, dark and a little bit cool.
* Get up at the same time every morning.

Chinese Herbal Medications for Dysmenorrhea: A Best Evidence Review

Charles P. Vega, MD

Abstract

The study that this review is based on was selected from Medscape Best Evidence, which uses the McMaster Online Rating of Evidence System. Out of a possible top score of 7, this study was ranked as 7 for newsworthiness and 6 for relevance by clinicians who used this system.

Summary

Primary dysmenorrhea is a common condition that can have a significant impact on the lives of women. Although currently available treatments may be effective for dysmenorrhea, many young women may not seek treatment and are unaware of treatment options. Chinese herbal medications may be an attractive treatment alternative for many women, but there are questions regarding their efficacy. The current review highlights this issue as well as challenges in applying medical practices across different cultures.

Commentary

Background

Primary dysmenorrhea may occur in more than half of young women. A population-based study in Canada found that 60% of respondents met diagnostic criteria for primary dysmenorrhea.[1] More than half of these

women had moderate or severe pain, and 51% also reported that dysmenorrhea symptoms limited their activities. Whereas increasing age and smoking increased the risk for dysmenorrhea, age at menarche and nulliparity status did not affect the risk for symptoms.

Another survey of young women in secondary school demonstrated an even higher rate of primary dysmenorrhea, with a prevalence of 80%.[2] More than one third of subjects reported that dysmenorrhea interfered with their school activities, but only 18% had seen a physician for their symptoms. Women in this trial were generally naive regarding the treatment of dysmenorrhea. Medications had been used by 58% of the subjects to treat their symptoms, but most of these women had used only simple analgesics. These medications were considered effective in only 53% to 59% of those using them.

Given the lack of knowledge and perceived inefficacy of commonly used medications for dysmenorrhea, many patients may consider the use of complementary treatment for their symptoms. This reflects a larger healthcare trend in Western countries. A survey of medication use in American households between 1998 and 2004 demonstrated that the rate of use of natural and herbal supplements was 9.5%, 12%, and 19% among African Americans, Hispanics, and non-Hispanic white respondents.[3] Hispanics used the widest variety of different products.

Another recent study examined factors associated with the use of herbal therapy in the United States.[4] These factors included:

* Age between 45 and 64 years old;
* Female gender;
* Having a higher education level;
* Being uninsured; and
* Living in the Western United States.

Of subjects who used herbal medications, 72% were also receiving prescription medications. The most popular herbal medications were echinacea, ginseng, and ginkgo.

Current Review

The current systematic review generally supports the use of Chinese herbal medicine for the treatment of primary dysmenorrhea, but it also highlights some of the difficulties in applying Western standards of evidence-based medicine to treatments used for thousands of years in the Far East. The review considered only trials of treatment of primary dysmenorrhea, and of interest, focused on trials in which women had previously received nonsteroidal anti-inflammatory medications (NSAIDs) or hormones for dysmenorrhea. The main study outcome was the reduction in pain associated with treatment; others included additional analgesia and quality of life.

Thirty-nine trials of Chinese herbal medication for dysmenorrhea were fully reviewed, but many of these trials had methodologic problems. In particular, 18 trials were not randomized, and 4 other trials failed to mention randomization.

Most research was conducted in mainland China, and the use of traditional Chinese medicine significantly affected the way the research was conducted. Chinese medicine emphasizes a different approach to patient symptoms and diagnosis compared with Western medicine, with a greater emphasis on clusters of symptoms across different organ systems. The clusters of symptoms in most of the studies examining the treatment of dysmenorrhea were consistent with the Western definitions of dysmenorrhea, but 19 studies used variations in the herbal treatment protocol based on individual participant's diagnostic patterns.

Only 3 studies compared Chinese herbal medications with placebo; most of the other trials compared herbal treatments with:

* NSAIDs;
* Hormonal therapy; or
* Other Chinese herbal treatments.

The size of all included studies was small, with only 1 trial involving more than 100 patients. Most participants in the trials received multiple herbal treatments, although the dosage ranges of these many different therapies (19 main herbs were investigated) generally conformed to standard Chinese practice.

Results of The Cochrane Review

Regardless of these study limitations, Chinese herbal medications were generally effective against dysmenorrhea. Herbal medications were approximately twice as likely to improve pain compared with conventional therapy. In particular, Meiguihua (Rosa rugosa Thunb) was demonstrated to reduce dysmenorrhea-associated symptoms (pain, stress, and anxiety) over a 6-month time course:

Chinese herbal medications can also be rapidly effective against dysmenorrhea; one trial demonstrated an analgesic effect within 30 minutes. There was evidence as well that Chinese herbal medications may reduce patients' use of other analgesic medications for dysmenorrhea.

Chinese herbal medications were superior to over-the-counter health supplements in improving dysmenorrhea. A tailored herbal regimen was more than twice as likely to improve dysmenorrhea as a routine herbal preparation available without a prescription. However, the lack of standardization of herbal preparations and t that there was little confirmatory research to establish the efficacy of a specific herbal remedy precluded any recommendation for a particular treatment regimen. Chinese herbal medication was also found to be superior to acupuncture for dysmenorrhea in 2 trials.

Adverse events associated with study therapy were reported in only 8 of the 39 trials. There were no significant events found with either Chinese herbal medications or the comparator agents.

How to apply the results of this meta-analysis in Western medical practice is a difficult dilemma. First, the methodologic limitations of these studies must be considered. More practically speaking, it seems clear that some experience with Chinese herbal medications would be necessary before effectively prescribing these treatments for dysmenorrhea. Although the herbal formulas may be generally effective, they involve multiple agents in each treatment regimen, and this regimen appears to be most effective when it is individualized to each patient's symptoms.

Context -- Other Research of Chinese Herbal Medication

Given the barriers of translating research about Chinese herbal medications into Western medical practice, healthcare providers would be well-advised to focus on objective, evidence-based reviews by individuals with some expertise in the field of Chinese medicine. The Cochrane Database of Systematic Reviews has previously examined the potential role of Chinese herbal medications for the treatment of type 2 diabetes.[5] This review examined 66 different trials involving 8302 participants. Similar to the current review regarding dysmenorrhea, there was significant heterogeneity between studies in almost every aspect, and the methodologic quality of studies was generally low. The studies included 69 different treatments, and the majority of studies compared herbal medications with established medications for diabetes, usually sulfonylureas.

At least 6 different herbal preparations were demonstrated to have hypoglycemic effects, and 15 herbal preparations were synergistic with traditional diabetes medications in improving glycemic control. Ginseng, which is one of the most popular supplements in the United States, was not effective in improving glucose control. Despite these generally positive results, the review recommended further study of any of the Chinese herbal medications prior to their routine use in treating type 2 diabetes.

Chinese Herbs and the Common Cold. Healthcare providers have multiple options to effectively treat dysmenorrhea and type 2 diabetes, but there are no truly effective treatment options for the common cold. Another systematic review examined the efficacy of Chinese herbal medications for this familiar malady.[6] Researchers focused on 14 studies involving 2440 participants. This research was limited because herbal medications were compared with drugs that were considered to be effective for viral upper respiratory infections rather than with placebo, which would have been a more effective means to study this issue. Another overall limitation of these studies was the poor quality of randomization in the clinical trials.

Nonetheless, this review also provides some positive results for Chinese herbal medications. Five studies demonstrated superior efficacy of herbal preparations over active control medications in promoting recovery from the common cold, and another 8 studies demonstrated equivalence of the herbal medication and active control in this outcome.

Conclusion

Traditional Chinese medicine has proven itself through the test of time, and it has much to offer patients around the world. However, the previous studies of the efficacy of Chinese herbal medications as well as the current review of herbal preparations for dysmenorrhea highlight the difficulty of translating medical treatment across cultures. The currently available research is not only limited regarding methodology in determining the efficacy of Chinese herbal medications, but also of importance, many of these studies do not adequately address concerns regarding tolerability and safety.

More high-quality research focused on Chinese herbal medications is forthcoming, but until that time, it appears that the most prudent approach for the incorporation of these medications in clinical practice is to partner with a practitioner who has significant experience in their use. The wealth of experience and knowledge accumulated over time is the strength of traditional Chinese medicine, and healthcare providers should build relationships and treatment teams with experienced providers to provide the most complete and effective care for a variety of patient conditions.

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Best Evidence Reference *Chinese Herbal Medicine for Primary Dysmenorrhea*
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Cochrane Database of Systemic Reviews. 2007; Issue 4. Article No. CD005288

Well

Raves (Yes, It's True) for New Hearing Aid

By TARA PARKER-POPE

Few products are hated as much as hearing aids.

The devices can squeal with feedback and overamplify background noises like the click of a turn signal or whir of a ceiling fan. They must be removed for showering or sleeping, and their batteries die frequently. Many users, out of exasperation, decide they'd rather live with hearing loss.

But now scientists have come up with a different kind of hearing aid. While the device, called the Lyric, is being used in only 500 patients, it appears to have overcome many of the problems associated with traditional hearing aids — without the expense and uncertainty of surgery and anesthesia.

The Lyric, made by InSound Medical of Newark, Calif., is hidden deep inside the ear canal, just four millimeters (about one-sixth of an inch) from the ear drum. While doctors for years have been implanting hearing devices in the middle ear, the Lyric is not an implant: it can be removed with a small magnet. It is worn 24 hours a day, and its batteries last one to four months.

Stuart Bradford

Typically, anything that clogs the ear canal would trap moisture and pose an infection risk, but the Lyric is surrounded by a spongy material that allows moisture to escape. Because it sits so close to the ear drum, doctors say that it works more efficiently and that sounds are more natural because they don't have to be amplified as much.

When the Lyric's battery dies, the entire device is replaced. Patients do not pay for a new device every time; instead, they pay an annual subscription fee of $2,900 to $3,600 for both ears (less if the hearing loss is in only one ear). Insurance plans typically do not cover the cost of the Lyric, or any other hearing device.

A magnet is used to control the volume, turn it on and off and remove it when the battery runs out. It takes only a few minutes for a doctor to insert a replacement device.

The Lyric does not work for everyone. In particular, some ear canals are too narrow to accommodate it, and the company estimates that it is not suitable for up to half of potential patients. A planned newer version should work for about 85 percent of patients, it says.

Still, it is already getting an enthusiastic reception from patients and from hearing specialists not connected with the company. "There are a certain number of patients who just can't get over having something in their ear, just as there are a certain number of patients who can't wear contact lenses," said Dr. Chester F. Griffiths, chairman of the department of surgery at the Santa Monica U.C.L.A. Medical Center. "But that's the minority. The patients that have them love them."

Dr. Griffiths says he has no financial ties to the Lyric, nor does he receive a commission for referring patients.

One patient who swears by the device is Mike Waufle, the 53-year-old defensive line coach for the New York Giants. After a stint in the Marines and regular exposure to the sounds of gunfire, Mr. Waufle suffered hearing loss that grew worse and worse as he aged.

On the football field, he just turned up the volume on his headset. But the locker room was a different story. Some voices were impossible to hear (including that of his last boss, Jon Gruden, the former Oakland Raiders head coach). Players learned they needed to face him when they spoke to him. Using a traditional hearing aid, he found it difficult to control his own voice.

"I teach a lot in a classroom as a coach, but when I would wear a hearing aid my voice pattern wasn't very good," he said. "It was all over the place. I just took it out most of the time. I missed an awful lot."

As it happened, a team doctor was one of a handful of physicians test-marketing the Lyric, which has been available for about 16 months. Mr. Waufle tried it, and he says it has changed his life.

"My voice pattern is so natural, and I hear so much better," he said. "Obviously, it's easier to carry on normal conversations without having to always say, 'Huh? What did you say?' And it helps just enjoying life over all and being able to hear the simple things like birds and other sounds you take for granted."

Mr. Waufle says he has no financial ties to the company and receives no benefit for talking about his experience with the device. (The company says none of the people featured in testimonials on its Web site, www.lyrichearing.com, receive any form of compensation for their endorsements.)

Right now, the Lyric is offered only through a dozen clinics in California, Florida and New Jersey, but it should be available at about 100 sites by the end of the year. Some patients who don't live near a clinic simply fly or drive to a site four or five times a year. InSound is a privately held firm, although the pharmaceutical giant Johnson & Johnson is a major investor.

Dr. Robert A. Schindler, a co-founder of InSound and chairman emeritus of the department of otolaryngology at the University of California, San Francisco, says he has had hearing loss most of his life and has worn a Lyric since 2005. He says he remembers listening to an orchestra and hearing the light ping of the triangle.

"I realized I hadn't heard it before," he said. "That was a very exciting moment for me."

Canada Likely to Label Plastic Ingredient 'Toxic'

By IAN AUSTEN

OTTAWA — The Canadian government is said to be ready to declare as toxic a chemical widely used in plastics for baby bottles, beverage and food containers as well as linings in food cans.

A person with knowledge of the government's chemical review program spoke on the condition he not be named because of a confidentiality agreement. He said the staff work to list the compound, called bisphenol-a, or B.P.A., as a toxic chemical was complete and was recently endorsed by a panel of outside scientists.

A public announcement by Health Canada may come as early as Wednesday but could be delayed until the end of May. Canada would be the first country to make a health finding against B.P.A., which has been shown to disrupt the hormonal systems of animals. The department's decision was first reported in The Globe and Mail, a Toronto newspaper, on Tuesday.

Also on Tuesday, a draft report from the United States Department of Health and Human Services' National Toxicology Program endorsed a scientific panel's finding that there was "some concern" about neural and behavioral changes in humans who consume B.P.A.

B.P.A. is widely used to make polycarbonate plastics, which are rigid and transparent like glass but very unlikely to shatter. Polycarbonates have many uses that pose no risk, like the cases of some iPod models. Because animal tests have shown that even small amounts of the chemical may cause changes in the body, however, researchers have focused on food- and drink-related applications of B.P.A., like the popular Nalgene brand beverage bottles.

"If the government issues a finding of toxic, no parent in their right mind will be using products made with this chemical," said Rick Smith, the executive director of Environmental Defence, a Canadian group that has been campaigning against B.P.A. "We will be arguing strongly for a ban on the use of this chemical in food and beverage containers."

The public and industry will have 60 days to comment on the designation once it is released, setting into motion a two-year process that could lead to a partial or complete ban on food-related uses of plastics made using B.P.A.

Alastair Sinclair, a spokesman for Health Canada, said, "When the minister has an announcement to make, he will make it." Mr. Sinclair declined to answer any questions.

A spokeswoman for the Canadian Plastics Industry Association referred a request for comment to the American Chemistry Council in Arlington, Va. The council did not respond to interview requests.

Some scientists question the significance to humans of studies indicating that even very small amounts of B.P.A. can induce changes in animals. There is also some dispute about how much of the chemical is released by plastics.

Jack Bend, a professor of pathology at the University of Western Ontario in London and one of the Canadian government's outside scientific advisers, declined to comment on what action Health Canada would take. But he said he was concerned about the widespread use of B.P.A.

"The first thing is that it's an endocrine disrupter, there's no question about that," Professor Bend said, referring to the chemical's impact on the hormonal system. "Should people that are exposed to these low

levels of this chemical be outrageously concerned? I'd err on the side of not creating panic. We simply don't know. But we should find out."

