http://www.sciencedaily.com/releases/2013/08/130824131405.htm

Linguistics Researcher Develops New System to Help Computers 'Learn' Natural Language

For more than 50 years, linguists and computer scientists have tried to get computers to understand human language by programming semantics as software.

Now, a University of Texas at Austin linguistics researcher, Katrin Erk, is using supercomputers to develop a new method for helping computers learn natural language.

Instead of hard-coding human logic or deciphering dictionaries to try to teach computers language, Erk decided to try a different tactic: feed computers a vast body of texts (which are a reflection of human knowledge) and use the implicit connections between the words to create a map of relationships.

"An intuition for me was that you could visualize the different meanings of a word as points in space," says Erk, a professor of linguistics who is conducting her research at the Texas Advanced Computing Center. "You could think of them as sometimes far apart, like a battery charge and criminal charges, and sometimes close together, like criminal charges and accusations ("the newspaper published charges…"). The meaning of a word in a particular context is a point in this space. Then we don't have to say how many senses a word has. Instead we say: 'This use of the word is close to this usage in another sentence, but far away from the third use.' "

To create a model that can accurately recreate the intuitive ability to distinguish word meaning requires a lot of text and a lot of analytical horsepower. "The lower end for this kind of a research is a text collection of 100 million words," she explains. "If you can give me a few billion words, I'd be much happier. But how can we process all of that information? That's where supercomputers come in."

http://www.eurekalert.org/pub_releases/2013-08/cmaj-plh082013.php

Patients leaving hospital against medical advice more likely to be readmitted or die

People who leave hospital against their doctors' orders are more likely to be readmitted to hospital or die, according to a new study in CMAJ (Canadian Medical Association Journal).

"Leaving the hospital against medical advice was associated with increased risks of readmission to hospital and death that persisted for at least 6 months," writes Dr. Allan Garland, Faculty of Medicine, University of Manitoba, Winnipeg, with coauthors. "Potential mechanisms for these associations directly related to the patients' acute illness include more severe illness or incomplete treatment of the illness."

Researchers looked at 1 916 104 adult admissions and live discharges over almost 20 years (1990) in Manitoba to determine rates of unplanned admission to hospital within 30 days and death within 90 days after discharge. There were 21 417 (1.1%) instances of patients leaving hospital against medical advice. People who left hospital against medical advice had 3 times the rate of readmission in the month following. Of readmissions within 30 days among patients who left hospital against medical advice, one-quarter occurred within 1 day and 75% within 2 weeks. People who were older, male, of lower socioeconomic status and who had multiple admissions to hospital in the preceding 5 years were more likely to be readmitted. The odds of death within 90 days were two and a half times higher for people who left hospital against medical advice.

"For both hospital readmission and death, the elevated rates among patients who left against medical advice started out high and then declined, but remained elevated to at least 180 days," write the authors.

They suggest that these elevated levels of risk may be linked to both the illness for which the patients were admitted to hospital or to their characteristics or health behaviors, such as not following medical advice or medication orders. Other smaller studies exist, but his study was large, with more than 21 000 instances of patients leaving hospital against medical advice.

"Although strategies targeted at trying to convince patients not to leave prematurely might diminish the early effects of leaving against medical advice, reducing the persistently elevated risk will likely require longitudinal interventions extending beyond hospital admission," conclude the authors.

http://www.medscape.com/viewarticle/810005?src=rss

Midwives Improve Outcomes, Says Cochrane Review

Most women whose prenatal and childbirth care are led by a midwife have better outcomes compared with those whose care is led by a physician or shared among disciplines, according to a systematic review of 13 trials involving 16,242 women published August 22 in the Cochrane Database of Systematic Reviews.

Troy Brown

Of the 13 trials reviewed, 8 included women at low risk for complications and 5 included women at high risk for complications. The researchers examined outcomes for mothers and babies including regional analgesia (epidural/spinal), caesarean delivery, instrumental vaginal birth (forceps/vacuum), spontaneous vaginal birth (as

defined by trial authors), intact perineum, preterm birth (less than 37 weeks), and overall fetal loss and neonatal death (fetal loss at 24 weeks' gestation or later, which is the cut-off for viability in many countries).
Women whose pregnancy care was led by a midwife were less likely to have regional analgesia (average risk ratio [RR], 0.83; 95% confidence interval [CI] 0.76 - 0.90), episiotomy (average RR, 0.84; 95% CI, 0.76 - 0.92), and instrumental birth (average RR, 0.88; 95% CI, 0.81 - 0.96).
Women who had midwife-led care were more likely to have no intrapartum analgesia/anesthesia (average RR, 1.16; 95% CI, 1.04 - 1.31), spontaneous vaginal birth (average RR, 1.05; 95% CI, 1.03 - 1.08), attendance at birth by a known midwife (average RR, 7.83; 95% CI, 4.15 - 14.80), and a longer mean length of labor (in hours) (mean difference, 0.50 hours; 95% CI, 0.27 - 0.74 hours).
The average risk ratio for caesarean births did not differ between the groups (average RR, 0.93; 95% CI, 0.84 - 1.02).
Women who were randomly assigned to receive midwife-led care were less likely to have preterm birth (average RR, 0.77; 95% CI, 0.62 - 0.94) and fetal loss before 24 weeks' gestation (average RR, 0.81; 95% CI, 0.66 - 0.99). There were no differences between the groups for fetal loss/neonatal death at 24 weeks' gestation or more (average RR, 1.00; 95% CI, 0.67 - 1.51) or in overall fetal/neonatal death (average RR, 0.84; 95% CI, 0.71 - 1.00).
Most studies reported higher maternal satisfaction in the midwifery-led model.
A total of 5 studies estimated costs associated with each care model, but they were inconsistent in how they measured those costs: One study found higher costs for postnatal care led by a midwife, and another study found no differences in cost when compared with medical-led care.
"There is a lack of consistency in estimating maternity care cost among the available studies; however, there seems to be a trend towards the cost-saving effect of midwife-led continuity of care in comparison with medical-led care," the authors write.

Delayed Care Can Be "Catastrophic," says Ob/Gyn

Nancy S. Roberts, MD, system department chairman of Obstetrics and Gynecology at Main Line Health in Bryn Mawr, Pennsylvania, commented on the review in a telephone interview with Medscape Medical News.
"If you look at other specialties, whether it's primary care..., physician assistants or advanced practice nurses, they can have a wonderful relationship with patients. The one problem...is figuring out when the patient requires a higher level of care. If there is a delay in obtaining that higher level of care, the results can be catastrophic," Dr. Roberts said.
"There are some very obvious high-risk situations, like twins, triplets, a woman who is over 40, a woman with medical complications, [or] a woman with medical complications of pregnancy, who would not be appropriate for a midwife's practice," Dr. Roberts explained.
The effects of midwife-led continuity models of care on the health and well-being of mothers and babies in the longer postpartum period are unclear, the authors write.
"Future research should pay particular attention to outcomes that have been under-researched, but are causes of significant morbidity, including postpartum depression, urinary and faecal incontinence, duration of caesarean incision pain, pain during intercourse, prolonged perineal pain and birth injury (to the baby)," the authors note in their conclusion.
This review was supported by the Women's Health Academic Centre, King's Health Partners, King's College; Sheffield Hallam University; Health Services Executive; and Trinity College Dublin; and the National Institute for Health Research in the UK. One coauthor is also a coauthor in one of the trials included in this review, one coauthor was and is principal investigator in 2 studies evaluating models of midwife-led continuity of care and is a coinvestigator on the Birthplace in England Research Programme, a comparison of birth outcomes for women who give birth at home, in various types of midwifery units, and in hospital units with obstetric services. Dr. Roberts has disclosed no relevant financial relationships.
Cochrane Database Syst Rev. 2013;8:CD004667. Abstract

http://www.eurekalert.org/pub_releases/2013-08/uops-cpb082313.php

Comprehensive Parkinson's biomarker test has prognostic and diagnostic value

First biomarker results from Parkinson's progression markers initiative detect differences in subtypes of Parkinson's disease

PHILADELPHIA - Perelman School of Medicine researchers at the University of Pennsylvania report the first biomarker results reported from the Parkinson's Progression Markers Initiative (PPMI), showing that a comprehensive test of protein biomarkers in spinal fluid have prognostic and diagnostic value in early stages of Parkinson's disease. The study is reported in JAMA Neurology.