Professor Bend added that the impact of B.P.A. on the development of human fetuses was worrisome. It may prove to cause damage in much the same way as early exposure to mercury, he said.

But Warren G. Foster, director of the center for reproductive care and reproductive biology at McMaster University in Hamilton, Ontario, is more skeptical.

"In my experience working with bisphenol-a, it's a relatively benign chemical," said Professor Foster, who once headed the reproductive toxicology group at Health Canada. "There's room here for a lot more research."

He added that substances could be declared toxic under Canada's chemical management system if they had the potential for adverse effects in animals but not humans.

"If I was a fish and there was bisphenol-a in the water, I'd be concerned," he said. "If I was a fetus and my mother was using a plastic water bottle, I wouldn't be bothered."

While the Canadian plastics association referred a reporter to Professor Foster, he said that he had no ties to it or the chemical industry.

The draft report released in the United States is effectively a call for further research on the chemical.

Michael D. Shelby, the director of the toxicology program's center for the evaluation of risks to human reproduction, said he wanted to see further confirmation that the test results could be repeated and more data about the long-term consequences of exposure to the chemical.

But he said that research strongly suggested that polycarbonate food and beverage containers and food cans were the main source of human exposure to B.P.A. When asked if people should stop using them, Dr. Shelby replied: "That becomes kind of a personal choice. These are certainly two things people can get around."

In a statement, the American Chemistry Council said the draft report "affirms that there are no serious or high-level concerns for adverse effects of bisphenol-a on human reproduction and development."

Basics

Adored, Deplored and Ubiquitous

By NATALIE ANGIER

Come next Tuesday, in a move flagrantly timed to coincide with Earth Day, the Whole Foods supermarket chain will no longer offer its customers the plastic bag option. Seeing that "it can take more than 1,000 years for a plastic bag to break down in a landfill" and that "in the U.S. alone, about 100 billion plastic bags are thrown away each year," the company said it could not in good conscience contribute to the crisis.

Bravo. Now tell me this: What am I supposed to line my garbage cans with? I always use plastic supermarket bags, and the Whole Foods ones were by far my favorites — roomy and springy enough to hold a lot of sodden waste without fear of breakage, always a plus when one is disposing of, say, fish skins or cat litter. So if I have to buy plastic bags by the box, that's better for the environment how? Forget about paper bags for this purpose. When we were growing up in the Bronx, my older brother recently reminded me, we lined our garbage can with newspapers, a solution satisfactory to none but the roaches.

A century ago, the Belgian-born chemist Leo Hendrik Baekeland ushered in a materials revolution with his invention of Bakelite, a synthetic resin that was molded into radio cases, lamps, buttons, dressers and other Antiques Roadshow reliables. We have been emotional bobbleheads about plastics ever since. We adore plastics for their versatility, lightness, strength and affordability, and it seems we can't get enough: the United States produced 6.5 billion pounds of raw plastic in December alone, up 2.3 percent from a year earlier. We deplore plastics for being cheap petroleum products and fear we'll never get rid of them.

Yet scientists point out that the class of substances lumped together under the plastics postmark is so broad and diverse that to condemn or condone them categorically makes no sense. Moreover, the field is evolving rapidly, as researchers strive to spin plastics from renewable sources like sugar cane and grass clippings in lieu of fossil fuels, and to outfit their creations with the chemical grace to decay once discarded. "We can do a lot of interesting things, but there's more research that needs to be done," said James A. Moore, a professor of chemistry at Rensselaer Polytechnic Institute. The biggest catch in reaching the new, greener stage of the plastics age, he said, "is that we have to accept that it's going to cost money."

Glancing around my office, I see how difficult it would be for me to live plastic-free. I'm typing on a computer keyboard made partly of molded polyvinyl chloride, which also serves as the source material for that ultimate plastic item, the credit card. Some components of the two black telephones on my desk are built of injection-molded acrylonitrile butadiene styrene, a material that has the strength and toughness to resist cracking when dropped, and hence is also used in motorcycle helmets and luggage. My earrings are made of Lucite, a lightweight acrylic that is embarrassingly popular among jewelry makers now. A cottontop tamarin doll on my bookcase stares down through beady brown eyes — probably acrylic as well — and its chirpy fake

fur is woven from polyester fibers. My desk and bookshelves are made of particle board, a composite of wood chips and a plastic resin. Lining my wastebasket is, yes, a plastic shopping bag, this one from Safeway, and like most plastic bags it's made of polyethylene, "the largest-volume plastic" of all, said Richard A. Gross, a professor of chemistry and biology at Polytechnic University in Brooklyn. In fact, all my views arrive as though Saran-wrapped, for I'd be blind without the blend of plastics from which my rigid gas permeable lenses are cast.

Uniting these and the hundreds of other plastics that pad our mattresses, elasticize our comfort-fit jeans, suture our wounds, plug our dental cavities, encapsulate our pills, replace our lost limbs, lighten our cars and jets and crisscross our Kevlar vests is the state of being a synthetic polymer. The term polymer refers to any long molecular chain made up of smaller chemical units, or monomers, which polymer chemists habitually compare to beads on a necklace or, when they're going out for a nice dinner, to pearls on a strand.

Life abounds with polymers. DNA, proteins and starches are polymeric molecules, all concatenations of smaller molecules. Plastics are just polymers in which humans, rather than nature, string the beads. Granted, we're still pretty crude jewelers by comparison. The synthetic polymers in the plastic skin of a garbage bag, for example, are monotonous skeins of a single type of chemical bauble, ethylene, while the protein polymers in a fish's skin are intricate arrays of as many as 20 distinct amino acids, the monomers of which proteins are built.

What's more, whereas nature knows how to make thousands of different polymers and can make them the same length and shape every time, chemists have yet to master such fine control over their product line. "The typical way a polymer is made is you throw your monomers into a big pot and let them all react, as opposed to building them up one piece at a time the way the body does," said Elliot P. Douglas, an associate professor of materials science and engineering at the University of Florida. "When we make a mixture, it's a mixture of all different lengths."

But our bodies and our plastics are by no means antithetical beasts. The polymers in both cases tend to feature a lot of carbon atoms, carbon having a readily linkable structure that makes it an ideal component of life — of the lives we live now, and of the ancient, squeezed and subliminated lives that constitute fossil fuels. It's also an ideal constituent for monomers you want to toss together into your pot and have a product with useful properties come out the other side, like stretchiness, stickiness, ductility, disdain for electrical flow.

The reason petroleum so often serves as the foundation for plastics production is that it offers an ultraconcentrated source of carbon, but carbon is carbon and with the right manipulations other handier biosources like lawn litter will do. Add chlorine to your carbon backbone for hardness and heat resistance. Tack little methyl groups to the carbon backbone for durability, compactness and a ropy indifference to chemical abuse. Extrude your melted mixture through die holes to form pipes, hoses, drinking straws and fibers. Inject it into moldings shaped like Barbie, Ken or a comb. Blow it out like a balloon and you've got a new bag. When you're done, hand it over: I will put it to use.

Citing Ethics, Some Doctors Are Rejecting Industry Pay

By GINA KOLATA

With little fanfare, a small number of prominent academic scientists have made a decision that was until recently all but unheard of. They decided to stop accepting payments from food, drug and medical device companies.

No longer will they be paid for speaking at meetings or for sitting on advisory boards. They may still work with companies. It is important, they say, for knowledgeable scientists to help companies draw up and interpret studies. But the work will be pro bono.

The scientists say their decisions were private and made with mixed emotions. In at least one case, the choice resulted in significant financial sacrifice. While the investigators say they do not want to appear superior to their colleagues, they also express relief. At last, they say, when they offer a heartfelt and scientifically reasoned opinion, no one will silently put an asterisk next to their name.

They are part of a group responding to accusations of ethical conflicts inherent in these arrangements, and their decisions repudiate decades of industry influence, says Dr. Jerome P. Kassirer, a professor at the Tufts School of Medicine, who has written a book on conflicts of interest.

Five years ago, "nobody paid any attention to taking money from industry," he said, adding: "They just took it. In some instances, I think people thought they were suckers if they didn't."

Even last year, the Food and Drug Administration decided that it could not altogether ban researchers from its advisory boards who took industry consulting fees.

Now, Dr. Kassirer said, he keeps finding experts who are rejecting the money.

"I don't think there's any question that the atmosphere has changed," Dr. Kassirer said.

He attributes the change to publicity about conflicts and what can be almost a public shaming when researchers' conflicts are published. "Finally, it's gotten to people," Dr. Kassirer said.

Here are the accounts of three scientists who have lost their asterisks.

Dr. Peter Libby, chief of cardiovascular medicine at Harvard's Brigham and Women's Hospital, said that when he first began receiving offers from drug companies, in the early 1980s, they seemed like a natural reflection of his burgeoning reputation.

"When you start emerging as an opinion leader or as a researcher who has knowledge and expertise, the pharmaceutical industry takes an interest in either having you consult to help them with their research or to speak," he said.

Dr. Libby wanted to assist. Like many scientists, he feels that it is important for researchers to consult with drug companies to help develop therapies and set up studies. He never owned stock in companies that he consulted for. He always disclosed the fact that he consulted and spoke for companies. And, he added, he thought that he was protected from accusations of favoring any particular company's products because he consulted for so many.

"I lived safely in that comfort zone for many years," Dr. Libby said.

Then he was hit with a moment of truth. He had spent four years working without pay to help create a public television series, "The Mysterious Human Heart." The project was, he thought, a worthy effort to educate the public about what heart disease was and how to prevent it. He was proud and pleased when the series was broadcast in October.

But to his dismay, bloggers immediately attacked him and the other medical experts who appeared on the programs for having consulted for manufacturers of pharmaceuticals and medical devices, Dr. Libby said, adding: "They said we were biased. What I thought was four years of public service was impugned.

"That was a wake-up call for me. I was singed in the blogosphere."

This year, he made his decision. He would continue speaking at forums sponsored by the pharmaceutical industry and would continue consulting for companies. But he would no longer accept payment.

Since then, Dr. Libby said, company executives and lawyers have asked whether they offended him. Does he have some secret agenda?

His motives are straightforward, he replies. "I want to speak out about the beliefs I am passionate about regarding prevention and medical advances that I think can reduce disease and save lives," he said. "It is not worth it to be under suspicion."

Kelly D. Brownell, director of the Rudd Center for Food Policy and Obesity at Yale, made a similar decision. His was to protect his integrity when he began to wonder whether his industry associations were subtly affecting his objectivity. "The money offers started happening about 20 years ago, at the point that I became a visible person in the field," Dr. Brownell said.

First it was drug companies developing obesity drugs. Then it was food companies. Eventually, Dr. Brownell said, he began to worry. Were his associations unconsciously affecting his objectivity? He said the money could be substantial. He was offered, for example, $50,000 to be on an advisory board.

"It is easy to offer subtle statements that would favor a drug," Dr. Brownell said. "You do it for two reasons. You've got a money stream coming in, and you get to like the people who work for the companies. You feel like you're on a team."

About 10 years ago, he decided he had to stop accepting money, he recounted. It was one factor, along with higher taxes and his wife's decision to work fewer hours, that led him to sell his house and move to a less expensive one. And that $50,000? He turned it down. The offer arrived after he had made his decision.

Dr. Eric P. Winer, director of the Breast Oncology Center at the Dana-Farber Cancer Institute at Harvard, made his decision about a year ago. "Several times when I was interviewed for stories, after my comments there would be the obligatory phrase, 'Dr. Winer has accepted honoraria,' " he said. "I was tired of having to see that."

He had also accepted a position as chief scientific adviser for a group that advocates for women with breast cancer, Susan G. Komen for the Cure. Those asterisks, he decided, could hinder his ability to help the group.

Dr. Winer, like many other investigators, points out that conflicts are not so simple. His honoraria were typically on the order of $2,000 or $3,000 for attending an advisory board meeting for a day and a half or two days. "It truly is not a large amount of money we are talking about here," he said.

There are many other sorts of conflicts that attract little comment but that can be much more significant, Dr. Winer added. There is the researcher's need to run a clinical trial because that can help the researcher's career or obtaining financing. The reward is not money, but career advancement and prestige.

In today's atmosphere of intense scrutiny of scientists who accept industry money, he said, he felt he had little choice.

"I am responding to a societal pressure," Dr. Winer said. "I just said enough is enough. And in truth, it has made my life simpler. I no longer debate can I take this, can I not take this. It is simpler when I talk to reporters. It is simpler when I give lectures."

On the other hand, he mused, the decision had a subtle effect. Now that he receives no compensation, he is less willing to help pharmaceutical companies research treatments.

"My willingness to go to an advisory board meeting has gone down," Dr. Winer said. "Do I want to spend my Saturdays and Sundays at a meeting? As much as I am a dedicated researcher, I have to have a life."

"This is a complicated arena," he added. "And on some level I resent the fact that I had to make this decision."

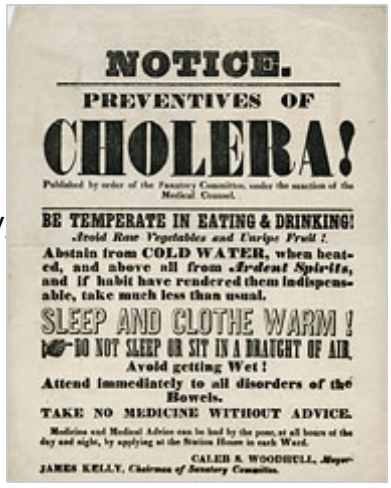
How Epidemics Helped Shape the Modern Metropolis

By JOHN NOBLE WILFORD

On a Sunday in July 1832, a fearful and somber crowd of New Yorkers gathered in City Hall Park for more bad news. The epidemic of cholera, cause unknown and prognosis dire, had reached its peak.

People of means were escaping to the country. The New York Evening Post reported, "The roads, in all directions, were lined with well-filled stagecoaches, livery coaches, private vehicles and equestrians, all panic-struck, fleeing the city as we may suppose the inhabitants of Pompeii fled when the red lava showered down upon their houses."

An assistant to the painter Asher B. Durand described the scene near the center of the outbreak. "There is no business doing here if I except that done by Cholera, Doctors, Undertakers, Coffinmakers, &c," he wrote. "Our bustling city now wears a most gloomy & desolate aspect — one may take a walk up & down Broadway & scarce meet a soul."


NOTICE.

PREVENTIVES OF

CHOLERA!

Published by order of the Sanitary Committee, under the sanction of the Medical Council.

BE TEMPERATE IN EATING & DRINKING!

Avoid Raw Vegetables and Unripe Fruit!

Abstain from COLD WATER, when heated, and above all from Ardent Spirits, and if habit have rendered them indispensable, take much less than usual.

SLEEP AND CLOTHE WARM!

DO NOT SLEEP OR SIT IN A DRAUGHT OF AIR.

Avoid getting Wet!

Attend immediately to all disorders of the Bowels.

TAKE NO MEDICINE WITHOUT ADVICE.

Medicine and Medical Advice can be had by the poor, at all hours of the day and night, by applying at the Station House in each Ward.

CALEB S. WOODHULL, Mayor.

JAMES KELLY, Chairman of Sanitary Committee.