Compared to healthy adults, the study found that people with early Parkinson's had lower levels of amyloid beta, tau and alpha synuclein in their spinal fluid. In addition, those with lower concentrations of tau and alpha synuclein had greater motor dysfunction. And early Parkinson's patients with low levels of amyloid beta and tau were more likely to be classified as having the postural instability-gait disturbance- dominant (PIGD) motor type of disease, where falling, freezing, and walking difficulty are common.

"Biomarkers for Parkinson's disease such as these could help us diagnose patients earlier, and we've now shown that the simultaneous measurement of a variety of neurodegenerative disease proteins is valuable," said study senior author Leslie M. Shaw, PhD, professor of Pathology and Laboratory Medicine at Penn Medicine. Dr. Shaw and John Q. Trojanowski, MD, PhD, director of the Penn Udall Center for Parkinson's Research, are co-leaders of the Bioanalytics Core for the Parkinson's Progression Markers Initiative, an international observational clinical study sponsored by The Michael J. Fox Foundation for Parkinson's Research.

The team evaluated spinal fluid collected from baseline visits of the first 102 PPMI participants - 63 with early, untreated Parkinson's disease and 39 healthy controls. The spinal fluid was evaluated for levels of five biomarkers: amyloid beta, total tau, phosphorylated tau, alpha synuclein and the ratio of total tau to amyloid beta. Spinal fluid measures of amyloid and tau are currently used in research to distinguish Alzheimer's disease from other neurodegenerative diseases. In contrast to Alzheimer's, where tau levels are higher than healthy controls, the study found that early Parkinson's patients had lower levels of tau than healthy controls. One reason, researchers suggest, could be that interactions between tau and alpha synuclein may limit the release of tau into the cerebrospinal fluid of Parkinson's patients.

"Through PPMI, we are hoping to identify subgroups of Parkinson's patients whose disease is likely to progress at a different rate, as early as possible," said Dr. Trojanowski. "Early prediction is critical, for both motor and dementia symptoms."

The Parkinson's PIGD motor subtype has been associated with a more rapid cognitive decline as well as greater functional disability. Using the biomarker test, this initial study found that levels of all spinal fluid biomarkers were lower in the PIGD motor subtype than other types of PD as well as healthy controls. In addition, amyloid beta and phosphorylated tau were at lower levels in the PIGD motor subtype, but were no different in tremor or indeterminate subtypes compared to normal controls.

This spinal fluid testing procedure is only being used in research studies, and will be continued to be evaluated and validated in a larger study of the PPMI cohorts.

In addition to leading the Bioanalytics Core of PPMI, Penn's Parkinson's Disease and Movement Disorders Center is one of the two dozen trial sites where volunteers are evaluated throughout the PPMI study. The Penn PDMDC has been part of the PPMI group studying people with early Parkinson's disease as well as healthy adults since 2010, and began enrollment for a new, pre-symptomatic arm of the study in the summer of 2013. The pre-motor arm of PPMI is enrolling participants who do not have Parkinson's disease and are living with one of three potential risk factors for PD: a reduced sense of smell (hyposmia); rapid eye movement sleep behavior disorder (RBD; a disorder in which the individual acts out his/her dreams); or a mutation in the LRRK2 gene (the single greatest genetic contributor to PD known to date).

"In addition to biomarker tests, validating risk factors could enable earlier detection of the disease and open new avenues in the quest for therapies that could slow or stop disease progression," said PPMI trial site study leader Matthew Stern, MD, professor of Neurology and director of Penn's Parkinson's Disease and Movement Disorders Center.

http://www.eurekalert.org/pub_releases/2013-08/tjnj-tut082313.php

Terminology used to describe preinvasive breast cancer may affect patients' treatment preferences

More women report that they would opt for nonsurgical treatments When ductal carcinoma in situ is described as a high-risk condition rather than cancer

When ductal carcinoma in situ (DCIS, a preinvasive malignancy of the breast) is described as a high-risk condition rather than cancer, more women report that they would opt for nonsurgical treatments, according to a research letter by Zehra B. Omer, B.A., of Massachusetts General Hospital—Institute for Technology Assessment, Boston, and colleagues.

A total of 394 healthy women without a history of breast cancer participated in the study and were presented with three scenarios that described a diagnosis of DCIS as noninvasive breast cancer, breast lesion, or abnormal cells. After each scenario, the women chose among three treatment options (surgery, medication, or active surveillance).

Overall, nonsurgical options (medication and active surveillance) were more frequently selected over surgery. When DCIS was described using the term noninvasive cancer, 53 percent (208 of 394) preferred nonsurgical options, whereas 66 percent (258 of 394) preferred nonsurgical options when the term was breast lesion and 69 percent (270 of 394) preferred nonsurgical options when the term was abnormal cells. Significantly more women changed their preference from a surgical to a nonsurgical option than from a nonsurgical to a surgical option depending on terminology, according to the study results.

"We conclude that the terminology used to describe DCIS has a significant and important impact on patients' perceptions of treatment alternatives. Health care providers who use 'cancer' to describe DCIS must be particularly assiduous in ensuring that patients understand the important distinctions between DCIS and invasive cancer," the study concludes.

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http://www.eurekalert.org/pub_releases/2013-08/wfbm-ocs082313.php

Oxygen-generating compound shows promise for saving tissue after severe injury

The same compound in a common household clothes detergent shows promise as a treatment to preserve muscle tissue after severe injury.

WINSTON-SALEM, N.C. Researchers at the Wake Forest Baptist Medical Center's Institute for Regenerative Medicine hope the oxygen-generating compound could one day aid in saving and repairing limbs and tissue. The research in rats, published online ahead of print in PLOS ONE, found that injections of the compound sodium percarbonate (SPO) can produce enough oxygen to help preserve muscle tissue when blood flow is disrupted.

"Some commercial detergents generate oxygen bubbles to help clean clothes or remove stains," said Benjamin Harrison, Ph.D., co-author and associate professor of regenerative medicine at Wake Forest Baptist. "We modified the material so it can be injected into muscle and provide a boost of oxygen to slow down muscle death until surgery can restore blood flow. Potential applications include treating amputations, crush injuries from car accidents or even blast injuries suffered by those in combat zones."

SPO is a combination of sodium carbonate and hydrogen peroxide molecules. In the presence of water, it decomposes into oxygen and other salts. The current formulation used by the researchers generates oxygen for about three hours.

"Normally, when blood flow to muscle tissue is reduced due to severe injury, the muscle begins to die," said Harrison. "Providing extra oxygen to oxygen-deprived muscle following injury is currently a major medical challenge. The few treatments that are available are primarily aimed at increasing the oxygen-carrying capacity of blood and require an intact system of blood vessels to carry that fluid, which we don't always have in damaged tissue."

When muscles don't have enough oxygen, they lose the ability to contract and their delicate metabolic balance (homeostasis) is impaired. The current project measured the effects of injecting oxygen-starved muscles with SPO. The first phase of this study, involving laboratory studies of muscle outside the body, compared SPO-treated muscles with non-treated muscles and found that SPO was effective at preserving both function and homeostasis in oxygen-deprived muscles.

"Our surprising finding was that even after exercising isolated leg muscles in the absence of oxygen, the muscles injected with the SPO compound could generate 20 percent more force than untreated muscles," said Harrison. "These studies were conducted using a standard laboratory test to evaluate muscle function outside the body."

Another part of the study involved rats in which the blood flow to a leg was interrupted and muscle function was studied while still in the body. The scientists measured flexion of the foot in response to nerve stimulation, which causes contraction of the tibialis anterior muscle. Even 30 minutes after the start of exercise (muscle stimulation), oxygen-deprived muscles injected with SPO maintained 30 percent of normal force. In muscles not treated with SPO, there was nearly complete cessation of contraction under identical conditions.

"This research, which evaluated muscles both outside and within the body, is the first to demonstrate that an oxygen-generating compound helps preserve muscle function and metabolic balance after oxygen-deprivation," said Harrison. "It may be a way to get oxygen to muscles when blood flow is severely compromised."

Harrison said additional work is still needed to determine if SPO will be effective in larger muscles and can be dispersed throughout the muscle, as well as if it can be applied to humans.

If successful, Harrison said the treatment could potentially extend the window of time, known as the "golden hour" in emergency medicine, when treatment has the highest chance of preventing death.