New York Historical Society

The epidemic left 3,515 dead out of a population of 250,000. (The equivalent death toll in today's city of eight million would exceed 100,000.) The dreadful time is recalled in art, maps, death tallies and other artifacts in an exhibition, "Plague in Gotham! Cholera in Nineteenth-Century New York," at the New-York Historical Society. The show will run through June 28.

The outbreak, as portrayed in the exhibition and other documentation, highlighted the vulnerabilities of life in overcrowded cities in a time of deplorable sanitation and before medical science recognized the role of germs in disease. Cities were growing faster in population than in understanding what it took to make them fit places to live — an urban problem probably as old as the Sumerians of Mesopotamia.

The initial response to the epidemic, Kenneth T. Jackson, a professor of history at Columbia University, said recently, exposed more than ever the city's divisions of class, race and religion. The disease hit hardest in the poorest neighborhoods, particularly the slum known as Five Points, where African-Americans and immigrant Irish Catholics were crowded in squalor and stench.

"Other New Yorkers looked down on the victims," said Dr. Jackson, editor of The Encyclopedia of New York City. "If you got cholera, it was your own fault."

Unlike most upper-class residents, John Pintard, the respected civic leader who was the historical society's founder, remained in the stricken city. His letters to one of his daughters are included in the exhibition.

The epidemic, he wrote in an attitude typical of his peers, "is almost exclusively confined to the lower classes of intemperate dissolute & filthy people huddled together like swine in their polluted habitations."

In another letter, his judgment was even harsher. "Those sickened must be cured or die off, & being chiefly of the very scum of the city, the quicker [their] dispatch the sooner the malady will cease."

Dr. David D. Ho, a biomedical scientist at Rockefeller University, noted the similarities between the views on cholera and the initial reaction to a more recent epidemic that took science by surprise: AIDS.

When the first AIDS cases were reported in 1981, the victims were almost all white gay men. They were treated as outcasts.

"It was a repeat of the cholera experience," said Dr. Ho, the founding chief executive of the Aaron Diamond AIDS Research Center. "The cause of the disease was unknown, and it affected a subset of the population. It was easy to brand the victims and blame the disease on their lifestyle."

Scientists moved quickly and effectively to isolate the virus that causes AIDS, which is by no means confined to gay men and is rampant in developing countries, particularly in Africa.

Science and medicine advanced more slowly in the 19th century. It was 1883 before the bacterium Vibrio cholerae was discovered to be the agent causing the gastrointestinal disease. But a turning point in prevention came in 1854, when a London physician, Dr. John Snow, established the connection between contaminated water and cholera.

Dr. Snow tested the idea by plotting cholera cases on a map of Soho. This showed that most of the victims drew their water from a public pump on Broad (now Broadwick) Street. An infected baby's diapers had been dumped into a cesspool near the well. A recent book, "Ghost Map," by Steven Johnson, recounts the discovery.

The cholera research was an early application of mapping in medical investigations, a technique that has become widespread now that computers facilitate the display and analysis of such data. Historians of medicine credit Dr. Snow with advancing the modern germ theory of disease and laying the foundations of scientific epidemiology.

The cholera menace thus prompted cities to begin cleaning up their fouled nests. This came too late for victims of the 1832 epidemic in New York, or one that followed in 1849. By then, the city's population had doubled, to 500,000, and deaths by cholera rose to 5,071.

The city in 1832 had expanded as far north as 14th Street. People were squeezed out of the lower wards by the influx of immigrants. Some, escaping earlier outbreaks of malaria and yellow fever, had sought a haven in the clean air and open land of the village called Greenwich.

Walking in Greenwich Village today, one is struck by the number of small brick houses bearing markers with dates immediately after 1832. It may be no coincidence that John Blauvelt, a carter working the piers, built his on West 10th Street (then Amos Street) the year after the cholera epidemic.

New Yorkers should have suspected that the scourge was on its way. Cholera, originally confined to South Asia, had started spreading in 1817 from seaport to seaport, presumably carried by infected sailors. The disease struck London in 1831 and reached New York the next June.

No one was prepared, not even doctors. They generally believed that miasmas, the noxious vapors from rotting organic matter, carried infections, an idea inspiring literature of death in Rome and Venice. The cholera in Five Points seemed to bear out the hypothesis.

Five Points was a slum that had metastasized from an intersection of five streets north of City Hall through the area that is now Foley Square and Chinatown. "All that is loathsome, drooping and decayed is here," Charles Dickens wrote after a visit. Martin Scorsese's movie "Gangs of New York" captures the lowlife there later in the 19th century, when it was still an urban sinkhole.

The exhibition includes illustrations of the thugs and gamblers, the stray dogs and pigs that inhabited the streets of mud and manure. The pigs at least were useful as garbage collectors and sources of food.

For victims, the onset of cholera was sudden: an attack of diarrhea and vomiting, followed by abdominal cramps and then acute shock, signaling the collapse of the circulatory system. Some survived the illness, despite the lack of effective remedies.

Posters from the time described recommended treatments, including laudanum (morphine), calomel (mercury) as a binding laxative, and camphor as an anesthetic. High doses sometimes did more harm than good. Poultices of mustard, cayenne pepper and hot vinegar were also applied, as well as opium suppositories and tobacco enemas.

Many victims, nearly half the cases at one hospital, died within a day of admission. After private hospitals began turning away patients, the city set up emergency public hospitals in schools and other buildings. One, on Rivington Street, bore the brunt, and sketches of its patients' faces contorted in the throes of death look down from the exhibition walls.

In stark contrast, Asher Durand, who had escaped with his family to their country home in New Jersey, painted his children happily eating apples in a sunny orchard. The idyllic canvas hangs a few feet, and a world, away from the scenes of Five Points.

While many Protestants sat out the epidemic at safe distances, the city's Catholics, many of whom were poor immigrants, mostly Irish, had no choice but to stay. Their nuns and priests also remained to offer comfort and some help, and they emerged as the few heroes in the ordeal. "The Sisters of Charity performed heroic service, and many of them died," said Stephen R. Edidin, co-curator of the exhibition, with Joseph Ditta. "As a result, there was some reduction of anti-Catholic sentiments and a new respect for the Catholic clergy, who risked their lives in the epidemic. The feeling didn't last, of course."

Despite the epidemics of '32 and '49, people still flocked to New York and other teeming cities. But the first outbreak bolstered support for the Croton Aqueduct system to bring clean upstate water to the city, a project, completed in 1842, that led to the phasing out of private and neighborhood wells that were often polluted with human and animal waste. In 1849, the municipal government banished more than 20,000 pigs to the outer reaches of the city. A similar effort in previous years had provoked riots, but this time a public chastened by epidemic complied.

Finally, after the work of Dr. Snow in London and a lesser cholera outbreak in New York in 1866, the Metropolitan Board of Health was established with doctors in commanding roles and broad powers to clean up the city. Inspectors went to houses and burned clothing of people who had just died. They cleared the filth, spread lime and instructed survivors in proper sanitation.

Cities had learned, or should have, that epidemics as a consequence of urbanization were their responsibility to prevent and control.

Cholera is still a threat wherever drinking water is polluted. But Dr. Ho says that people should no longer die of it, if they are treated promptly and properly with rehydration fluids to restore their ravaged bodies.

Creatinine Increase in Elderly Means Increased Renal Disease, Mortality

- ***10-year study of 87,094 patients***
- ***Small creatinine changes increase long term mortality and kidney failure***
- ***Mortality and kidney failure greatest with larger creatinine changes***

BIRMINGHAM, Ala. -- Even small increases in serum creatinine levels during hospitalization raise the risk of end stage renal disease and mortality of elderly patients over the long term, according to a University of Alabama at Birmingham (UAB) study in the March issue of the Archives of Internal Medicine.

The 10-year retrospective study, led by UAB nephrologist Britt Newsome, M.D, is the first systematic description of creatinine increase and longer-term end stage renal disease and mortality risk. Previous studies showed a relationship between reductions in kidney function during hospitalization and higher mortality rates.

"Previous studies have shown that a rise in serum creatinine level of 0.3 milligrams per deciliter or more during hospitalization is associated with higher in-hospital mortality, longer stays and higher costs," Newsome said. "However, little was known about the long-term risks of subsequent end-stage renal disease and mortality in this population. The long-term risks we observed suggest that even the least severe category of kidney injury may indicate a worse prognosis."

The study looked at 87,094 Medicare beneficiaries admitted to 4,473 hospitals across the country suffering from a heart attack, or acute myocardial infarction. They studied changes in creatinine levels of those patients from 0.1 to 3.0 milligrams per deciliter. The mean age of the patients was 77.1 years old.

Incidences of end stage renal disease and death were greatest among patients with larger changes in creatinine level, and all levels of serum creatinine increase were associated with a greater risk of end stage renal disease and death.

"We chose to examine a population of Medicare beneficiaries because the incidence of acute kidney injury has been increasing in this population for the past 10 years," Newsome said. "Further, patients with cardiovascular disease are at a particularly high risk of chronic kidney disease as well as acute kidney injury. In future studies we will want to determine if this relationship exists in patients admitted to the hospital for other conditions."

With these findings, the study calls for clinicians to closely monitor and aggressively treat patients experiencing increases in creatinine levels.

"The study also shows that giving patients beta blockers and aspirin can help treat these patients and possibly prevent death in the long term, regardless of creatinine change during hospitalization," Newsome said

Other UAB authors on the paper were Jeroan J. Allison, M.D.; David Warnock, M.D.; and Catarina I. Kiefe, M.D., Ph.D.

Additional authors are William M. McClellan, M.D., Emory University School of Medicine; Charles A. Herzog, M.D., Cardiovascular Special Studies Center, U.S. Renal Data System, Minneapolis, Minn.; and Paul W. Eggers, Ph.D., the National Institute of Diabetes and Digestive and Kidney Diseases.

Disturbances in Brain Circuitry Linked to Chronic Exposure to Solvents

Annals of Neurology Research News Alert
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Disturbances in Brain Circuitry Linked to Chronic Exposure to Solvents

Chronic occupational exposure to organic solvents, found in materials such as paints, printing and dry cleaning agents, is widespread all over the world, and is thought to damage the central nervous system. The pattern of cognitive impairment, involving memory, attention and psychomotor function, frequently persists even after exposure has ceased, is usually referred to as chronic solvent-induced encephalopathy (CSE). Although CSE is an acknowledged occupational disease in an increasing number of western countries, and is classified according to the World Health Organization criteria and is included in the Diagnostic and Statistical Manual for Mental Disorders, it is still a controversial diagnosis, with still some debating whether or not it is a bonafide condition.

Various studies have attempted to pinpoint brain abnormalities caused by CSE, but their methodologies have been questioned. It has been proposed that deterioration within the frontal-striatal-thalamic (FST) circuitry, which is also associated with the psychomotor and attention impairment that takes place with natural aging, may play a role in CSE. A new study was the first to show that disturbances in this region are related to the clinical characteristics of CSE as well as to the severity of exposure. The study was published in the April 2008 issue of Annals of Neurology (www.interscience.wiley.com/), the official journal of the American Neurological Association.

Led by Ieke Visser of the Academic Medical Center in Amsterdam , the study included 10 CSE patients who had been exposed to solvents and had mild to severe cognitive impairment, 10 participants who had been exposed to solvents but had no CSE symptoms, and 11 participants who were not exposed to solvents and had no symptoms. Subjects were classified according to the duration and level of exposure, symptoms of

acute intoxication and the use of personal protection equipment. They also underwent MRI and single photon emission computed tomography (SPECT) scans to evaluate various aspects of FST-circuitry, as well as a battery of neuropsychological tests to assess attention and psychomotor speed.

The results showed that CSE patients had reduced striatal dopamine D2 receptor (D2R) binding ratios (dopamine receptor density is thought to play a role in psychomotor speed) which were predictive of impaired psychomotor speed and attention and were also linked to exposure severity. The exposed controls showed similar reductions, although to a lesser extent. Both groups also showed reduced levels of choline, which plays a role in neurotransmission, in the frontal grey matter. These findings suggest that certain parts within the FST-circuitry are compromised in CSE patients and also exposed workers who don't show any symptoms, according to the authors. "A better understanding of the nature, severity and specificity of these suspected biological markers may further validate diagnostic procedures, this reinforcing medical and social recognition, and underlining the importance of prevention," they state.

The authors acknowledge that the study was small and that using higher field scanners would no doubt shed further light in assessing chemical interactions in the brain. However, they note that this is the first study in CSE patients to show pronounced disturbances in the FST-circuitry that are related to the clinical findings and to the severity of solvent exposure. They conclude: "Our results can be an important incentive for further study, clarifying the nature and specificity of these disturbances, thereby improving diagnostic procedures and acknowledgement of CSE patients, as well as worldwide prevention of chronic occupational solvent exposure."

Article: "Frontal-striatal-thalamic impairment in Chronic Solvent-Induced Encephalopathy," Ieke Visser, Cristina Lavini, Jan Booij, Liesbeth Reneman, Charles Majoie, Angela de Boer, Elizabeth Wekking, Elisabeth de Joode, Gert van der Laan, Frank van Dijk, Aart Schene, Gerard den Heeten, Annals of Neurology, April 2008.

Combining liver cancer treatments doubles survival rates, UVA researchers find

Charlottesville, Va., April 15, 2008 – By combining the use of stents and photodynamic therapy, also called SpyGlass, physicians at the University of Virginia have been able to significantly increase survival rates for patients suffering from advanced cholangiocarcinoma, cancer of the liver bile duct.

"Most patients who develop this type of cancer cannot have surgery as it is diagnosed at such a late stage, so there was not much we could do except offer them palliative care," said University of Virginia Gastroenterologist Michel Kahaleh, M.D., lead investigator of the study. "By combining therapies, we saw an improved survival rate from just more than 7 months to more than 16 months."

In the study, recently published in the March 2008 issue of Clinical Gastroenterology and Hepatology, 48 patients were treated with advanced cholangiocarcinoma over a five year period. Twenty-nine patients were treated with biliary stents, with the remaining 19 being treated with the stents and photodynamic therapy (PDT). The stents decompress the bile ducts, maintaining liver function. The combined therapy group received treatment every three months, at which time all stents were replaced.

The combined therapy group had survival rates of 16.2 months compared to the stent-only group's 7.4 months. Mortality rates in the group that received PDT was 0, 16, and 56 percent at three, six, and 12 months respectively. Mortality rates in the stent-only group were 28, 52, and 82 percent respectively. Kahaleh said the number of stent-replacement procedures and PDT sessions were the only factors which significantly impacted survival.

Photodynamic Therapy treatment uses a photosensitizing agent (porfimer sodium in this study) which is activated using light of a specific wavelength, which then kills the targeted cells. PDT has been used for more than a decade to destroy cancer cells and reduce tumor size.

Cancer of the liver bile ducts is the second most common liver cancer and has significant mortality and mortality. Of the approximately 2,000 cases diagnosed each year, the vast majority of patients survive up to three months without intervention or four to six months with decompression treatment.

"Stents alone do not destroy or shrink the tumors or cancer cells. We were not surprised that the combined therapy offers a significant benefit to the patient, as this is accepted treatment in Europe," said Kahaleh. "However the FDA (Food and Drug Administration) wants to see more data so we have completed what we believe is the first published comparative American study on the treatment."

Kahaleh hopes to begin a multi-center trial within six months.

Health risks, benefits come with delayed umbilical cord clamping

Waiting just a few minutes to clamp the umbilical cord after a baby is born could boost iron stores in the newborn's blood, but delayed cord clamping comes with an increased risk of jaundice, according to a new review of studies.

Clamping the cord within 30 to 60 seconds after birth is one of three steps in an "active management" approach to the third stage of labor, a time when a new mother is vulnerable to excessive blood loss. Studies show that active management reduces the risk for hemorrhage, but now lead review author Susan McDonald and other investigators are refining that research.

"We've started to ask 'Is it necessary that we do all three" Which part of this is most important" Did timing of clamping the cord make a difference"" said McDonald, a professor of midwifery at La Trobe University and the Mercy Hospital for Women in Melbourne, Australia.

McDonald said of the studies included in the review: "We found in terms of the amount of bleeding, delayed clamping did not increase the mother's risk of bleeding."

The review appears in the latest issue of The Cochrane Library, a publication of The Cochrane Collaboration, an international organization that evaluates medical research. Systematic reviews draw evidence-based conclusions about medical practice after considering both the content and quality of existing medical trials on a topic.

The review of 11 studies evaluates the maternal and infant benefits of delaying cord clamping until after the cord stops pulsing, a sign that blood is no longer flowing between the mother's placenta and the baby.

McDonald said in most cases the time difference between early and late cord clamping is just one or two minutes, but the delay allows for an additional infusion of blood from mother to child.

McDonald's analysis found that newborns in the delayed-clamping group had larger stores of iron in their blood. The amount of iron in the blood at birth can influence health, particularly an infant's risk for anemia in the first months of life.

However, the study also found that infants in the delayed-clamping group were more vulnerable to jaundice. Many babies get a mild form of jaundice at birth because the liver is immature and cannot process bilirubin, a yellow byproduct of the breakdown of old red blood cells.

"When the liver can't process all the bilirubin it tends to get pushed out to the tissue and the baby looks a little bit yellow," McDonald said.

Most newborn jaundice subsides without treatment or is treated with simple exposure to sunlight. The review found that infants in the delayed-clamping group had a higher risk for jaundice that needed extra treatment with phototherapy.

"In most places in Western countries where there is a higher income, people have access to hospitals where babies can get that therapy," McDonald said.

"But if you are working in an area where you don't have easy access to treat a child with more severe jaundice, then as a clinician you would need to weigh up the benefits and risks. Allowing the baby to get the extra blood and maybe become jaundiced is a particular problem if you don't have the facilities. In that case, perhaps, you would err on the side of clamping the cord a little earlier," she said.

"There's a happy medium you try to strike," said Joyce Roberts, a certified nurse midwife, professor and coordinator of the Nurse-Midwifery Track at the University of Michigan School of Nursing.

Roberts said many midwives put the baby on the mother's abdomen, above the level of the placenta, so blood continues to flow, but not to excess.

FOR MORE INFORMATION:

Health Behavior News Service: Lisa Esposito at (202) 387-2829 or hbns-editor@cfah.org.

McDonald SJ, Middleton P. "Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes (Review)." Cochrane Database of Systematic Reviews 2008, Issue 2.

IU Health & Wellness: New research findings from the Kinsey Institute

When It Comes To Sex, Some Men Are From Mars, Others From Venus

A study by researchers at the Kinsey Institute for Research in Sex, Gender, and Reproduction at Indiana University finds that men report a variety of different experiences involving sexual desire and arousal.

Men participating in focus groups expressed a range of experiences and feelings relating to such matters as the relationship between erections and desire, the importance of scent and relationships, and a woman's intelligence. The Kinsey Institute study, appearing in the April issue of the journal "Archives of Sexual Behavior," is unique because few studies so far have examined how closely the findings of decades of laboratory studies on sex actually reflect the experiences of men.

"We have a lot of assumptions about how men think and feel and behave sexually," said Erick Janssen, associate scientist at the Kinsey Institute. "We use all kinds of methods to measure men's sexual responses; in addition, we use questionnaires and surveys to ask about sexual behaviors. It's less common to sit down with men and ask them to talk about their experiences."

The focus groups involved 50 men divided into three groups based on their age (18-24 years, 25-45 years and 46 and older). Below are some examples of the different experiences reported by the men:

* Some factors, such as depression or a risk of being caught having sex, were reported by some men as inhibiting sex, while other men found that they can enhance their desire and arousal.

* An erection is not the main cue for men to know they are sexually aroused. Most of the men responded that they can experience erections without feeling aroused or interested, leading researchers to suggest that erections are not good criteria for determining sexual arousal in men.

* Many men found it difficult to distinguish between sexual desire and sexual arousal, a distinction prominent in most sexual response models used by researchers and clinicians.

* The changes in the quality of older men's erections had a direct effect on their sexual encounters, including, for some, a shifting focus to the partner and her sexual enjoyment. Older men also consistently mentioned that as they aged, they became more careful and particular in choosing sexual partners.

* The sexual history of women also mattered to the men -- but differently for different age groups. Sexually experienced women were considered more threatening by younger men, who had concerns about "measuring up," but such women were considered more arousing for older men.

Janssen and his colleagues at the Kinsey Institute have been working for more than 10 years on a theoretical model that focuses on sexual excitation and sexual inhibition. They refer to this as the dual control model of sexual response. It holds that separate and relatively independent activating and suppressing sexual systems exist within the central nervous system and that the balance between these two systems determines a person's sexual response in any particular situation. Janssen relates this to the gas and break pedals in a vehicle -- both can influence a car's behavior (you can slow down by letting go of the gas or by pressing the brake) but they do so in different ways.

This model is used around the world by sex researchers in studies on topics as varied as sexual dysfunction and sexual risk taking. To measure the propensity for sexual excitation and inhibition, the researchers designed a questionnaire.

The original questionnaire was developed for men, leading researchers at the Kinsey Institute to conduct focus groups with women in an effort to create a similar questionnaire that would be more relevant for women. Janssen said the success of women's focus groups led him and his colleagues to conduct the focus groups with men.

The findings of this latest study ultimately could lead to a more effective questionnaire for the dual control model but also can inform research efforts to better understand the variability in sexual behavior.

"One of the main conclusions of the focus group study is that, just like women, men are different," Janssen said. "Sex researchers tend to focus a lot on differences between men and women, while not giving as much attention to the differences that exist among men, and women. This research is part of a larger agenda at the Kinsey Institute of looking at individual differences. This dates back to Alfred Kinsey's original research, but in our current research we not only try to capture the variations in men and women's sexual experiences -- we also try to understand better what explains variations in those experiences."

Co-authors of the study are Kimberly R. McBride, IU School of Medicine; William Yarber, Department of Applied Health Science; Brandon J. Hill, Department of Gender Studies; and Scott M. Butler, Georgia College and State University. To speak with Janssen or to obtain a copy of the study, contact Jennifer Bass at 812-855-7686 or jbass@indiana.edu.

One Step Closer To Understanding The Causes Of Sexual Difficulties In Women

Researchers at the Kinsey Institute for Research in Sex, Gender and Reproduction are shedding light on why some women experience sexual problems and others do not.

A study published in the April issue of the journal "Archives of Sexual Behavior" found connections between personality traits such as sexual inhibition and sexual problems.

While previous studies have explored the role demographics such as age, education and socio-economic status play in sexual functioning among women, few have explored the role differences in personality play in predicting current and lifetime sexual problems. In this study, women's sexual inhibition tendencies were more important than other factors in predicting sexual problems.

"Although further research is needed to confirm these findings with other samples, particularly clinical samples of women seeking help for sexual problems, these findings suggest that high scores on sexual inhibition may help predict which women are vulnerable to experience sexual problems," said Cynthia Graham, research fellow at the Kinsey Institute and co-author of the paper. "They may also be used as prognostic factors in treatment studies."

Researchers studied the responses of 540 women on the Sexual Excitation/Sexual Inhibition Inventory for Women that rated current and sexual problems, lifetime arousal difficulty and lifetime problems with low sexual interest. The strongest predictors of reports of sexual problems were women's sexual inhibition scores. Below are some of the findings:

* Sexual inhibition scores were the strongest predictor of current and past sexual problems including lifetime arousal difficulty and low sexual interest. They were better predictors than demographic and background factors such as age, socio-economic status, and whether or not women were in a sexual relationship.

* "Arousal Contingency" or the ease with which arousal can be disrupted by situational factors, and "Concerns about Sexual Function" were the two most predictive of women's sexual problems.

The Kinsey Institute has been developing, testing and fine-tuning the dual control model of sexual response, which is the basis for the Sexual Excitation/Sexual Inhibition Inventory for Women used in this study. This theoretical model reflects the idea that sexual response in individuals is the product of a balance between excitatory and inhibitory processes. Researchers believe these two systems operate somewhat independent of each other and are different in each person.

Researchers are using the dual control model to better understand such complex issues as sexual difficulties, sexual compulsivity and high-risk sexual behaviors. Prior studies have found that while sexual inhibition plays an important protective role in restraining sexual responses, individuals who score highly in inhibition might be more likely to experience sexual problems.

This particular study aimed to gain insight into the role of inhibition and excitation proneness in predicting sexual problems in a non-clinical sample of women.

Co-authors of the study are Stephanie A. Sanders, Kinsey Institute; and Robin R. Milhausen, University of Guelph in Ontario, Canada. To speak with Graham or to obtain a copy of the study, contact Jennifer Bass, 812-855-7686 or jbass@indiana.edu.

"Factors that Influence Sexual Arousal in Men: A Focus Group Study," Archives of Sexual Behavior, April, 2008. Vol. 37, No. 2.

Neanderthals speak out after 30,000 years

* 15:00 15 April 2008

* NewScientist.com news service

*** Ewen Callaway**

Talk about a long silence – no one has heard their voices for 30,000 years. Now the long-extinct Neanderthals are speaking up – or at least a computer synthesiser is doing so on their behalf.

Reconstruction of a Neanderthal child's face **(Image: Anthropological Institute, University of Zürich)**

Robert McCarthy, an anthropologist at Florida Atlantic University in Boca Raton has used new reconstructions of Neanderthal vocal tracts to simulate the voice. He says the ancient human's speech lacked the "quantal vowel" sounds that underlie modern speech.

Quantal vowels provide cues that help speakers with different size vocal tracts understand one another, says McCarthy, who was talking at the annual meeting of the American Association of Physical Anthropologists in Columbus, Ohio, on April 11.

"They would have spoken a bit differently. They wouldn't have been able to produce these quantal vowels that form the basis of spoken language," he says.

Talking heads

In the 1970s, linguist Phil Lieberman, of Brown University in Providence, Rhode Island, inferred the dimensions of the larynx of a Neanderthal based on its skull. His team concluded that Neanderthal speech did not have the subtlety of modern human speech.

Some researchers have criticised this finding, citing archaeological evidence of an oral culture and even errors in Lieberman's original vocal tract reconstruction.

Undeterred, the linguist teamed with McCarthy to simulate Neanderthal speech based on new reconstructions of three Neanderthal vocal tracts. The 50,000-year old fossils all came from France.

By modelling the sounds the Neanderthal pipes would have made, McCarthy's team engineered the sound of a Neanderthal saying "E". He plans to eventually simulate an entire Neanderthal sentence***. Listen to McCarthy's simulation of a Neanderthal voice***

In contrast to a modern human "E", the Neanderthal version doesn't have a quantal hallmark, which helps a listener distinguish the word "beat" from "bit," for instance. ***Listen to a simulation of a modern human voice***

Though subtle, the linguistic difference would have limited Neanderthal speech, McCarthy says.

The language gene

That conclusion doesn't fit in with Neanderthals' large brains, which may have been an adaptation to language, says Erik Trinkaus, an anthropologist at Washington University in St Louis. "Ultimately what is important is not the anatomy of the mouth but the neuronal control of it."

Neanderthals may have also boasted the genes for language, Trinkaus says. Last year, researchers discovered that Neanderthals shared a version of a gene called FOXP2 with humans.

People missing a copy of FOXP2 suffer from language and speech disorders, and humans have a version of the gene that is different from other animals – including chimpanzees, our nearest relatives.

Yet other genetic evidence suggests that spoken language shaped the recent evolution of humans. John Hawks, a biological anthropologist at the University of Wisconsin in Madison, also spoke at the Ohio meeting. He says that some genes important to hearing changed rapidly in modern humans, perhaps because the genes helped decode new, more complex spoken languages.

"Something's changing in the last 40,000 years," he says. "Maybe this is because our ears are becoming tuned to listening to sounds that have recently been changing."

Gene activity may explain cancer's racial divide

* 20:00 15 April 2008
* NewScientist.com news service
*** Peter Aldhous**

Prostate and breast cancer are more deadly for African Americans than for whites. Now it seems that differences in the activity of key genes may be partly to blame.

Black men in the US are around 60% more likely to develop prostate cancer than their white counterparts, and are more than twice as likely to die from the disease.

In large part, these differences are thought to be due to socioeconomic factors such as access to healthcare. But at the annual meeting of the American Association for Cancer Research (AACR) in San Diego on 15 April, Tiffany Wallace of the US National Cancer Institute in Bethesda, Maryland, argued that biological differences between the tumours of blacks and whites are also involved.

Wallace and her colleagues used "gene chips" to scan for gene activity in prostate tumours removed from 33 African-American and 36 white patients. There were significant differences between blacks and whites for the activity of more than 160 genes, many of which were involved in regulating the immune system.

These differences could simply reflect greater inflammation in the tumours of African Americans. But given that some of the genes are involved in the production of interferons, one of the body's defences against viruses, the higher incidence of prostate cancer in African Americans could be due to a higher rate of infection with an unknown cancer-causing virus. To test this possibility, the researchers are now looking for viral genes in prostate tumour samples.

Sex differences

African American women, meanwhile, are slightly less likely to develop breast cancer than whites – but the disease seems to strike them younger, and is more likely to kill. Differences in gene activity between the tumours of blacks and whites may again be involved, Lori Field of the Windber Research Institute in Pennsylvania told the AACR meeting.

Field's team compared breast tumours taken from 26 pairs of black and white women, matched for age and the stage of their cancer, who were either serving in the US military, or were the dependent of a service member. All of the patients were being treated at the Walter Reed Army Medical Center in Washington DC, minimising biases due to differences in access to healthcare between the races.

The researchers found 65 genes with significantly different levels of activity between tumours from blacks and whites. Unlike the prostate cancer study, there was no clear link with the immune system. And while some of the genes involved have previously been linked to cancer suppression or tumour development, most had not.

Mystery changes

What caused these differences is unclear. Field suggests that mutations in some of the genes may be involved. Alternatively, the differences may be linked to chemical alterations, known as epigenetic changes, to the DNA that regulates the genes' activity.

"We really don't know at this time," Field says. The long-term goal, she says, is to identify new targets for drugs – which could prove particularly valuable in treating African Americans.

That prospect is welcomed by Funmi Olopade of the University of Chicago, who studies racial disparities in breast cancer outcomes. "I'm happy that people are trying to look at plausible biological explanations," she says.