"The major implication of these findings is that oxygen-generating compounds can potentially reduce the magnitude of the permanent functional deficits resulting from traumatic injury to muscle, said George Christ, Ph.D., co-author and professor of regenerative medicine at Wake Forest Baptist. "This effect alone would be extremely valuable to both wounded warriors and civilians. However, it is also conceivable that the technology, because it delivers oxygen independent of blood flow, may also have diverse applications to the salvage, repair and regeneration of soft tissue following trauma."

The research was funded by the National Institutes of Health and the Armed Forces Institute for Regenerative Medicine. Co-authors are Catherine L. Ward, Ph.D., Benjamin T. Corona, Ph.D., James J. Yoo, M.D., Ph.D., Wake Forest Baptist.

http://www.eurekalert.org/pub_releases/2013-08/fhcr-fco082613.php

4 cups of coffee a day may keep prostate cancer recurrence and progression away

Bioactive compounds in coffee may have anti-inflammatory and antioxidant effects

SEATTLE – Coffee consumption is associated with a lower risk of prostate cancer recurrence and progression, according to a new study by Fred Hutchinson Cancer Research Center scientists that is online ahead of print in Cancer Causes & Control.

Corresponding author Janet L. Stanford, Ph.D., co-director of the Program in Prostate Cancer Research in the Fred Hutch Public Health Sciences Division, conducted the study to determine whether the bioactive compounds in coffee and tea may prevent prostate cancer recurrence and delay progression of the disease.

Stanford and colleagues found that men who drank four or more cups of coffee per day experienced a 59 percent reduced risk of prostate cancer recurrence and/or progression as compared to those who drank only one or fewer cups per week.

They did not, however, find an association between coffee drinking and reduced mortality from prostate cancer, although the study included too few men who died of prostate cancer to address that issue separately.

First study to assess the link between tea and prostate cancer outcomes

Regarding tea consumption, the researchers did not find an associated reduction of prostate cancer recurrence and/or progression. The study also did not draw any conclusions regarding the impact of tea drinking on prostate-specific death.

"To our knowledge, our study is the first to investigate the potential association between tea consumption and prostate cancer outcomes," the authors wrote. "It is important to note, however, that few patients in our cohort were regular tea drinkers and the highest category of tea consumption was one or more cups per day. The association should be investigated in future studies that have access to larger populations with higher levels of tea consumption."

The population-based study involved 1,001 prostate cancer survivors, aged 35-74 years old at the time of diagnosis between 2002-2005, who were residents of King County, Wash. Participants answered questions regarding their diet and beverage consumption two years prior to prostate cancer diagnosis using a validated food frequency questionnaire, and were interviewed about demographic and lifestyle information, family history of cancer, medication use and prostate cancer screening history.

The researchers followed up with patients more than five years after diagnosis to ascertain whether the prostate cancer had recurred and/or progressed. Those who were still living, willing to be contacted and had been diagnosed with non-metastatic cancer were included in the follow-up effort.

Of the original 1,001 patients in the cohort, 630 answered questions regarding coffee intake, fit the follow-up criteria and were included in the final analysis. Of those, 61 percent of the men consumed at least one cup of coffee per day and 12 percent consumed the highest amount: four or more cups per day.

The study also evaluated daily coffee consumption in relation to prostate cancer-specific death in 894 patients using data from the initial food frequency questionnaire. After the median follow-up period of eight-and-a-half years, 125 of the men had died, including 38 specifically from prostate cancer. Daily coffee consumption was not associated with prostate cancer-specific mortality or other-cause mortality, but with few deaths these analyses were limited.

"Our study differs from previous ones because we used a composite definition of prostate cancer recurrence/progression," said first author Milan Geybels, a doctoral student at Maastricht University in the Netherlands who was a graduate student in Stanford's Prostate Studies group at Fred Hutch when the study was conducted. "We used detailed information on follow-up prostate-specific antigen levels, use of secondary treatment for prostate cancer and data from scans and biopsies to assess occurrence of metastases and cause-specific mortality during follow up. Using these detailed data, we could determine whether a patient had evidence of prostate cancer recurrence or progression."

The results are consistent with findings from Harvard's Health Professionals Follow-up Study, which found that men who drank six or more cups of coffee per day had a 60 percent decreased risk of metastatic/lethal prostate

cancer as compared to coffee abstainers. Phytochemicals in coffee have anti-inflammatory and antioxidant effects

Further research is required to understand the mechanisms underlying the results of the study, but biological activities associated with consumption of phytochemical compounds found in coffee include anti-inflammatory and antioxidant effects and modulation of glucose metabolism. These naturally occurring compounds include:

Caffeine, which has properties that inhibit cell growth and encourage apoptosis, or programmed cell death. Previous studies have found that caffeine consumption may reduce the risk of several cancer types, including basal-cell carcinoma, glioma (a cancer of the brain and central nervous system) and ovarian cancer.

Diterpenes cafestol and kahweol, which may inhibit cancer growth.

Chlorogenic acid, which, along with caffeic acid, can inhibit DNA methylation, a biochemical process involved in the development and progression of many cancer types.

Additional studies needed to confirm whether coffee can prevent cancer recurrence

The researchers emphasize that coffee or specific coffee components cannot be recommended for secondary prevention of prostate cancer before the preventive effect has been demonstrated in a randomized clinical trial. Further, there's ongoing debate about which components in coffee are anti-carcinogenic, and additional large, prospective studies are needed to confirm whether coffee intake is beneficial for secondary prevention.

Coffee drinking may even be problematic for some men, Geybels said.

"Although coffee is a commonly consumed beverage, we have to point out that increasing one's coffee intake may be harmful for some men. For instance, men with hypertension may be vulnerable to the adverse effects of caffeine in coffee. Or, specific components in coffee may raise serum cholesterol levels, posing a possible threat to coronary health. Patients who have questions or concerns about their coffee intake should discuss them with their general practitioner," he said.

The investigators also noted limits to their study, which included a lack of data on how coffee consumption might have changed following diagnosis, whether the coffee that participants consumed was caffeinated or decaffeinated, and how the coffee was prepared (espresso, boiled or filtered), a factor that may affect the bioactive properties of the brew.

The National Cancer Institute, Fred Hutchinson Cancer Research Center, Prostate Cancer Foundation and Dutch Cancer Society funded the research.

http://www.sciencedaily.com/releases/2013/08/130826095829.htm

New Study Supports Intracerebral Injections of Bone Marrow-Derived Stem Cells to Prevent or Reduce Post-Stroke Cognitive Deficits

Cognitive deficits following ischemic stroke are common and debilitating, even in the relatively few patients who are treated expeditiously so that clots are removed or dissolved rapidly and cerebral blood flow restored.

A new study in Restorative Neurology and Neuroscience demonstrates that intracerebral injection of bone-marrow-derived mesenchymal stem cells (BSCs) reduces cognitive deficits produced by temporary occlusion of cerebral blood vessels in a rat model of stroke, suggesting that BSCs may offer a new approach for reducing post-stroke cognitive dysfunction.

According to the American Heart Association, almost half of ischemic stroke survivors older than 65 years of age experience cognitive deficits, contributing to functional impairments, dependence, and increased mortality. The incidence of cognitive deficits triples after stroke and about one quarter of cognitively impaired stroke patients' progress to dementia. For these reasons, "there is an underlying need for restorative therapies," says lead investigator Gary L. Dunbar, PhD, of the Field Neurosciences Institute Laboratory for Restorative Neurology, and Director of the Central Michigan University Program in Neuroscience.

In order to see whether mesenchymal stem cells derived from bone marrow could attenuate or prevent cognitive problems following a stroke-like ischemic event, the investigators mimicked stroke in rats by injecting the hormone endothelin-1 (ET-1) directly into the brain in order to constrict nearby blood vessels and block blood flow temporarily. Control animals underwent similar surgery but were injected with saline, not ET-1.

Seven days after the "stroke," some of the rats received intrastriatal injections of BSC, while others received control injections. Cognition was evaluated using a spatial operant reversal task (SORT), in which the animals were trained to press a lever a certain number of times when it was illuminated to receive a food reward.

The investigators found that animals that underwent a stroke but were then injected with BSC made significantly fewer incorrect lever presses than stroke rats who received control injections. In fact, the BSC-treated stroke animals performed as well as those who did not have a stroke. "Importantly, there were no significant between-group differences in the total number of lever presses, indicating the deficits observed were cognitive, rather than motor in nature," said Dr. Dunbar. No differences were observed in infarct size between the BSC-treated and control groups.

The authors emphasize that the BSCs were effective even when transplanted seven days after the induced stroke, a finding that offers hope to patients who may not present for treatment immediately. The authors suggest that BSCs may work by creating a microenvironment that provides trophic support to remaining viable cells, perhaps by releasing substances such as brain-derived neurotrophic factor (BDNF).

SA Lowrance, KD Fink, A Crane, J Matyas, ND Dey, JJ Matchynski, T Thibo, T Reinke, J Kippe, C Hoffman, M Sandstrom, J Rossignol, and GL Dunbar. Bone-marrow-derived mesenchymal stem cells attenuate cognitive deficits in an endothelin-1 rat model of stroke. Restorative Neurology and Neuroscience, 2013 DOI: 10.3233/RNN-130329

http://www.medscape.com/viewarticle/809238?src=rss

5 Important Developments in *C difficile* Management

Important Findings in C difficile Infection

John G. Bartlett, MD

The Role of Infection Control

Standard teaching is that *Clostridium difficile* infection (CDI) is a hospital-acquired infection that reflects a failure of infection control, but it may be more closely related to antibiotic control. A recent report from the Centers for Disease Control and Prevention (CDC), based on an analysis of 10,342 cases of CDI in 111 hospitals and 310 nursing homes, showed that 75% of the patients were already colonized with *C difficile* at the time of admission.[1] Nearly all (94%) of these cases were "healthcare-associated," meaning that acquisition occurred during an outpatient visit, a nursing home stay, the current hospitalization, or a previous hospitalization. Only 25% of patients actually acquired the pathogen in the same hospital where clinical expression of CDI occurred.

Clinical relevance. The CDC study suggests that infection control personnel and physicians need to be aware of this association, because this may require changes in infection control practice. The implication is that to prevent CDI, clinicians need to find ways to identify patients who are already colonized to protect them from obvious risks, and also to consider them to be potential sources of infection to others. This could substantially change infection control practice for prevention of CDI.

Fidaxomicin

Fidaxomicin is the second drug approved by the US Food and Drug Administration (FDA) for the treatment of CDI. The first was oral vancomycin, which was approved in 1978 on the basis of a 16-patient randomized controlled trial.[2] The fidaxomicin trials included approximately 1200 patients randomly assigned to receive fidaxomicin vs oral vancomycin.[3,4] Results showed similar initial response rates (88% vs 86%), but a significantly reduced rate of relapse in fidaxomicin recipients (15% vs 25%).[3] A subsequent trial showed that fidaxomicin was also superior to vancomycin in prevention of a second relapse in patients who had already experienced a relapse of CDI (36% vs 20%).[5] The presumed mechanism for reduced rates of relapse is a less pronounced alteration of the colonic microbiome with fidaxomicin,[6] which is presumed to be the ultimate control of *C difficile* toxin production.

Clinical relevance. It appears that fidaxomicin is a good drug for CDI because it is FDA-approved; similar to oral vancomycin with respect to cure rates; and clearly superior in terms of "global cure" rates, which include initial responses without relapses. Nevertheless, the cost of fidaxomicin (which reflects the high cost of FDA trials) is intimidating.

Does the Nose Know?

It has long been claimed that nurses can identify patients with CDI by the odor in an infected patient's room or the odor of the stool, although this has not been verified in clinical trials.[7] Because dogs have an olfactory sense that is approximately 300 times that of humans, investigators in The Netherlands[8] trained a beagle to detect the odor of *p*-cresol (a phenolic compound that results from the fermentation of tyrosine), which is thought to be the source of the odor of *C difficile*. The dog was taught to sit if the specimen was positive. The beagle's performance in a trial was near perfect. Compared with results of clinical and laboratory studies for *C difficile*, the dog recognized positive cases in 30 of 30 instances of CDI and identified negative tests in 270 of 270 specimens from patients without CDI. In fact, the dog was even able to recognize a case by exposure to the patient's ward in 25 of 30 cases (83%) and correctly eliminated CDI by the ward walk-through in 265 of 270 negative cases.

Clinical relevance. Although the original investigators suggest that dogs could be used in hospitals to "sniff out" CDI if precautions are taken to protect patients, it is unlikely that this method will be widely adopted.

Surgical Treatment for CDI

A new surgical procedure for CDI has been developed: diverting loop ileostomy with colonic vancomycin lavage. The surgical experience with CDI has previously consisted of colectomy in patients who are critically

ill, often with toxic megacolon. Mortality rates are high, and surviving patients suffer the consequences of living without a colon.

Surgeons at the University of Pittsburgh had extensive experience in the midst of a CDI epidemic and have subsequently reported a new surgical approach, consisting of a diverting ileostomy in place of colectomy. A retrospective comparison of 42 patients who underwent the new procedure with 42 who had previously had colectomy for refractory CDI showed mortality rates of 19% vs 50% favoring the new procedure.[9]

Clinical relevance. It is hoped that diverting loop ileostomy procedure will replace colectomy as the standard surgical procedure for most patients with severe CDI who require surgery.

Stool Transplantation

Fecal microbiota transplantation has become a relatively common method to manage the patient with multiple relapses of CDI. This technique was initially attempted in the early 1980s for CDI, with multiple reviews showing good results. Meta-analyses of these studies, including approximately 300 reported cases, generally showed cure rates of 85%-90% with minimal morbidity.[10]

One of the problems with this strategy (besides the "yuck" factor) has been the anecdotal nature of the published reports. A controlled trial was finally conducted in The Netherlands to clearly substantiate the benefit of stool transplantation and silence the critics,[11] with results that were already clear to those who were using this treatment.

More recently, the FDA decided that stool used in this fashion was a "drug," and required the massive paperwork that accompanies an application for an investigational new drug. However, they have subsequently repealed this requirement. Stool transplant cannot be considered new, because the procedure actually goes back to 1958.

A variation of this procedure is the recent attempt to achieve the same goal by implanting not human stool, but cultured organisms that dominate the normal microbiome.[12] The product is called "RePOOPulate" and has been tested in 2 patients, with good results.[12]

Clinical relevance. Stool transplants are highly effective, and physicians who see patients with multiple relapses need to be aware of local resources with expertise in this procedure. RePOOPulate is interesting and has nothing to do with probiotics, because it is composed of the dominant colonic bacteria that require special handling. This treatment will require substantial testing before it can become available in the marketplace.

Web Resources

C difficile: 10% of Patients Are Carriers at Hospitalization
Fidaxomicin Noninferior to Vancomycin for Treatment of C difficile Infection
Dog Sniffs Out Deadly C. diff Infection
An Alternative to Colectomy for Severe C difficile Colitis
Fecal Transplant by Enema Works for Stubborn C difficile: Study
Fecal Transplantation for C difficile: A How-To Guide
Fecal Transplantation for C difficile: An Evolving "Art"
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FDA OKs First Topical Agent for Facial Erythema of Rosacea

The US Food and Drug Administration (FDA) has approved brimonidine topical gel 0.33% (Mirvaso, Galderma Laboratories) for facial redness resulting from rosacea in adults aged 18 years or older, the company announced today.

Megan Brooks

Rosacea is a chronic skin condition that affects an estimated 16 million Americans. According to the company, this is the first and only FDA-approved topical treatment specifically developed and indicated for the facial erythema of rosacea.

"Facial redness is the most common symptom of rosacea, but until now, physicians have been without prescription treatment options to specifically address this patient need," Mark Jackson, MD, who is clinical professor of medicine at the University of Louisville in Kentucky, a dermatologist, and a principal investigator for the phase 3 studies of Mirvaso, said in a company statement.

"The FDA approval of Mirvaso marks a turning point in rosacea treatment: we are now able to provide patients who deal with the daily frustrations caused by the redness of rosacea with an effective therapy," he added.

In clinical testing, the alpha 2 adrenergic agonist brimonidine topical gel yielded significantly greater improvement in the facial redness of rosacea than vehicle gel, the company said. Testing included 2 phase 3 clinical trials involving more than 550 patients, each lasting 1 month, and a long-term trial with 276 patients lasting up to 12 months.

Brimonidine topical gel may work by constricting dilated facial blood vessels to reduce the redness of rosacea, the company said. It should be applied in a pea-sized amount once daily to the forehead, chin, nose, and each cheek.