Drug giant Merck accused of deaths cover-up

* 21:00 15 April 2008
* NewScientist.com news service
*** Jim Giles**

It is perhaps the biggest drug scandal of recent years. Before Merck withdrew Vioxx in 2004, the popular painkiller was linked to heart attacks in tens of thousands of people. Now researchers have alleged that Merck knew of the dangers years earlier, but tweaked statistics and hid data so that regulators remained in the dark.

Vioxx was a blockbuster drug for Merck in the 5 years it was on the market, generating billions of dollars in revenue. After it was linked to heart attacks and strokes, the firm pulled its product, and earlier this year Merck agreed to provide almost US$5 billion in compensation to those claiming to have been harmed.

But an analysis of documents released during the litigation process that led to that settlement, carried out by Richard Kronmal, a statistician at the University of Washington, Seattle, who acted as an expert witness in the Merck lawsuits, suggests that company scientists were aware of the problems well before 2004.

Internal report

Kronmal's study, co-authored with colleague Bruce Psaty, focuses on a 2001 internal company report. In it, Merck staff describe two recently completed trials involving around 1000 patients on Vioxx and a roughly equal number taking a placebo. Thirty-four people taking the drug died, compared with just 12 on the placebo.

But when Merck submitted the results to the US Food and Drug Administration (FDA) the same year, the company analysed the data in a different way. Deaths that occurred after patients completed their course of Vioxx appear to have been removed from the results, even though the drug can cause problems after patients stop taking it. Removing the deaths reduced the risk attributed to Vioxx.

The studies still prompted the FDA to ask whether the risk associated with the drug was enough to warrant stopping another ongoing trial, but Merck replied that it wasn't. According to documents cited by Psaty and Kronmal, the company described the increase in mortality – which its own report revealed to be threefold – as "small numeric differences… most consistent with chance fluctuations".

A Merck statement, released to coincide with the Psaty and Kronmal paper, does not address the allegations in detail, but says that the company has analysed the trials and "found that there was no pattern suggesting the deaths had any connection to Vioxx; some of the deaths were caused by car accidents, poisonings, infections and other causes that are not related to Vioxx".

The full set of documents released during the trials also contains details of other possible tactics employed by Merck. When a study suggested that Vioxx was more dangerous than a rival drug, for example, the company is alleged to have decided not to publish the results or properly inform the FDA.

Expert witness

David Egilman, a public health researcher and advocate at Brown University in Attleboro, Massachusetts, acted as an expert for Vioxx plaintiffs and has also analysed the internal documents. He says the documents contain descriptions of an experiment, known as Protocol 906, that compared the response of around 450 arthritis patients to Vioxx and Pfizer's drug, Celebrex. The two drugs performed equally well, but the rate of side effects among Vioxx users – around 10% – was roughly twice that of those on Celebrex.

Egilman says the documents also contain an email in which a Merck employee tells a co-worker that "this is a very serious result and you will hardly be surprised by the idea of keeping this VERY TIGHT for the moment".

Egilman adds that the results of Protocol 906 were never published or made clear to the FDA. Merck did not respond to a request from New Scientist for comment on Egilman's analysis.

Critics say problems with data manipulation are due to intense pressure on drug companies to chase the multi-billion revenues generated by blockbuster drugs.

"It completely clouds your ethical responsibility," says Merrill Goozner, director of the Center for Science in the Public Interest in Washington, D.C.

Journal reference: Journal of the American Medical Association (vol 299, p 1813)

Euro MPs urged to save tigers

MEPs are being urged to use their influence to force nations with wild tiger populations to halt poaching and the illegal trade in tiger parts.

The European Parliament's first Tiger Day is being held to focus attention on the plight of the endangered animals.

Scientists estimate that only 2,500 breeding adults are left in the wild.

However, campaigners say tiger numbers could reach 10,000 within a decade if attempts to protect the animals receive additional support and resources.

Figures show that only about 2,500 breeding tigers remain in the wild

'Tiger farms'

There are growing fears among campaign groups that some nations, such as China, could soon legalise the trade in farmed tiger parts.

"A few Chinese businessmen who invest in industrialised tiger farming are petitioning the government to lift a 15-year trade ban that has successfully reduced the market for tiger parts used in traditional Chinese medicine," said Grace Ge Gabriel from the International Fund for Animal Welfare (Ifaw).

"Overturning the trade ban would open the floodgates of consumption, and stimulate more poaching of wild tigers."

Dirk Sterckx, a Belgian MEP and chairman of the Parliament's Delegation to China, said it was "absolutely essential" for China to support the international efforts to save wild tigers.

"I would urge the Chinese authorities to fulfill their international obligations by declaring their commitment to the 1993 ban on the trade in tiger parts," he commented, "and by destroying existing stockpiles of tiger parts."

Alasdair Cameron, from the London-based Environmental Investigation Agency (EIA), called for the phasing out of China's tiger farms.

"It is essential that all parties, including the European Parliament, do all that they can to prevent the extinction of the wild tiger and other Asian big cats," he said.

During the course of Brussels Tiger Day, which is being hosted by UK MEP Neena Gill, politicians are being invited to a range of events, including a meeting with a number of the world's leading experts on tigers.

'Big brain' keeps dementia at bay

Having a large hippocampus - a part of the brain involved with memory - seems to provide protection against the symptoms of dementia, a study suggests.

A US team compared the brains of 35 people who had Alzheimer's "plaques", some of whom died with sharp minds and others who showed no dementia symptoms.

The hippocampus, an area at the base of the brain, was on average 20% larger in those with cognitive functions intact.

The Alzheimer's Society cautioned that it was a "relatively small study".

The research was presented at a meeting of the American Academy of Neurology.

It has long been recognised that people can die with all the biological evidence of Alzheimer's - such as a build-up of plaques and tangles within the brain - but having remained perfectly lucid until the last.

Researchers at Oregon Health and Science University in Portland compared the brains of 12 such people with 23 others who had similar levels of plaques, but had been diagnosed with Alzheimer's before death.

Prevention strategies

The hippocampus is located close to the junction with the spinal cord and is believed to "encode" experiences so they can be stored as long-term memories in another part of the brain.

"This larger hippocampus may protect these people from the effects of Alzheimer's disease-related brain changes," said lead researcher Deniz Erten-Lyons.

"Hopefully this will lead us eventually to prevention strategies."

The Alzheimer's Society said it remained unclear from this "relatively small study" whether the larger hippocampus really was the reason why people with dementia did not display the signs.

"However this work is consistent with increasing research that has shown that people with higher levels of education or cognitive reserve may be protected from some of the effects of dementia," said Professor Clive Ballard.

"This is an exciting area of research which needs more exploration."

Forecast for big sea level rise

By Richard Black Environment correspondent, BBC News website, Vienna

Sea levels could rise by up to one-and-a-half metres by the end of this century, according to a new scientific analysis.

This is substantially more than the Intergovernmental Panel on Climate Change (IPCC) forecast in last year's landmark assessment of climate science.

Sea level rise of this magnitude would have major impacts on low-lying countries such as Bangladesh.

The findings were presented at a major science conference in Vienna.

The research group is not the first to suggest that the IPCC's forecast of an average rise in global sea levels of 28-43cm by 2100 is too conservative.

The IPCC was unable to include the contribution from "accelerated" melting of polar ice sheets as water temperatures warm because the processes involved were not yet understood.

Melt water

The new analysis comes from a UK/Finnish team which has built a computer model linking temperatures to sea levels for the last two millennia.

"For the past 2,000 years, the [global average] sea level was very stable, it only varied by about 20cm," said Svetlana Jevrejeva from the Proudman Oceanographic Laboratory (POL), near Liverpool, UK.

"But by the end of the century, we predict it will rise by between 0.8m and 1.5m.

"The rapid rise in the coming years is associated with the rapid melting of ice sheets."

The model, she told reporters here at the European Geosciences Union (EGU) annual meeting, is able to mimic accurately sea levels reliably observed by tide gauges over the last 300 years.

There is little concrete evidence on sea levels for the thousands of years before that, explained POL's Simon Holgate, who was not involved in the new study.

"There is some limited archaeological evidence [based on] the sill heights of fish enclosures that the Romans used, that's probably the strongest evidence that there hasn't been any significant change in sea level over the last 2,000 years."

Against that, he said, the currently observed rise of about three mm per year is significant, and many scientists working in the field expect to see an acceleration.

Last year, German researcher Stefan Rahmstorf used different methodology but reached a similar conclusion to Dr Jevrejeva's group, projecting a sea level rise of between 0.5m and 1.4m by 2100.

Space-eye view

The latest satellite data indicates that the Greenland and West Antarctic ice sheets are losing mass, though the much bigger East Antarctic sheet may be gaining mass.

A full melting of Greenland and West Antarctica would raise sea levels by many metres; but the process, if it happened, would take centuries.

"We know what's happening today from satellite data, but trying to predict what that means in the future is very difficult science," noted Steve Nerem from the University of Colorado, whose own research concerns global sea levels.

"There's a lot of evidence out there that we're going to see at least a metre of sea level rise by 2100," he said.

"We're seeing big changes in Greenland, we're seeing big changes in West Antarctica, so we're expecting this to show up in the sea level data as an increase in the rate we've been observing."

However, a rise of even a metre could have major implications for low-lying countries - especially, noted Dr Holgate, those whose economies are not geared up to build sophisticated sea defence systems.

"Eighty to 90% of Bangladesh is within a metre or so of sea level," he said, "so if you live in the Ganges delta you're in a lot of trouble; and that's an awful lot of people."

Dr Jevrejeva's projections have been submitted for publication in the scientific journal Proceedings of the National Academy of Sciences.

Flu tracked to viral reservoir in tropics

Each winter, strains of influenza A virus infect North Americans, causing an average of 36,000 deaths. Now, researchers say the virus comes from a viral reservoir somewhere in the tropics, settling a key debate on the source of each season's infection.

"We now know where the influenza A virus comes from every year," said Edward Holmes, professor of biology at Penn State. "And because we now know how the virus evolves, we have a much better chance of controlling it."

Currently, there are many strains of the influenza virus that appear only in birds, which are natural viral reservoirs. So far three of these viral strains -- H1N1, H2N2 and H3N2 – have caused epidemics in humans as influenza A.

Of the three, H3N2 is the dominant strain, responsible for most influenza infections each winter, with lower levels of H1N1. However, little is known about how these two strains spread on a geographical scale, and how whole genome of influenza A virus evolves.

Holmes and his colleagues analyzed complete genomes of 1,032 strains of H1N1 and H3N2 viruses sampled over a 12-year period from New York state in the northern hemisphere and New Zealand in the southern hemisphere.

The researchers noticed that over time, both strains follow a distinctive pattern. In seasons where the H3N2 strain is dominant, H1N1 is not and vice versa.

"We found that the two strains peak at different times, and seem to be directly competing with each other" said Holmes, whose findings appear today online in Nature. The results also indicate that compared to the H3N2 strain, the H1N1 strain exhibits far less genetic diversity, although it is not clear why.

Holmes says his results also show that the influenza A virus is frequently exchanging genes by reassortment – when multiple human influenza viruses infect a single person and shuffle their genes – which sometimes allows the virus to acquire a new haemagglutinin, a protein that facilitates the entry of viral particles into the host cells.

These new haemagglutinins sometimes cause vaccines to fail, explained Holmes, whose work is funded by the National Institutes of Health.

"The critical thing is unless you understand the way the genome evolves, you will not understand why vaccines work during some years and fail during others," he added. "We can now show that vaccines failed in some years because new haemagglutinins appeared."

The Penn State researcher says his analysis not only indicates how the influenza virus is evolving, but also where new strains are being generated.

Each year new strains appear in the northern hemisphere, infect people and then burn out. However, patterns of genetic diversity within the viruses suggest the strains are coming from a global source population. The researchers believe that there must be some reservoir somewhere that every year generates new strains that are injected each season into the north and the south, and then burn themselves out.

"We know the strains are dying out every year in the northern and southern hemispheres. So they're surviving somewhere else, and we think it is a reservoir in the tropics," Holmes said. "It tells us that to really understand how the influenza virus evolves on a seasonal basis, and to make the best vaccine, we need to focus our surveillance on the source population in the tropics, especially in places such as Southeast Asia." Other researchers on the paper include Andrew Rambaut, University of Edinburgh; Oliver Pybus, University of Oxford; Martha Nelson, graduate student, Penn State; Jeffery K. Taubenberger, Laboratory of Infectious Diseases, NIH, and Cecile Viboud, Fogarty International Center, NIH.

Intelligence and rhythmic accuracy go hand in hand

People who score high on intelligence tests are also good at keeping time, new Swedish research shows. The team that carried out the study also suspect that accuracy in timing is important to the brain processes responsible for problem solving and reasoning.

Researchers at the medical university Karolinska Institutet and Umeå University have now demonstrated a correlation between general intelligence and the ability to tap out a simple regular rhythm. They stress that the task subjects performed had nothing to do with any musical rhythmic sense but simply measured the capacity for rhythmic accuracy. Those who scored highest on intelligence tests also had least variation in the regular rhythm they tapped out in the experiment.

"It's interesting as the task didn't involve any kind of problem solving," says Fredrik Ullén at Karolinska Institutet, who led the study with Guy Madison at Umeå University. "Irregularity of timing probably arises at a more fundamental biological level owing to a kind of noise in brain activity."

According to Fredrik Ullén, the results suggest that the rhythmic accuracy in brain activity observable when the person just maintains a steady beat is also important to the problem-solving capacity that is measured with intelligence tests.

"We know that accuracy at millisecond level in neuronal activity is critical to information processing and learning processes," he says.

They also demonstrated a correlation between high intelligence, a good ability to keep time, and a high volume of white matter in the parts of the brain's frontal lobes involved in problem solving, planning and managing time.

"All in all, this suggests that a factor of what we call intelligence has a biological basis in the number of nerve fibres in the prefrontal lobe and the stability of neuronal activity that this provides," says Fredrik Ullén.
Publication: '*Intelligence and variability in a simple timing task share neural substrates in the prefrontal white matter',* Fredrik Ullén, Lea Forsman, Örjan Blom, Anke Karabanov and Guy Madison, The Journal of Neuroscience, 16 April 2008. Download image: http://ki.se/pressbilder

Is there anybody out there?

Is there anybody out there? Probably not, according to a scientist from the University of East Anglia. A mathematical model produced by Prof Andrew Watson suggests that the odds of finding new life on other Earth-like planets are low, given the time it has taken for beings such as humans to evolve and the remaining life span of Earth.

Structurally complex and intelligent life evolved late on Earth and it has already been suggested that this process might be governed by a small number of very difficult evolutionary steps.

Prof Watson, from the School of Environmental Sciences, takes this idea further by looking at the probability of each of these critical steps occurring in relation to the life span of Earth, giving an improved mathematical model for the evolution of intelligent life.

According to Prof Watson a limit to evolution is the habitability of Earth, and any other Earth-like planets, which will end as the sun brightens. Solar models predict that the brightness of the sun is increasing, while temperature models suggest that because of this the future life span of Earth will be 'only' about another billion years, a short time compared to the four billion years since life first appeared on the planet.

"The Earth's biosphere is now in its old age and this has implications for our understanding of the likelihood of complex life and intelligence arising on any given planet," said Prof Watson.