The most common adverse reactions (incidence ≥ 1%) seen in the short-term trials were erythema, flushing, skin burning sensation, and contact dermatitis. In the long-term study, the most common adverse events (≥4% of subjects) included flushing (10%), erythema (8%), rosacea (5%), nasopharyngitis (5%), skin burning sensation (4%), increased intraocular pressure (4%), and headache (4%).

Galderma expects Mirvaso to be available in pharmacies in September.

http://www.sciencedaily.com/releases/2013/08/130826182803.htm

Disabling Enzyme Reduces Tumor Growth, Cripples Cancer Cells, Finds New Study

Knocking out a single enzyme dramatically cripples the ability of aggressive cancer cells to spread and grow tumors, offering a promising new target in the development of cancer treatments, according to a new study by researchers at the University of California, Berkeley.

The paper, published today (Monday, Aug. 26), in the journal Proceedings of the National Academy of Sciences, sheds new light on the importance of lipids, a group of molecules that includes fatty acids and cholesterol, in the development of cancer.

Researchers have long known that cancer cells metabolize lipids differently than normal cells. Levels of ether lipids -- a class of lipids that are harder to break down -- are particularly elevated in highly malignant tumors, although the nature of that correlation has been unclear for decades.

"Cancer cells make and use a lot of fat and lipids, and that makes sense because cancer cells divide and proliferate at an accelerated rate, and to do that, they need lipids, which make up the membranes of the cell," said study principal investigator Daniel Nomura, assistant professor in UC Berkeley's Department of Nutritional Sciences and Toxicology. "Lipids have a variety of uses for cellular structure, but what we're showing with our study is that lipids can also send signals that fuel cancer growth."

In the study, Nomura and his team tested the effects of reducing ether lipids on human skin cancer cells and primary breast tumors. They targeted an enzyme, alkylglycerone phosphate synthase, or AGPS, known to be critical to the formation of ether lipids.

The researchers first confirmed that AGPS expression increased when normal cells turned cancerous. They then found that inactivating AGPS substantially reduced the aggressiveness of the cancer cells.

"The cancer cells were less able to move and invade," said Nomura.

The researchers also compared the impact of disabling the AGPS enzyme in mice that had been injected with cancer cells. "Among the mice that had the AGPS enzyme inactivated, the tumors were nonexistent," said Nomura. "The mice that did not have this enzyme disabled rapidly developed tumors."

The researchers determined that inhibiting AGPS expression depleted the cancer cells of ether lipids. They also found that AGPS altered levels of other types of lipids important to the ability of the cancer cells to survive and spread, including prostaglandins and acyl phospholipids.

"The effect on other lipids was unexpected and previously unknown," said study lead author Daniel Benjamin, doctoral student in the Nomura Research Group. "Other studies have investigated specific lipid signaling pathways, but what makes AGPS stand out as a treatment target is that the enzyme seems to simultaneously regulate multiple aspects of lipid metabolism important for tumor growth and malignancy."
Future steps include the development of AGPS inhibitors for use in cancer therapy, said Nomura.
"This study sheds considerable light on the important role that AGPS plays in ether lipid metabolism in cancer cells, and it suggests that inhibitors of this enzyme could impair tumor formation," said Benjamin Cravatt, professor and chair of chemical physiology at The Scripps Research Institute, who is not part of the UC Berkeley study. Cravatt is an expert in the role enzymes play in human diseases.
Other study co-authors include Kunxin Luo, UC Berkeley professor of molecular and cell biology and faculty scientist at the Lawrence Berkeley National Laboratory.
The National Institutes of Health and the Searle Scholar Foundation helped support this research.
Daniel I. Benjamin, Alyssa Cozzo, Xiaodan Ji, Lindsay S. Roberts, Sharon M. Louie, Melinda M. Mulvihill, Kunxin Luo, and Daniel K. Nomura. Ether lipid generating enzyme AGPS alters the balance of structural and signaling lipids to fuel cancer pathogenicity. PNAS, August 26, 2013 DOI: 10.1073/pnas.1310894110

http://www.eurekalert.org/pub_releases/2013-08/uosf-ntb082713.php

New treatments better than standard ones just over half the time

That's evidence the randomized clinical trial system works, University of South Florida researcher reports in Nature

Tampa, FL - University of South Florida Distinguished Professor Benjamin Djulbegovic, MD, PhD, has studied the ethics of randomized clinical trials and their effectiveness in evaluating the outcomes of new treatments for decades.
Now, in a paper published Aug. 22 in the top journal Nature, Dr. Djulbegovic and colleagues report that on average new treatments work better than existing ones just over half the time. On scientific and ethical grounds, they say, the randomized controlled trial (RCT) system's little more than 50-50 success rate over the past half century is evidence that the system is working as intended.
The researchers analyzed 860 phase III published and unpublished RCTs performed by academic institutions or pharmaceutical companies. These trials collectively involved more than 350,000 patients.
"Our retrospective review of more than 50 years of randomized trials shows that they remain the 'indispensable ordeals' through which biomedical researchers' responsibility to patients and the public is manifested," the researchers conclude. "These trials may need tweak and polish, but they're not broken."
People who consent to participate RCTs are willing to be randomly allocated to new or existing treatments. While RCTs are considered the gold standard for comparing the effects of one treatment to another, the gradual progress they yield can seem frustratingly slow -- particularly for patients with poor standard treatment options. Yet, the genuine uncertainty associated with individual RCTs has been vital to the gains in therapeutics, said Dr. Djulbegovic, professor of medicine and oncology at the USF Health Morsani College of Medicine and Moffitt Cancer Center. If there was significant likelihood that one treatment in a comparison was better than the other, it would be unethical to deny some patients the superior treatment, and well-informed patients would probably refuse to participate in the study, he said.
Incremental advances in treatment generated by RCTs over time – such as childhood leukemia cure rates moving from zero to 80 percent even though only 2 to 5 percent of new treatments provided a breakthrough – have translated into important improvements in health and lifespan, the authors say. However, they suggest trials could still benefit from more rigorous design, implementation and reporting –with widespread publication of trial results, including negative findings.
"Medical research: Trial unpredictability yields predictable therapy gains;" Benjamin Djulbegovic, Ambuj Kumar, Paul Glasziou, Branko Miladinovic, and Iain Chalmers, Nature, August 22, 2013, pp 395-96.

http://www.eurekalert.org/pub_releases/2013-08/uons-frp082713.php

Fukushima radioactive plume to reach US in 3 years

Tracking the movement of the Fukushima radioactive plume in our oceans

Tuesday, August 27: The radioactive ocean plume from the 2011 Fukushima nuclear plant disaster will reach the shores of the US within three years from the date of the incident but is likely to be harmless according to new paper in the journal Deep-Sea Research 1.
While atmospheric radiation was detected on the US west coast within days of the incident, the radioactive particles in the ocean plume take considerably longer to travel the same distance.
In the paper, researchers from the Centre of Excellence for Climate System Science and others used a range of ocean simulations to track the path of the radiation from the Fukushima incident.

The models identified where it would likely travel through the world's oceans for the next 10 years.
"Observers on the west coast of the United States will be able to see a measurable increase in radioactive material three years after the event," said one of the paper's authors, Dr Erik van Sebille.
"However, people on those coastlines should not be concerned as the concentration of radioactive material quickly drops below World Health Organisation safety levels as soon as it leaves Japanese waters."
Two energetic currents off the Japanese coast - the Kuroshio Current and the Kurushio Extension – are primarily responsible for accelerating the dilution of the radioactive material, taking it well below WHO safety levels within four months.
Eddies and giant whirlpools – some tens of kilometres wide – and other currents in the open ocean continue this dilution process and direct the radioactive particles to different areas along the US west coast.
"Although some uncertainties remain around the total amount released and the likely concentrations that would be observed, we have shown unambiguously that the contact with the north-west American coasts will not be identical everywhere," said Dr Vincent Rossi.
"Shelf waters north of 45°N will experience higher concentrations during a shorter period, when compared to the Californian coast. This late but prolonged exposure is due to the three-dimensional pathways of the plume. The plume will be forced down deeper into the ocean toward the subtropics before rising up again along the southern Californian shelf."
Interestingly, the great majority of the radioactive material will stay in the North Pacific, with very little crossing south of the Equator in the first decade. Eventually over a number of decades, a measurable but otherwise harmless signature of the radiation will spread into other ocean basins, particularly the Indian and South Pacific oceans.
"Australia and other countries in the Southern Hemisphere will see little if any radioactive material in their coastal waters and certainly not at levels to cause concern," Dr van Sebille said.
"For those interested in tracking the path of the radiation, we have developed a ***website*** to help them.
"Using this website, members of the public can click on an area in the ocean and track the movement of the radiation or any other form of pollution on the ocean surface over the next 10 years."
The paper: Multi-decadal projections of surface and interior pathways of the Fukushima Cesium-137 radioactive plume. (dx.doi.org/10.1016/j.dsr.2013.05.015)

http://www.bbc.co.uk/news/science-environment-23849334

Evidence for new periodic table element boosted

Scientists have presented new evidence for the existence of an unconfirmed element with atomic number 115.
The element is highly radioactive and exists for less than a second before decaying into lighter atoms.
First proposed by Russian scientists in 2004, the super-heavy element has yet to be verified by the governing body of chemistry and physics.
The new evidence by a Swedish team is published in the journal Physical Review Letters.
"This was a very successful experiment and is one of the most important in the field in recent years", said Dirk Rudolph, professor at the division of atomic physics at Lund University, who led the research.
After the discovery of element 115, independent confirmation to measure the exact proton number was required, Prof Rudolph told BBC News.
He said the finding "goes beyond the standard measurement" which had been observed previously.
A new isotope of a potential new element was produced, which transformed into other particles via a radioactive process named alpha decay.
The researchers also gained access to data that they say gives them a deeper insight into the structure and properties of super-heavy atomic nuclei.
The team bombarded a thin film of the element americium with calcium ions, which allowed them to measure photons in connection with the new element's alpha decay.
Certain energies of the photons (light particles) agreed with the expected energies for X-ray radiation, which acts as a "fingerprint" of a given element.
The experiment was conducted at the GSI research facility in Germany, where scientists have previously discovered six other new elements.
The potential new element will now be reviewed by a committee which consists of members of the international unions of pure and applied physics and chemistry.
They will decide whether to recommend further experiments before the discovery of the new element is acknowledged.

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Researchers Solve Biological Mystery about the Common Genesis of Many Serious Diseases

Scientists solve a biological mystery about the common genesis of many serious diseases, discovering a trigger to important biologic responses such as the control of cell death and production of inflammatory mediators.

A Yale-led team of researchers has solved a biological mystery about the common genesis of many serious diseases such as asthma and metastatic melanoma, identifying the first known pathway by which their cellular functions turn abnormal, and a healthy process goes haywire. The study is published in Cell Reports.

The team focused on an ancient gene family known as "18 glycosyl hydrolase (GH 18)," and in particular, one protein known as chitinase 3-like-1 (Chi3l1). This protein plays a critical role in the body's response to foreign pathogens, augmenting the killing of bacteria while controlling inflammation and cell death to keep the immune response from harming normal tissue.

Although previous studies from this Yale team and colleagues have helped define the roles of Chi3l1 in biology, the mechanism by which it works — and triggers disease when overexpressed — was not known. The Yale team knew that Chi3l1 was not functioning as an enzyme would. They theorized that it acted, instead, by binding to a cellular receptor. Their studies led them to focus on a receptor known as IL-13Rα2, which was thought to be a so-called "decoy receptor" that binds molecules but does not induce cellular signaling or activate a biologic response.

Their experiments in mice proved that IL-13Rα2 was no decoy at all, but an active participant in the signaling pathway. The binding of overexpressed Chi3l1 and the receptor IL-13Rα2 began a cascade of subsequent reactions in the mice that resulted in lung disease, lung melanoma metastasis, and a host of other diseases.

"What we discovered was that when Chi3l1 is produced, IL-13Rα2 binds it and acts as a catalyst, triggering important biologic responses such as the control of cell death and production of inflammatory mediators," said senior author Dr. Jack A. Elias, chair of internal medicine at Yale School of Medicine and a member of Yale Cancer Center.

Elias hopes that further research will identify more receptors in this family, and he sees a potential for developing therapies based on his team's findings. "These molecules are expressed abnormally in a number of diseases, so the idea that you can control them is exciting. Perhaps we can develop an antibody or a small molecule that blocks their action and changes cellular function."

Other authors are Chuan Hua He, Chun Geun Lee, Charles S. Dela Cruz, Chang-Min Lee, Yang Zhou, Farida Ahangari, Bing Ma, Erica L. Herzog, Stephen A. Rosenberg, Yue Li, Adel M. Nour, Chirag R. Parikh, Yorgo Modies, and Lloyd Cantley of Yale; and Insa Schmidt of Yale and Hanover Medical School in Germany.

The study was supported by grants from the National Institutes of Health (grants HL-R01 HL093017 and U01HL108638). Publication: Chuan Hua He, et al., "Chitinase 3-like 1 Regulates Cellular and Tissue Responses via IL-13 Receptor α2," Cell Reports, 22 August 2013; doi:10.1016/j.celrep.2013.07.032

http://www.eurekalert.org/pub_releases/2013-08/eaog-wma082613.php

We may all be Martians -- new research supports theory that life started on Mars

New evidence has emerged which supports the long-debated theory that life on Earth may have started on Mars.

Professor Steven Benner will tell geochemists gathering today (Thursday 29 Aug) at the annual Goldschmidt conference that an oxidized mineral form of the element molybdenum, which may have been crucial to the origin of life, could only have been available on the surface of Mars and not on Earth. "In addition", said Professor Benner "recent studies show that these conditions, suitable for the origin of life, may still exist on Mars."

"It's only when molybdenum becomes highly oxidized that it is able to influence how early life formed," explains Professor Benner, from The Westheimer Institute for Science and Technology in the USA. "This form of molybdenum couldn't have been available on Earth at the time life first began, because three billion years ago the surface of the Earth had very little oxygen, but Mars did. It's yet another piece of evidence which makes it more likely life came to Earth on a Martian meteorite, rather than starting on this planet."

The research Professor Benner will present at the Goldschmidt conference tackles two of the paradoxes which make it difficult for scientists to understand how life could have started on Earth.

The first is dubbed by Professor Benner as the 'tar paradox'. All living things are made of organic matter, but if you add energy such as heat or light to organic molecules and leave them to themselves, they don't create life. Instead, they turn into something more like tar, oil or asphalt.

"Certain elements seem able to control the propensity of organic materials to turn into tar, particularly boron and molybdenum, so we believe that minerals containing both were fundamental to life first starting," says Professor Benner. "Analysis of a Martian meteorite recently showed that there was boron on Mars; we now believe that the oxidized form of molybdenum was there too."

The second paradox is that life would have struggled to start on the early Earth because it was likely to have been totally covered by water. Not only would this have prevented sufficient concentrations of boron forming – it's currently only found in very dry places like Death Valley – but water is corrosive to RNA, which scientists believe was the first genetic molecule to appear. Although there was water on Mars, it covered much smaller areas than on early Earth.

"The evidence seems to be building that we are actually all Martians; that life started on Mars and came to Earth on a rock," says Professor Benner. "It's lucky that we ended up here nevertheless, as certainly Earth has been the better of the two planets for sustaining life. If our hypothetical Martian ancestors had remained on Mars, there might not have been a story to tell."

1. The Goldschmidt Conference is jointly sponsored by the European Association of Geochemistry and the Geochemical Society. The annual, five-day event brings together around 4000 of the world's leading geochemists, covering topics as diverse as planetary formation, volcanoes, tectonics, climate change and oceans.

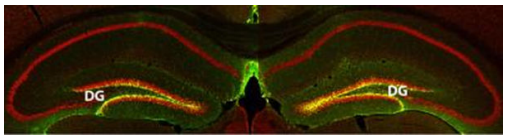
http://www.eurekalert.org/pub_releases/2013-08/cumc-amc080913.php

A major cause of age-related memory loss identified

Study points to possible treatments and confirms distinction between memory loss due to aging and that of Alzheimer's

NEW YORK, NY - A team of Columbia University Medical Center (CUMC) researchers, led by Nobel laureate Eric R. Kandel, MD, has found that deficiency of a protein called RbAp48 in the hippocampus is a significant contributor to age-related memory loss and that this form of memory loss is reversible. The study, conducted in postmortem human brain cells and in mice, also offers the strongest causal evidence that age-related memory loss and Alzheimer's disease are distinct conditions. The findings were published today in the online edition of Science Translational Medicine.