"At present, Earth is the only example we have of a planet with life. If we learned the planet would be habitable for a set period and that we had evolved early in this period, then even with a sample of one, we'd suspect that evolution from simple to complex and intelligent life was quite likely to occur. By contrast, we now believe that we evolved late in the habitable period, and this suggests that our evolution is rather unlikely. In fact, the timing of events is consistent with it being very rare indeed."

Prof Watson suggests the number of evolutionary steps needed to create intelligent life, in the case of humans, is four. These probably include the emergence of single-celled bacteria, complex cells, specialized cells allowing complex life forms, and intelligent life with an established language.

"Complex life is separated from the simplest life forms by several very unlikely steps and therefore will be much less common. Intelligence is one step further, so it is much less common still," said Prof Watson.

His model, published in the journal Astrobiology, suggests an upper limit for the probability of each step occurring is 10 per cent or less, so the chances of intelligent life emerging is low – less than 0.01 per cent over four billion years.

Each step is independent of the other and can only take place after the previous steps in the sequence have occurred. They tend to be evenly spaced through Earth's history and this is consistent with some of the major transitions identified in the evolution of life on Earth.

World's oldest living tree discovered in Sweden

The world's oldest recorded tree is a 9,550 year old spruce in the Dalarna province of Sweden

The world's oldest recorded tree is a 9,550-year-old spruce in the Dalarna province of Sweden.

The spruce tree has shown to be a tenacious survivor that has endured by growing between erect trees and smaller bushes in pace with the dramatic climate changes over time.

For many years the spruce tree has been regarded as a relative newcomer in the Swedish mountain region.

" Our results have shown the complete opposite, that the spruce is one of the oldest known trees in the mountain range," says Leif Kullman, Professor of Physical Geography at Umeå University.

A fascinating discovery was made under the crown of a spruce in Fulu Mountain in Dalarna. Scientists found four "generations" of spruce remains in the form of cones and wood produced from the highest grounds.

The discovery showed trees of 375, 5,660, 9,000 and 9,550 years old and everything displayed clear signs that they have the same genetic makeup as the trees above them. Since spruce trees can multiply with root penetrating braches, they can produce exact copies, or clones.

The tree now growing above the finding place and the wood pieces dating 9,550 years have the same genetic material. The actual has been tested by carbon-14 dating at a laboratory in Miami, Florida, USA.

Previously, pine trees in North America have been cited as the oldest at 4,000 to 5,000 years old.

In the Swedish mountains, from Lapland in the North to Dalarna in the South, scientists have found a cluster of around 20 spruces that are over 8,000 years old.

Although summers have been colder over the past 10,000 years, these trees have survived harsh weather conditions due to their ability to push out another trunk as the other one died.

" The average increase in temperature during the summers over the past hundred years has risen one degree in the mountain areas," explains Leif Kullman.

Therefore, we can now see that these spruces have begun to straighten themselves out. There is also evidence that spruces are the species that can best give us insight about climate change.

The ability of spruces to survive harsh conditions also presents other questions for researchers.

Have the spruces actually migrated here during the Ice Age as seeds from the east 1,000 kilometres over the inland ice that that then covered Scandinavia? Do they really originate from the east, as taught in schools? "My research indicates that spruces have spent winters in places west or southwest of Norway where the climate was not as harsh in order to later quickly spread northerly along the ice-free coastal strip," says Leif Kullman.

"In some way they have also successfully found their way to the Swedish mountains."

The study has been carried out in cooperation with the County Administrative Boards in Jämtland and Dalarna.

Different mutations in a single gene suggests Parkinson's disease is primarily an inherited genetic disorder

JACKSONVILLE, Fla. – Two new international studies by researchers at the Mayo Clinic site in Florida are rounding out the notion that Parkinson's disease is largely caused by inherited genetic mutations that pass through scores of related generations over hundreds, if not thousands of years. These genetic influences, which can be small but additive, or large and causative, overturn common beliefs that the neurodegenerative disease mostly occurs in a random fashion or is due to undetermined environmental factors.

These latest studies bring the total of number of disease-related mutations in an as yet poorly understood gene, leucine-rich repeat kinase 2 (LRRK2), to seven, all of which are linked, either weakly or strongly, to typical, late onset development of Parkinson's disease in people around the world. One mutation (R1628P) doubles the risk of Parkinson's disease in ethnic Chinese, according to a study published on Wednesday, April 16, 2008 in the online edition of the Annals of Neurology. The second study, published April 15 in Neurology, demonstrates that another very rare mutation (R1441C), found in people on three continents, increases risk by more than 10-fold.

The R1628P was identified by the strong collaborative effort of researchers from Taiwan, Singapore, Japan, and the U.S. The research institutions included the National Taiwan University Hospital, led by Dr. Ruey-Meei Wu, Chang Gung Memorial Hospital led by Dr. Yih-Ru Wu, National Neuroscience Institute of Singapore led by Dr. Eng-King Tan and Juntendo University, led by Dr. Nobutaka Hattori. This group believes the R1628P mutation arose from a single individual in the Han Chinese population about 2,500 years ago and has since spread through generations of descendants, wherever they live. This is the second common LRRK2 mutation discovered in Asians –a mutation labeled G2385R believed to have originated 4,500 years ago was first reported in the journal 'Neurogenetics' in 2006 and subsequently confirmed by several groups. Lrrk2 G2385R and R1628P predispose over 100 million Chinese people to Parkinson's disease.

"The picture that is emerging of Parkinson's disease is one in which genetic risk factors, passed down through the population for hundreds or thousands of years, add up to substantial susceptibility within a single individual, and, with some possible environmental influences, can result in disease," says Mayo Clinic neuroscientist Owen A. Ross, Ph.D., first author on the Annals of Neurology study.

"These types of mutations are important because the goal of this research is to be able to screen people who are most at risk because of their genetic profiles, and design therapies that interfere with the disease process," Dr. Ross says.

The stronger R1441C mutation, also currently being reported, originated from several different "founders" and is now found in 20 families on three continents. It is relatively causative in nature, meaning the majority of people with the mutation are likely to develop the disease.

"Parkinson's disease is fascinating to study because we can now roughly trace when and where mutations occur, and how they travel through offspring and in populations," says Kristoffer Haugarvoll, M.D., a visiting scientist at Mayo Clinic and lead author on the Neurology study. "It also shows us that disease that appears to be the same in the majority of patients can originate from different genetic mutations – either genes that increase risk substantially, or by several risk factors, genetic and environmental, that each have minor but additive effects."

Same mutations in familial and sporadic forms of the disease

Only about 10 percent of patients diagnosed with Parkinson's disease have a strong family history of the disease, and Mayo Clinic researchers in Florida have been part of a worldwide effort to discover whether common genes may explain the origin of the other 90 percent, the so-called "sporadic" form. In 2004, they were part of a team that discovered that the LRRK2 gene is linked to both familial and non-familial cases of the disease.

Since then, they have found LRRK2 mutations that can cause the same clinical manifestations of Parkinson's disease in people with and without a family history – discoveries that "have caused a paradigm shift in the field," says Dr. Ross. For example, a mutation labeled G2019S causes both familial and non-familial Parkinson's disease in a high number of Berber Arabs and Ashkenazi Jews. "This shows that the effect of mutations in different areas of the Lrrk2 protein lead to the same disease, although it may not manifest in each generation and so did not appear to be familial," he says.

In the latest study, Dr Ross and colleagues studied 1079 ethnic Han Chinese diagnosed with Parkinson's disease, of which 44 reported a family history of the disease. These patients were compared with 907 ethnically matched Han Chinese who did not have Parkinson's disease, and results showed the R1628P variant was approximately twice as frequent in Parkinson's disease patients as in the control population. From this, the researchers estimated that for every 100 Chinese, 3 will have the gene variant. Further research then suggested that the R1628P carriers were related to a single common founder that dated from about 2,500 years ago.

The researchers then searched for evidence of the mutation in Japanese patients and controls – but did not find it. "The theory is that this mutation arose in China after the Japanese and Chinese segregated their populations, which explains why the G2385R mutation, which is 2,000 years older than R1628P, is found in both populations and is more common," Dr. Ross says.

"Inheriting one or both of these mutations doesn't mean that a person will develop Parkinson's disease, but that an individual's risk is increased," he says. "The basis of population genetics is that disease is familial; people are so distantly related that they don't know they may have inherited specific genes. While there may be an environmental component to development of the disease, none have been identified that have risks as large as those seen by the LRRK2 gene mutations."

Generations that carry rare but critical mutations

In the Neurology study, Dr. Haugarvoll, who is from Norway, worked with researchers from a number of countries to collect genetic information from discrete populations of people representing three continents who had previously been found to be carriers of the R1441C mutation. "This was a completely collaborative effort,"

he says. "Rare mutations affect relatively few patients, but if we join forces in a worldwide initiative, we have larger samples to look at, and that is the only way you can advance the science."

The scientists identified 33 affected and 15 unaffected R1441C mutations from 20 families, including four patients with no family history of Parkinsonism. These patients all developed disease that mimicked the typical, late onset disease normally seen in non-familial, sporadic Parkinson's disease, Haugarvoll says. The scientists believe the same disease-causing mutation has occurred independently on several occasions; however, most patients seem to originate from two different founders. One variant was found in Italian, German, Spanish, and American patients. The second was discovered in patients from Belgium and from a single American family, located in Nebraska.

Dr. Haugarvoll says the region of R1441C appears to be "a hotspot for mutation events" because other mutations occur in this general area. What is most interesting, he says, is that "even though there are familial mutations in different locations of the gene, it produces the same effect, the same disease."

"It seems like mutations are occurring in a few founders, and that these founders have a lot of offspring over generations that carry the mutation. Even in sporadic disease, then, familial genes are inherited but symptoms may skip some generations, making the disease appear sporadic" Dr. Haugarvoll says.

Major funding for both studies came from NIH (including the Morris K. Udall Center for Excellence in Parkinson's Disease Research at the Mayo Clinic) and several international funding agencies.

Slowly-developing primates definitely not dim-witted

DURHAM, N.C. -- Some primates have evolved big brains because their extra brainpower helps them live and reproduce longer, an advantage that outweighs the demands of extra years of growth and development they spend reaching adulthood, anthropologists from Duke University and the University of Zurich have concluded in a new study.

The four investigators compared key benchmarks in the development of 28 different primate species, ranging from humans living free of modern trappings in South American jungles to lemurs living in wild settings in Madagascar.

"This research focused specifically on the balance between the costs and benefits of growing a large brain," said Nancy Barrickman, a graduate student in Duke's Department of Biological Anthropology and Anatomy, who is first and corresponding author of a report now posted online for a future print edition of the Journal of Human Evolution.

"Growth rates are much slower in large-brained organisms, and that causes a delay in reproduction," Barrickman said. "If individuals wait too long to reach maturity then they run the risk of dying before they've had the chance to reproduce. So there must be some benefit to large brain size at the same time these costs are incurred.

"Is larger brain size causing life histories to become extended and slowed down? We think so," Barrickman added. "That obviously fits in very well with humans, who take forever to grow up and live a really long time. So we have the opportunity to have lots of offspring over that long period."

Barrickman drew these conclusions working with Carel van Schaik, a Duke adjunct professor on her doctoral studies committee who directs the University of Zurich's Anthropological Institute and Museum. Other coauthors include Duke graduate student Meredith Bastian, and Karin Isler, a collaborator of van Schaik's in Switzerland.

"Our main finding is that brain size is a far better predictor of the duration of immaturity than body size, at least among primates," said van Schaik. "This study is also useful because it allows us to understand why humans develop so slowly and live so long -- we have no other choice!"

Other studies have linked primate brain size to life span and other factors, but those results have been contradictory, according to the new report. Previous studies were "polluted" by mixing data on captive and wild animals, van Schaik said. "Because development and survival are highly responsive to conditions, this variability made it impossible to do clean comparisons."

Their study was supported by the scientific research society Sigma Xi, the American Museum of Natural History and the Ruggles Gates Fund for Biological Anthropology in the United Kingdom.

Barrickman and her colleagues focused on primates living in the wild because "animals tend to grow up faster in captivity," she said. In the case of humans, they studied the Ache, a tropical forest culture in eastern Paraguay.

"Their food is exclusively wild food they forage from the forest," she said of the Ache. "And they don't have other things like modern birth control methods that you'd find in an industrial population like ours. My argument is that we're basically captive primates by comparison."

After analyzing available data on life history benchmarks such as length of pregnancy, years from birth to maturity, pre- and post-natal brain development and lifespan, the researchers found that humans and other big-brained species such as chimpanzees share certain survival traits.

It takes longer to grow a bigger brain, thus leaving immature offspring in need of extra care for longer periods. But larger brains also provide adult caretakers with "more complex foraging techniques, predator avoidance and social skills," the researchers wrote.

Greater skill allows adults to live longer, which in turn gives them longer reproductive lives. Humans have added to this adaptive advantage by using their cognitive and social skills to work together in providing shelter and nourishment for the young, they said.

Additionally, human females can live well beyond their reproductive years. And the contributions of non-reproducing grandmothers may further enhance their own children's reproductive effort and decrease infant mortality, Barrickman said. That's because grandmas offer extra assistance in child rearing and food gathering.

Studies of some primitive societies, such as the Hadza in East Africa, show that "grandchildren are more likely to survive if they have a grandmother present," she said.

Some studies suggest that starting life with a brain that is still developing itself confers some survival advantages to offspring, according to Barrickman. Extended interactions with mothers and their surroundings can help "wire their brain" as it grows, she said.

"They wind up with very plastic brains that can adjust to whatever environmental stimulations come at them," she said.

Your belly fat could be making you hungrier

Researchers in London, Canada identify new source of appetite stimulant

The extra fat we carry around our middle could be making us hungrier, so we eat more, which in turn leads to even more belly fat. Dr. Kaiping Yang and his colleagues at the Lawson Health Research Institute affiliated with The University of Western Ontario found abdominal fat tissue can produce a hormone that stimulates fat cell production. The researchers hope this discovery will change in the way we think about and treat abdominal obesity.

Yang identified that the hormone Neuropeptide Y (NPY) is produced by abdominal fat tissue. Previously, it was believed to only be produced by the brain. Yang believes this novel finding may lead to new therapeutic targets for combating obesity. Their findings were reported in a recent issue of The FASEB Journal.

The traditional view is that one of the main reasons why overweight people eat more food is because their brains produce the hormone NPY in excessive amounts. NPY is the most potent appetite stimulating hormone known, sending signals to the individual that they are constantly hungry. However, Yang, a Professor in the Departments of Obstetrics & Gynaecology and Physiology & Pharmacology at the Schulich School of Medicine & Dentistry at The University of Western Ontario, has provided evidence that in obese rat models NPY is also produced locally by abdominal fat.

A fat cell cannot replicate itself. But the researchers found NPY increases fat cell number by stimulating the replication of fat cell precursor cells, which then change into fat cells.

Yang says "this may lead to a vicious cycle where NPY produced in the brain causes you to eat more and therefore gain more fat around your middle, and then that fat produces more NYP hormone which leads to even more fat cells."