"Our study provides compelling evidence that age-related memory loss is a syndrome in its own right, apart from Alzheimer's. In addition to the implications for the study, diagnosis, and treatment of memory disorders, these results have public health consequences," said Dr. Kandel, who is University Professor & Kavli Professor of Brain Science, co-director of Columbia's Mortimer B. Zuckerman Mind Brain Behavior Institute, director of the Kavli Institute for Brain Science, and senior investigator, Howard Hughes Medical Institute, at CUMC. Dr. Kandel received a share of the 2000 Nobel Prize in Physiology or Medicine for his discoveries related to the molecular basis of memory.



The researchers have identified a protein—RbAp48—that, when increased in aged wild-type mice, improves memory back to that of young wild-type mice. In the image, yellow shows the increased RbAp48 in the dentate gyrus. **Elias Pavlopoulos, Ph.D./Columbia University Medical Center**

The hippocampus, a brain region that consists of several interconnected subregions, each with a distinct neuron population, plays a vital role in memory. Studies have shown that Alzheimer's disease hampers memory by first acting on the entorhinal cortex (EC), a brain region that provides the major input pathways to the hippocampus. It was initially thought that age-related memory loss is an early manifestation of Alzheimer's, but mounting evidence suggests that it is a distinct process that affects the dentate gyrus (DG), a subregion of the hippocampus that receives direct input from the EC.

"Until now, however, no one has been able to identify specific molecular defects involved in age-related memory loss in humans," said co-senior author Scott A. Small, MD, the Boris and Rose Katz Professor of Neurology and Director of the Alzheimer's Research Center at CUMC.

The current study was designed to look for more direct evidence that age-related memory loss differs from Alzheimer's disease. The researchers began by performing microarray (gene expression) analyses of postmortem brain cells from the DG of eight people, ages 33 to 88, all of whom were free of brain disease. The team also analyzed cells from their EC, which served as controls since that brain structure is unaffected by aging. The analyses identified 17 candidate genes that might be related to aging in the DG. The most significant changes occurred in a gene called RbAp48, whose expression declined steadily with aging across the study subjects.

To determine whether RbAp48 plays an active role in age-related memory loss, the researchers turned to mouse studies. "The first question was whether RbAp48 is downregulated in aged mice," said lead author Elias

Pavlopoulos, PhD, associate research scientist in neuroscience at CUMC. "And indeed, that turned out to be the case—there was a reduction of RbAp48 protein in the DG."
When the researchers genetically inhibited RbAp48 in the brains of healthy young mice, they found the same memory loss as in aged mice, as measured by novel object recognition and water maze memory tests. When RbAp48 inhibition was turned off, the mice's memory returned to normal.
The researchers also did functional MRI (fMRI) studies of the mice with inhibited RbAp48 and found a selective effect in the DG, similar to that seen in fMRI studies of aged mice, monkeys, and humans. This effect of RbAp48 inhibition on the DG was accompanied by defects in molecular mechanisms similar to those found in old mice. The fMRI profile and mechanistic defects of the mice with inhibited RbAp48 returned to normal when the inhibition was turned off.
In another experiment, the researchers used viral gene transfer and increased RbAp48 expression in the DG of aged mice. "We were astonished that not only did this improve the mice's performance on the memory tests, but their performance was comparable to that of young mice," said Dr. Pavlopoulos.
"The fact that we were able to reverse age-related memory loss in mice is very encouraging," said Dr. Kandel. "Of course, it's possible that other changes in the DG contribute to this form of memory loss. But at the very least, it shows that this protein is a major factor, and it speaks to the fact that age-related memory loss is due to a functional change in neurons of some sort. Unlike with Alzheimer's, there is no significant loss of neurons."
Finally, the study data suggest that RbAp48 protein mediates its effects, at least in part, through the PKA-CREB1-CBP pathway, which the team had found in earlier studies to be important for age-related memory loss in the mouse. According to the researchers, RbAp48 and the PKA-CREB1-CBP pathway are valid targets for therapeutic intervention. Agents that enhance this pathway have already been shown to improve age-related hippocampal dysfunction in rodents.
"Whether these compounds will work in humans is not known," said Dr. Small. "But the broader point is that to develop effective interventions, you first have to find the right target. Now we have a good target, and with the mouse we've developed, we have a way to screen therapies that might be effective, be they pharmaceuticals, nutraceuticals, or physical and cognitive exercises."
"There's been a lot of handwringing over the failures of drug trials based on findings from mouse models of Alzheimer's," Dr. Small said. "But this is different. Alzheimer's does not occur naturally in the mouse. Here, we've caused age-related memory loss in the mouse, and we've shown it to be relevant to human aging."
The paper is titled, "A Molecular Mechanism for Age-Related Memory Loss: The Histone Binding Protein RbAp48." The other contributors are Sidonie Jones, Stylianos Kosmidis, Maggie Close, Carla Kim, and Olga Kovalerchik, all at CUMC.
The study was supported by grants from the Howard Hughes Medical Institute, the James S. McDonnell Foundation, the Broitman Foundation, the Henry M. Jackson Foundation for the Advancement of Military Medicine Inc., the McKnight Brain Research Foundation, and the National Institute on Aging (AG034618).

http://www.eurekalert.org/pub_releases/2013-08/msu-bil082813.php

Brain inflammation linked to more severe Parkinson's symptoms

Study analyzes biomarkers in fluid near brain cortex

GRAND RAPIDS, Mich. — Reversing inflammation in the fluid surrounding the brain's cortex may provide a solution to the complex riddle of Parkinson's, according to researchers who have found a link between pro-inflammatory biomarkers and the severity of symptoms such as fatigue, depression and anxiety in patients with the chronic disease.
Lena Brundin of Michigan State University's College of Human Medicine was part of a research team that measured inflammatory markers found in cerebrospinal fluid samples of Parkinson's patients and members of a control group.
"The degree of neuroinflammation was significantly associated with more severe depression, fatigue, and cognitive impairment even after controlling for factors such as age, gender and disease duration," said Brundin, an associate professor in the college and a researcher with the Van Andel Institute.
"By investigating associations between inflammatory markers and non-motor symptoms we hope to gain further insight into this area, which in turn could lead to new treatment options."
The results of the study were published in the journal Brain, Behavior, and Immunity.
Inflammation in the brain long has been suspected to be involved in the development of Parkinson's disease, specifically in non-motor symptoms such as depression, fatigue and cognitive impairment. Recent research suggests inflammation could drive cell death and that developing new drugs that target this inflammation might slow disease progression.
Parkinson´s disease is the second most common degenerative disorder of the central nervous system; the causes of the disease and its development are not yet fully understood.

"The few previous studies investigating inflammatory markers in the cerebrospinal fluid of Parkinson's patients have been conducted on comparatively small numbers of subjects, and often without a healthy control group for comparison," Brundin said.
In the study, 87 Parkinson's patients were enrolled between 2008 and 2012. For the control group, 37 individuals were recruited. Participants underwent a general physical exam and routine blood screening. Researchers looked at the following markers: C-reactive protein, interleukin-6, tumor necrosis factor-alpha, eotaxin, interferon gamma-induced protein-10, monocyte chemotactic protein-1 and macrophage inflammatory protein 1-β.
The study was carried out in collaboration with researchers from Lund University in Sweden, Skåne University Hospital in Sweden and the Mayo Clinic College of Medicine in Florida.