Being overweight, regardless of where the fat is located, is unhealthy. However, because of its anatomical location and its byproducts, abdominal fat or the apple-shape is known to be the most dangerous. People predisposed to the apple shape are at an elevated risk for heart disease, Type 2 diabetes, hypertension and some cancers.

Next, the researchers will be investigating whether NPY produced by fat is released into the body's circulatory system. "We want to know if NPY could potentially be transported in the blood to the brain where it in turn has an impact on the brain to stimulate feelings of hunger," says Yang. If the researchers find that NPY is in fact transported in the blood circulation then it may be possible to develop a simple blood test to detect increased levels of NPY. "If you can detect NPY early and identify those at risk for abdominal obesity we can then target therapy to turn off NPY. It would be much easier to use drugs to prevent obesity than to treat the diseases caused by obesity."

Using anti-cholinergic drugs may increase cognitive decline in older people

CHICAGO – Anticholinergic drugs, such as medicines for stomach cramps, ulcers, motion sickness, and urinary incontinence, may cause older people to experience greater decline in their thinking skills than people not taking the drugs, according to research that will be presented at the American Academy of Neurology 60th Anniversary Annual Meeting in Chicago, April 12–19, 2008.

The study looked at the effects of taking a medication with anticholinergic properties on the annual change in thinking abilities of 870 Catholic nuns and clergy members who were an average of 75 years old. All of the participants were part of the Rush Religious Orders Study, an ongoing, longitudinal, clinical study of older people without dementia.

All of the participants underwent annual cognitive tests and reported their medication use for an average followup period of eight years. During the study, 679 people took at least one medication with anticholinergic properties.

The study found those people who took anticholinergic drugs saw their rate of cognitive function decline 1.5 times as fast as those people who did not take the drugs.

"Our findings point to anticholinergic drugs having an adverse impact on cognitive performance in otherwise normal, older people," said study author Jack Tsao, MD, DPhil, Associate Professor of Neurology at Uniformed Services University in Bethesda, Maryland, and member of the American Academy of Neurology. "Doctors may need to take this into account before prescribing these commonly used drugs."

Tsao says more research is needed to determine the mechanism behind the rapid memory loss apparently associated with anticholinergic drugs and to identify which drugs, in particular, may be more likely to impair cognition.

The study was supported by the American Philosophical Society Daland Grant and grants from the National Institute on Aging.

Infantile esotropia linked to developmental delays

Babies' development 'catches up' after surgery to fix crossed eyes

Philadelphia, April 17, 2008 – Babies with an eye-alignment disorder called infantile esotropia have delays in motor development milestones, but development "catches up" after corrective surgery, reports a study in the April Journal of AAPOS (American Association for Pediatric Ophthalmology and Strabismus).

Led by James R. Drover, PhD, of the Retina Foundation of Southwest Texas, Dallas, the researchers assessed developmental milestones in 161 infants with infantile esotropia, or crossed eyes. These infants need surgery on the eye muscles to correct the alignment. However, it has been unclear whether surgery to correct esotropia influences other aspects of infant development.

To answer this question, the researchers had parents complete an infant development questionnaire before and/or after corrective surgery. The questionnaire assessed fine-motor skills, such as grasping a toy and handling a bottle (sensorimotor development); as well are large-muscle skills, such as sitting, standing, and walking (gross motor development). A group of children with normal eye alignment were studied for comparison.

Before surgery, infants with esotropia had delays in both milestones. The developmental delays appeared as early as four to five months of age and were still present at ten months.

The sensorimotor delays were "particularly profound," and probably reflected the importance of normal binocular vision (both eyes working together) in fine-muscle tasks. The delays in gross motor development, while not as severe, were still significant.

In contrast, infants tested after esotropia surgery had no delays in developmental milestones. In fact, they actually had a faster rate of sensorimotor development, suggesting that correcting their binocular vision helped their development to "catch up" to that of normal infants.

Infantile esotropia is one of a group of disorders called strabismus, in which the eyes are not aligned normally. Without surgery to correct the problem, depth perception cannot develop. Because vision develops rapidly between three to eight months of age, infantile esotropia might cause delays in developmental milestones—for example, grasping objects, crawling, or walking—that depend on normal vision. However, previous studies were unclear as to whether early surgery helps normal development, partly because many babies with esotropia are not sent for expert evaluation by a pediatric ophthalmologist until they are over one year old.

The new results show that babies with infantile esotropia have significant delays in developmental milestones before surgery, and, suggests that development catches up to normal after surgery to correct eye alignment. Dr. Drover and colleagues suspect that the rapid rate of development after surgery results from the improvement in binocular function.

"Doctors continue to disagree over when is the best time to correct strabismus in children, because most of the focus has been on when it can best help their vision," comments Dr. David G. Hunter of Children's Hospital Boston and editor-in-chief of the Journal of AAPOS. "This study says that surgery to correct strabismus doesn't just help the eyes—it helps the whole child."

Notes to Editors:

The article appears in Journal of AAPOS (April 2008), published by Elsevier on behalf of the American Association for Pediatric Ophthalmology and Strabismus. Full text of the article mentioned above is available upon request. Contact Jayne Dawkins at (215) 239-3674 or ja.dawkins@elsevier.com to obtain a copy or to schedule an interview.

Antidepressants enhance neuronal plasticity in the visual system

In the April 18 issue of Science, scientists from the Scuola Normale Superiore in Pisa, Italy and the Neuroscience Centre at the University of Helsinki, Finland, provide new information about the mechanism of action of antidepressant drugs. In addition, the study suggests that antidepressants could also be used for the treatment of amblyopia. However, to produce a functional effect, antidepressant treatment also seems to require environmental stimuli, such as rehabilitation or therapy

According to Professor Eero Castrén at the University of Helsinki, the original objective of the study was to learn more about why the antidepressant effect of fluoxetine (also known as Prozac) and other selective serotonin reuptake inhibitors develops so slowly, many weeks after starting treatment.

Castrén's research group has approached this question by examining the growth factor, brain-derived neurotrophic factor (BDNF), which influences plasticity of the nervous system or in other words, the ability of brain cells to change their structure or function in response to stimuli. Antidepressants seem to act through BDNF, thus enhancing the plasticity of the nervous system, at least in certain brain areas. However, it has been unclear how antidepressant-induced increases in BDNF could relieve depression.

Neuronal plasticity of the developing visual cortex has been well characterised. Therefore, this classical model of the visual cortex was utilised to examine the effect of fluoxetine on neuronal plasticity, although there was previously no evidence that antidepressants would act on the visual system. During early childhood, if one eye remains weaker than the other eye, the neuronal connections of the stronger eye take over the visual cortex while the connections of the weaker eye retract. During a critical period of early childhood, neuronal connections are in a highly plastic state, and the vision of the weaker eye can be strengthened by covering the better eye, thus reinforcing the connections of the weaker eye to the visual cortex. In adolescence however, after the critical period has closed, plasticity is reduced and covering the better eye no longer strengthens the connections of the weaker eye which remains poor in vision throughout adulthood.

The experiments, mainly conducted by the research group of Professor Lamberto Maffei in Pisa, showed that treatment with the antidepressant, fluoxetine reopened the critical period of plasticity in the visual cortex of adult rats. In experiments where one eye of a young rat was covered during the critical period and reopened only in adulthood, vision improved in the weaker eye to finally equal that of the healthy eye when fluoxetine treatment was combined with covering the healthy eye. This fluoxetine-induced enhancement of plasticity was associated with increased BDNF and reduced cortical inhibition in the visual cortex, which advanced reorganisation of the neuronal connections.

Since fluoxetine, when combined with covering the better eye, improved vision in the weaker eye of adult rats, it is possible that antidepressants could be similarly used in amblyopic humans. The results suggest that the improved plasticity induced by antidepressants leads to a functional neuronal reorganisation in the cerebral cortex. The ability of an antidepressant to facilitate the reorganisation of neuronal connections in a brain area not associated with mood, suggests that similar treatment strategies might also be useful in the treatment of other brain disorders.

It is important to note that fluoxetine improved vision in the weaker eye only if the better eye was covered. This suggests that while antidepressants provide the possibility of rearranging cortical connections, environmental stimuli are required to guide the rearrangement to produce the desired effect.

It is possible that defective neuronal connections in cortical areas related to mood regulation might predispose people to depression. The enhanced plasticity provided by the antidepressant might allow reorganisation of cortical connections and function. However, Castrén emphasises that antidepressants do not repair the network on their own, but that functional recovery also requires environmental guidance, such as social interaction, rehabilitation or therapy.

Rice and UT-Houston join DOD push for regenerative medicine

TMC program is part of $250M search for new treatments for wounded soldiers

The Department of Defense (DOD) today announced that Rice University and the University of Texas Health Science Center at Houston will spearhead the search for innovative ways to quickly grow large volumes of bone tissue for craniofacial reconstruction for soldiers wounded in Iraq and Afghanistan.

The program is part of a broad, $250 million national effort to rapidly apply the latest techniques in regenerative medicine to the treatment of wounded soldiers. DOD officials today unveiled the Armed Forces Institute for Regenerative Medicine (AFIRM). AFIRM is made up of two civilian research consortiums working with the U.S. Army Institute for Surgical Research at Fort Sam Houston in San Antonio.

"This is by far the largest federal investment ever made in regenerative medicine, and it's no coincidence that the Texas Medical Center is playing an important role," said Rice University President David Leebron. "Rice and UT-Houston's collaborative research in this area is at the forefront of this rapidly growing field."

One of AFIRM's civilian consortiums is led by the Wake Forest Institute for Regenerative Medicine and the McGowan Institute for Regenerative Medicine at the University of Pittsburgh. The other is led by Rutgers University and the Cleveland Clinic.

Rice bioengineer Antonios Mikos and UT-Houston surgeon Mark Wong are overseeing the Wake Forest consortium's research on craniofacial reconstruction. Mikos is Rice's J.W. Cox Professor in Bioengineering, professor of chemical and biomolecular engineering and the director of Rice's Center for Excellence in Tissue Engineering. Wong is associate professor and chairman of the Department of Oral and Maxillofacial Surgery at the University of Texas Dental Branch at Houston. Rice and UT-Houston will receive $2 million over the next five years to spearhead the development of new tissue engineering technologies, novel reconstructive surgical techniques and innovative drug therapies that can help wounded soldiers.

"Dr. Mikos and Dr. Wong have been pioneers in the development of new tissue-engineering technologies that can be used for facial reconstruction for victims of catastrophic injury," said Dr. Peter Davies, executive vice president for research at UT–Houston.

Tissue engineering is a fast-growing biomedical discipline that aims to quickly grow human tissues like bone, cartilage and skin that can be surgically transplanted without risk of rejection. Tissue engineers often use a patient's own cells as the basis for new tissue, placing them on biodegradable templates and stimulating them with chemical and physical cues.

"All of our efforts, both here in Houston and around the nation, are aimed at moving forward immediately to deliver therapies to the thousands of soldiers who have been wounded in this time of war," Mikos said.

Mikos, a founding editor of the journal Tissue Engineering and president-elect of the North American Tissue Engineering and Regenerative Medicine International Society, is one of the world's foremost experts on tissue engineering and regenerative medicine.

Technology investigated by the consortium partners in craniofacial reconstruction will include the use of biopolymers as matrices for tissue regeneration and the delivery of different drugs to prevent infection and promote wound healing. Additional tissue-engineering projects that employ adult stem cells to reconstruct lost appendages such as ears and noses will also be investigated.

"We are honored to be part of this consortium, which will allow us to bring to fruition many years of collaborative research with Rice University and apply novel techniques to aid the reconstruction of devastating facial defects sustained by our military personnel," Wong said.

Traditionally, it can take years for laboratory breakthroughs to be translated into clinical practice. Mikos said it is vital for engineers and doctors to work together closely -- at every stage of research -- if cutting-edge technology is to be quickly transitioned to patients.

Wong, the director of the UT Dental Branch at Houston's Oral and Maxillofacial Surgery residency training program, holds surgical appointments at Memorial Hermann Hospital-Texas Medical Center, Lyndon B. Johnson General Hospital, Ben Taub General Hospital and The Methodist Hospital. He said AFIRM's bench-to-bedside research efforts in Houston will help ensure that the technology developed for the military will also benefit civilian victims of trauma.

Davies said, "This is the sort of groundbreaking translational research that is being conducted in UT-Houston's new research facility, the Center for Clinical and Translational Sciences, a state-of-the-art clinical research facility funded by one of the first (Clinical and Translational Science Awards) made by the National Institutes of Health."

The long-standing partnership between Mikos and Wong is the foundation for the research. This partnership has been rewarded with several grants from the National Institutes of Health, the Oral and Maxillofacial Surgery Foundation and industry. It has also provided the basis for a joint educational program combining oral and maxillofacial surgery residency training at UT-Houston with a doctorate in bioengineering at Rice.

Thanks to an existing relationship between the military and the UT Dental Branch's oral and maxillofacial surgery residency program, the military's own trauma surgeons will get firsthand experience with all the new facial reconstruction techniques developed and tested by AFIRM. Under the residency program, surgeons from both the Army and Air Force spend time in Houston gaining experience in trauma management.

"We are fortunate to have a close relationship with UT-Houston where we can get experience with wider variety real-world trauma situations, similar to those we would see in Iraq and Afghanistan," said Capt. Curt Hayes, chief resident of oral and maxillofacial surgery at Lackland Air Force Base's Willford Hall Medical Center in San Antonio. "This new grant presents the opportunity for improving battlefield management and outcome for hard-tissue injuries that are sustained by our military members."

Each of AFIRM's civilian consortiums was awarded $42.5 million over a period of five years. In addition, the two consortia are bringing local public and private matching funds amounting to more than $180 million that will be added to their research budgets -- for a total of more than $250 million available for research.

Rice and UT–Houston are two of the 46 member institutions in the Texas Medical Center (TMC), one of the world's largest medical complexes. TMC institutions conduct more than $1 billion worth of research and see more than 5 million patients each year.

"Rice and UT-Houston's AFIRM research program calls for doctors and bioengineers to work side-by-side to rapidly translate new discoveries from the laboratory to the operating room," said Rice Provost Eugene Levy. "This is an outstanding example of the kind of joint, tightly interwoven research that will be greatly facilitated and that Rice plans to conduct with UT-Houston and its other TMC partners in the new Collaborative Research Center slated to open in mid-2009."

UT–Houston President Dr. James Willerson said, "This is a most significant endeavor and is a tribute to the strength we can achieve through collaboration in the Texas Medical Center."

On the Origin of Muffin Pudding, by Emma Darwin

* 00:01 17 April 2008
* NewScientist.com news service
*** Henry Nicholls**

Want to know when Charles Darwin first recorded his doubt about the stability of species? Or are you more interested in the puddings his wife prepared for him? Notes about both – and reams more – will appear online this week for the first time.

Until now the manuscripts, which the Darwin family donated to Cambridge University Library in 1942, have only been seen by a handful of scholars. Now the library has agreed to make some 20,000 items freely available through The Complete Works of Charles Darwin Online.

When Darwin Online launched 18 months ago, it hosted electronic versions of everything that Darwin ever published. But these are just the end product of his avid research programme, says project director John van Wyhe, a historian of science at Cambridge University.

Pencil sketch

"Behind every one of Darwin's publications, there's a mountain of private papers, notes, reading notes, press clippings and things that people sent to him," he says. "Now at the click of a button much of that material will be available to everyone in the world."

Amongst the mass of new material on the site are several noteworthy documents, including scans of Darwin's ornithological notes from the Beagle voyage in which he penned his first recorded doubt about the stability of species.

Then there's his first sketch of his species theory, which he jotted down in pencil in 1842. This runs to 61 scanned pages, although almost half of them have been crossed through as he reworked the text. There's also the memo written by Darwin's wife Emma in 1839 in which she expressed her concerns about his religious doubts.

Hearty puddings

The online dissemination of these private papers is extremely welcome, says Randal Keynes, a historian and Darwin's great-great-grandson. But they are of limited value to all but the most well-read scholars, he suggests. "The manuscripts aren't easy to make sense of because Darwin's handwriting is just a scrawl," says Keynes. "You also often need to understand the context and his ways of working to understand what he's writing about."

Adam Perkins, the archivist at Cambridge University Library in charge of the original papers, agrees. "These manuscripts will be most useful for Darwin scholars," he says. "But others will also find plenty of interest in there." One such document is a recipe book written in Emma's relatively legible hand. Crammed with details of hearty deserts, such as muffin pudding, lemon blancmange, burnt cream and gingerbread, it should perhaps come with a health warning, says van Wyhe. One of the rare savoury recipes, which appears in Darwin's own hand, gives detailed instructions on how to boil rice.

Dark matter may have been found on Earth

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* NewScientist.com news service
*** Anil Ananthaswamy**

Particles of invisible "dark matter" have been detected deep inside a mountain in Italy, a collaboration of Italian and Chinese physicists claims. But others remain sceptical of the result, because other experiments have failed to detect any dark matter at all.

On Wednesday 16 April, at a workshop in Venice, Italy, the Dark Matter (DAMA) collaboration announced the results of the 4-year second phase of its experiment. DAMA scientists claimed to see dark matter back in 2003, but some scientists believed the result was a quirk of statistics. Now the evidence is stronger.

"We are pretty sure now that this [signal] is not a statistical fluke. What it means is another matter," says Francis Halzen, an astroparticle physicist at the University of Wisconsin-Madison, US. He spoke to New

Scientist after attending the announcement by DAMA project leader Rita Bernabei of the University of Rome, Italy.

Unidentified substance

Astronomers believe our galaxy is awash with particles of dark matter, the invisible, unidentified substance that makes up nearly 90% of the matter in the universe. So far, the existence of dark matter in space has only been determined by its gravitational pull on normal stars and galaxies.

The DAMA experiment has looked more directly for dark matter particles hitting the Earth. The experiment takes place in an underground laboratory that lies beneath 1.4 kilometres of rock, inside the Gran Sasso mountain in Italy. The team looks for flashes of light in a sodium iodide detector.

The flashes mainly come from background "noise", such as ordinary neutrons from radioactivity in the surrounding rock. But some might also come from dark matter particles, and, if so, the scientists expect to see seasonal variations in the signal because the Earth's speed through our galaxy changes depending on its direction of motion.

This theory predicts that the Earth should be hit by more dark matter particles in June, when it is moving through the galaxy in the same direction as the Sun. There would also be fewer particles in December, when it is moving in the opposite direction.

Intense scepticism

That's exactly what the DAMA team reported in 2003, following the first phase of their experiment, which ran for 7 years with a 100-kilogram detector. But the results were met with intense scepticism, as none of the other experiments looking for dark matter had seen anything.

So the DAMA team renewed their search with a larger 250-kilogram detector. And they say they can now confirm that the new experiment has again shown an annual variation in the number of particles hitting their detector. There is a slight increase above the average in June rate and a corresponding decrease in December.

The team claims that the new result is highly significant. The odds that they are simply seeing a random fluctuation are less than one in several billion, they say. They also say they have ruled out the possibility that the signal is due to some systematic effect, such as seasonal variations in the temperature of their underground cavern.

But Halzen is wary. "The discussion about whether this is some unknown systematic effect remains," he says.

Richard Gaitskell from Brown University at Providence, Rhode Island, US, and a member of two dark matter experiments – the Cryogenic Dark Matter Search (CDMS) and the Xenon project – also remains sceptical, because no other experiment has seen signs of dark matter.

"Right now, it is very difficult to reconcile theoretically what they are seeing and what we are seeing," says Gaitskell.

But both Halzen and Gaitskell agree that the new DAMA results might prompt others to try and duplicate the results. "The issue of dark matter is important enough that we should pay attention to this; we should not just ignore it," says Halzen.

Breast cancers behave differently before and after the age of 70

Do the immune defense mechanisms play a role?

Berlin, Germany: Researchers in Belgium have discovered that increasing age affects the way breast cancer behaves. As women approach the age of 70, they become less likely to be diagnosed with aggressive tumours that have spread to the lymph nodes. But after 70, the cancer is increasingly likely to spread, particularly if the tumours are small.

Until now, there has been conflicting evidence on aging and lymph node involvement and this study is the first to show clearly how the link between the two changes before and after the age of 70.

Professor Hans Wildiers told the 6th European Breast Cancer Conference (EBCC-6) in Berlin today (Friday), that he suspects that women older than 70 have decreased immune defence mechanisms, which are less able to deal with tumours that are likely to metastasise to other sites in the body.

"The effect of age of lymph node positivity is not straightforward. There seems to be a different effect between women aged up to 70 years and women older than 70. For the younger group of women, age appears to have a negative effect on lymph node status – the older they become, the less likely the cancer is to have spread to the lymph nodes. For the older group of women (aged over 70), age appears to influence lymph node status in the opposite way – the older they become, the more likely they are to have cancer cells in the lymph nodes if the tumour is small," said Prof Wildiers, who is adjunct head of clinic in the department of general medical oncology at the Multidisciplinary Breast Centre, University Hospitals Leuven, Belgium.

"There is an interaction between age and tumour size, suggesting that, up to the age of 70, age mainly has a positive effect on lymph node status for older women with small tumours. A likely explanation is that breast tumours metastasise less frequently to lymph nodes with increasing age due to the decreased biological

aggressiveness in these tumours. On the other hand, over the age of 70, if the tumours have the potential to metastasise to lymph nodes, this occurs more rapidly in smaller tumours and this might be related to decreased immune defence mechanisms in elderly patients."

Prof Wildiers and his colleagues investigated 2,227 women who had been treated for breast cancer between 2000 and 2006 at the University Hospitals Leuven. Then they compared the results with a separate database of over 11,000 breast cancer patients on the Eindhoven Cancer Registry.

They found that for women aged 70 or younger, increasing age was associated with a decreased prevalence of cancer spreading to the lymph nodes. The women's risk of having positive lymph nodes decreased by 13% for every decade they aged, up to age 70.

Once aged 70 and over, the odds of lymph node involvement doubled with every 10-year increase in age for women who had tumours that were no bigger than 15mm across. If the tumours were larger than 42-43 mm, then risk of lymph node involvement continued to decrease.

Prof Wildiers said: "We know that the elderly have depressed immune defences, and, therefore, it is possible that these decreased defences are unable to prevent invasion of the lymph nodes by metastases in a subset of breast tumours in elderly women. Although breast cancer survival in older women appears to be similar to survival in the general population irrespective of disease status, it might well be that there is a balance in the elderly between, on the one hand, a less aggressive type of tumour, and, on the other hand, their decreased immunological defences."

He said the findings supported the idea that there are two types of tumour in elderly women: ones that are slow-growing and don't invade the lymph nodes even if the tumours are larger, and ones that are aggressive and metastasise very early to the lymph nodes. Women with slow-growing tumours might benefit from less aggressive treatment, while the smaller tumours in the women aged over 70 might need to be treated more aggressively.

"Further research now needs to be conducted into the role the immune system plays in lymph node invasion," he concluded.

Vitamin D and breast cancer risk

A connection between vitamin D level and the risk of developing breast cancer has been implicated for a long time, but its clinical relevance had not yet been proven. Sascha Abbas and colleagues from the working group headed by Dr. Jenny Chang-Claude at the German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ), collaborating with researchers of the University Hospitals in Hamburg-Eppendorf, have now obtained clear results: While previous studies had concentrated chiefly on nutritional vitamin D, the researchers have now investigated the complete vitamin D status. To this end, they studied 25-hydroxyvitamin D (25(OH)D) as a marker for both endogenous vitamin D and vitamin D from food intake.

The result of the study involving 1,394 breast cancer patients and an equal number of healthy women after menopause was surprisingly clear: Women with a very low blood level of 25(OH)D have a considerably increased breast cancer risk. The effect was found to be strongest in women who were not taking hormones for relief of menopausal symptoms. However, the authors note that, in this retrospective study, diagnosis-related factors such as chemotherapy or lack of sunlight after prolonged hospital stays might have contributed to low vitamin levels of breast cancer patients.

In addition, the investigators focused on the vitamin D receptor. The gene of this receptor is found in several variants known as polymorphisms. The research team of the DKFZ and Eppendorf Hospitals investigated the effect of four of these polymorphisms on the risk of developing breast cancer. They found out that carriers of the Taql polymorphism have a slightly increased risk of breast tumors that carry receptors for the female sex hormone estrogen on their surface. No effects on the overall breast cancer risk were found. A possible explanation offered by the authors is that vitamin D can exert its cancer-preventing effect by counteracting the growth-promoting effect of estrogens.

Besides its cancer-preventing influence with effects on cell growth, cell differentiation and programmed cell death (apoptosis), vitamin D regulates, above all, the calcium metabolism in our body. Foods that are particularly rich in vitamin D include seafish (cod liver oil), eggs and dairy products. However, the largest portion of vitamin D is produced by our own body with the aid of sunlight.

'Babelfish' to translate alien tongues could be built

* 15:30 18 April 2008
* NewScientist.com news service
*** Michael Reilly, Santa Clara**

If we ever make contact with intelligent aliens, we should be able to build a universal translator to communicate with them, according to a linguist and anthropologist in the US.

Such a "babelfish", which gets its name from the translating fish in Douglas Adams's book The Hitchhiker's Guide to the Galaxy, would require a much more advanced understanding of language than we currently have.

But a first step would be recognising that all languages must have a universal structure, according to Terrence Deacon of the University of California, Berkeley, US.

How language develops is highly controversial. Some theories argue that the process has been built into the human brain through evolution, and that the sounds we use to communicate are arbitrary.

If that is true, there could be an infinite set of possibilities for expressing an idea through language. An alien race that developed through a completely different process of evolution would probably speak a language indecipherable to humans.

But Deacon argues that all languages arise from the common goal of describing the physical world. That limits the way a language **could be constructed, he concludes.**

Scented words

An alien race could use a strange medium like scents as their language, Deacon says, but the scents would still describe objects in their world. An odour that communicates "rock" or "tree" would be analogous to our words for the same objects. So there must be an underlying universal code that can be deciphered, as in mathematics.

"In Carl Sagan's book Contact, aliens communicate to humans through prime numbers," says Deacon. "Why? Nature doesn't use prime numbers. But the numbers are intrinsic to the mathematical system, just as certain structures are intrinsic to language."

One of our most basic forms of communication is pointing, he says. Pointing directly references a physical object. When we invent a word for that object, that word is a symbol. Symbols can then convey meaning about objects even if they're not present in our immediate environment.

Abstract symbols

Deacon argues that no matter how abstract a symbol becomes, it is still somehow grounded in physical reality, and that limits the number of relationships it can have with other symbol words. In turn, this defines the grammatical structure that emerges from stringing words together.

If that is true, then in the distant future it might be possible to invent a gadget that uses complex software to decode alien languages on the spot, Deacon said. He presented his ideas on Thursday 17 April at the 2008 Astrobiology Science Conference in Santa Clara, California, US.

Testing the theory might be tough because we would have to make contact with aliens advanced enough to engage in abstract thinking and the use of linguistic symbols. But Denise Herzing of Florida Atlantic University in Boca Raton, US, points out that we might be able to test it by studying dolphins.

"Our work suggests that dolphins may be able to communicate using symbols," Herzing told New Scientist. "The word's not definitively in yet, but it's totally possible that we might show universality by understanding dolphin language."

Food miles don't feed climate change - meat does

* 17:00 18 April 2008
* NewScientist.com news service

*** Ewen Callaway**

That locally-produced, free-range, organic hamburger might not be as green as you think.

An analysis of the environmental toll of food production concludes that transportation is a mere drop in the carbon bucket. Foods such as beef and dairy make a far deeper impression on a consumer's carbon footprint.

"If you have a certain type of diet that's indicative of the American average, you're not going to do that much for climate while eating locally," says Christopher Weber, a researcher at Carnegie Mellon University in Pittsburgh who led a comprehensive audit of the greenhouse gas emissions of our meals.

Gassy foods

His analysis included emissions such as transporting and producing fertiliser for crops, methane gas emitted by livestock, and food's journey to market. All told, that final step added up to just 4% of a food's greenhouse emissions, on average.

But some items, particularly red meat, spewed out far more greenhouse gases than other foods, Weber and his colleague Scott Matthews found.

Environmentally savvy shoppers may want to take note.

"It seems much easier to shift one day of my beef consumption a week to chicken or vegetables, than going through and eating only Jerusalem artichokes for three months in the winter," says Weber, a "vegetarian bordering on vegan."

Every last molecule

Other researchers have quantified the greenhouse gas budget of foods, but most studies looked at a single food item, such as an apple, or ignored greenhouse gases more potent than CO2, such as methane and nitrous oxide.

Weber's team combined statistics on greenhouse gas emissions for different foods with estimated greenhouse footprints for transport for each step in a food's production and final delivery.

Food travelled an average of 1640 km in its final trip to the grocery store, out of total of 6760 km on the road for the raw ingredients. But some foods log more kilometres than others. Red meat averaged 20,400 km – just 1800 of those from final delivery.

Accounting for greenhouse gas emissions made those contrasts even starker. Final delivery "food-miles" make up just 1% of the greenhouse emissions of red meat, and 11% for fruits and vegetables.

To drive his point home, Weber calculated that a completely local diet would reduce a household's greenhouse emissions by an amount equivalent to driving a car 1600 km fewer per year. He assumed the car travels 10.6 km per litre of petrol (25 mpg). Switching from red meat to veggies just one day per week would spare 1860 km of driving.

"The differences between eating habits are very, very striking," Weber says.

Carbon grocery list

Edgar Hertwich, a researcher at the Norwegian University of Science and Technology in Trondheim, agrees that the obsession with food miles can obscure more significant environmental impacts of our food.

"Why not focus on what actually happens on the field and how much fertiliser we use," he says.

Whatever the source of greenhouse gas emissions from food, many are now calling for labelling that lets shoppers know how much carbon went into their goods. In the UK, the government-supported Carbon Trust offers a voluntary carbon label, and a proposed California law aims to regulate such labelling, much like organic food standards.

"Our goal is to get the most accurate information that’s available in the hands of consumer so they can make informed purchasing decisions," says Matthew Perry, head of Carbon Label California.

But based on Weber's study, consumers will face decisions tougher than buying local well water over bottles shipped from Fiji.

"If you're interested in the hamburger you're not going to switch to tofu, but you might switch to a chicken burger," Perry says.

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