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School-age drinking increases breast cancer risk

If a female averages a drink per day between her first period and her first full-term pregnancy, she increases her risk of breast cancer by 13 percent

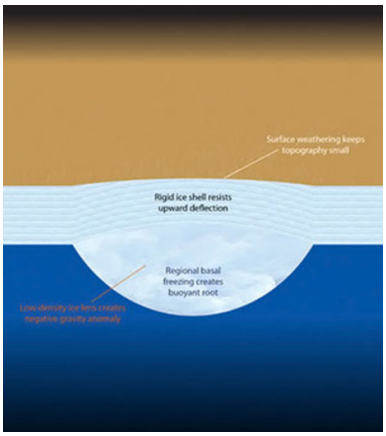
Here's a sobering fact for millions of young women heading back to school: The more alcohol they drink before motherhood, the greater their risk of future breast cancer. That's according to new research from Washington University School of Medicine in St. Louis that, for the first time, links increased breast cancer risk to drinking between early adolescence and first full-term pregnancy. Previous studies have looked at breast cancer risk and alcohol consumption later in life or at the effect of adolescent drinking on noncancerous breast disease.
“More and more heavy drinking is occurring on college campuses and during adolescence, and not enough people are considering future risk. But, according to our research, the lesson is clear: If a female averages a drink per day between her first period and her first full-term pregnancy, she increases her risk of breast cancer by 13 percent,” said co-author Graham Colditz, MD, DrPH, associate director for cancer prevention and control at Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine.
The study is published online Aug. 28 in the Journal of the National Cancer Institute.
Colditz also is the Niess-Gain Professor of Surgery at Washington University School of Medicine. He worked on the study with first author Ying Liu, MD, PhD, a School of Medicine instructor in the Division of Public Health Sciences, and colleagues from Brigham and Women's Hospital, Harvard Medical School, Beth Israel Deaconess Medical Center and Harvard School of Public Health.
The researchers also found that for every bottle of beer, glass of wine or shot of liquor consumed daily, a young woman increases her risk of proliferative benign breast disease by 15 percent. Although such lesions are noncancerous, their presence increases breast cancer risk by as much as 500 percent, Liu said.
"Parents should educate their daughters about the link between drinking and risk of breast cancer and breast disease," she said. "That's very important because this time period is very critical."
The findings are based on a review of the health histories of 91,005 mothers enrolled in the Nurses' Health Study II from 1989 to 2009. Colditz was key to the development and administration of that and similar studies that track disease risk in female nurses.
Colditz and Liu didn't consider the effects of adolescent and early adulthood drinking on women who didn't have a full-term pregnancy because not enough were represented among those studied, Liu said.
Breast tissue cells are particularly susceptible to cancer-causing substances as they undergo rapid proliferation during adolescence and later. Adding to the risk is the lengthening time frame between the average age of a girl's first menstrual cycle and the average age of a woman's first full-term pregnancy. Colditz doesn't foresee any shortening of that, which is why young women should drink less, he said – to lower average daily consumption and, therefore, risk.
"Reducing drinking to less than one drink per day, especially during this time period, is a key strategy to reducing lifetime risk of breast cancer," he said.
Colditz said the findings call for more research into what young women can do to counteract alcohol's adverse effects if they choose to drink. Past studies that didn't consider alcohol use suggest that eating more fiber and exercising more lowers cancer risk for everyone.

This work was supported by the National Cancer Institute, National Institutes of Health (NIH) (R01 CA050385, R01 CA046475). Colditz's work also is supported by an American Cancer Society Clinical Research Professorship and the Breast Cancer Research Foundation. Liu's research is supported by The Foundation for Barnes-Jewish Hospital.
Liu Y, Colditz GA, Rosner B, Berkey CS, Collins LC, Schnitt SJ, Connolly JL, Chen WY, Willett WC, Tamimi RM. Alcohol intake between menarche and first pregnancy: A prospective study of breast cancer risk. Journal of the National Cancer Institute. Online Aug. 28, 2013.

http://www.eurekalert.org/pub_releases/2013-08/uoc--ncd082813.php

New Cassini data from Titan indicate a rigid, weathered ice shell

An analysis of gravity and topography data from Saturn's largest moon, Titan, has revealed unexpected features of the moon's outer ice shell.



A rigid ice shell resists the upward pressure of a buoyant root, whose low density produces a negative gravity anomaly. Upward deflection of the ice shell creates positive topography, but surface weathering keeps that topography small. **Credit: Doug Hemingway**

The best explanation for the findings, the authors said, is that Titan's ice shell is rigid and that relatively small topographic features on the surface are associated with large roots extending into the underlying ocean. The study is published in the August 29 issue of the journal Nature.

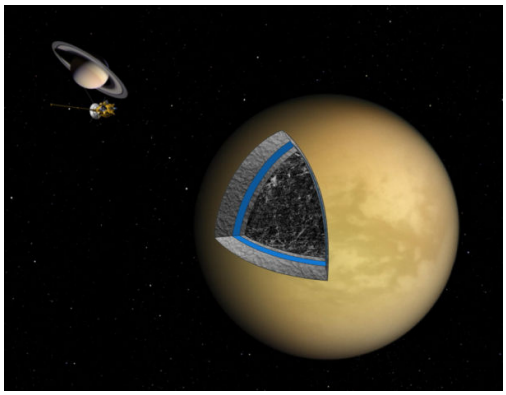
Led by planetary scientists Douglas Hemingway and Francis Nimmo at the University of California, Santa Cruz, the study used new data from NASA's Cassini spacecraft. The researchers were surprised to find a negative correlation between the gravity and topography signals on Titan.

"Normally, if you fly over a mountain, you expect to see an increase in gravity due to the extra mass of the mountain. On Titan, when you fly over a mountain the gravity gets lower. That's a very odd observation," said Nimmo, a professor of Earth and planetary sciences at UC Santa Cruz.

To explain that observation, the researchers developed a model in which each bump in the topography on the surface of Titan is offset by a deeper "root" big enough to overwhelm the gravitational effect of the bump on the surface. The root is like an iceberg extending below the ice shell into the ocean underneath it. "Because ice is lower density than water, you get less gravity when you have a big chunk of ice there than when you have water," Nimmo explained.

An iceberg floating in water is in equilibrium, its buoyancy balancing out its weight. In this model of Titan, however, the roots extending below the ice sheet are so much bigger than the bumps on the surface that their buoyancy is pushing them up against the ice sheet.

"It's like a big beach ball under the ice sheet pushing up on it, and the only way to keep it submerged is if the ice sheet is strong," said Hemingway, a doctoral candidate in planetary geophysics at UCSC and lead author of the paper. "If large roots are the reason for the negative correlation, it means that Titan's ice shell must have a very thick rigid layer."



This artist's illustration shows the likely interior structure of Saturn's moon Titan deduced from gravity field data collected by NASA's Cassini spacecraft. The investigation by Cassini's radio science team suggests that Titan's interior is a cool mix of ice studded with rock. **NASA/JPL**

The researchers calculated that, in this model, Titan's ice shell would have to have a rigid layer at least 40 kilometers thick. They also found that hundreds of meters of surface erosion and deposition are needed to account for the observed imbalance between the large roots and small surface topography.

The results from their model are similar to estimates obtained by geomorphologists studying the erosion of impact craters and other features on Titan.

These findings have several implications. For example, a thick rigid ice shell makes it very difficult to produce ice volcanoes, which some have proposed to explain certain features seen on the surface.

Unlike Earth's geologically active crust, Titan's ice shell isn't getting recycled by convection or plate tectonics. "It's just sitting there, and weather and erosion are acting on it, moving stuff around and redepositing sediments," Nimmo said. "It may be like the surface of Earth would be if you turned plate tectonics off."

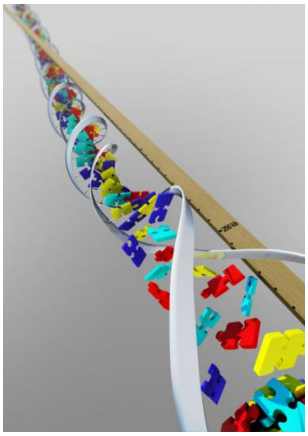
The researchers are not sure what could have given rise to Titan's topographical features with their deep roots. Titan's eccentric orbit around Saturn generates tides that flex the moon's surface and create tidal heating, which could cause variations to develop in the thickness of the ice shell, Hemingway said.

In addition to Hemingway and Nimmo, the coauthors of the paper include Howard Zebker at Stanford University and Luciano Iess at the Sapienza University of Rome. This research was supported in part by NASA. The Cassini-Huygens mission is a cooperative project of NASA, the European Space Agency, and the Italian Space Agency. More information on the Cassini mission is available online from NASA and the Jet Propulsion Laboratory.

http://www.eurekalert.org/pub_releases/2013-08/uonc-rda082813.php

Researchers discover a potential cause of autism

Key enzymes are found to have a 'profound effect' across dozens of genes linked to autism, the insight could help illuminate environmental factors behind autism spectrum disorder and contribute to a unified theory of how the disorder develops



CHAPEL HILL, N.C. -- Problems with a key group of enzymes called topoisomerases can have profound effects on the genetic machinery behind brain development and potentially lead to autism spectrum disorder (ASD), according to research announced today in the journal Nature. Scientists at the University of North Carolina School of Medicine have described a finding that represents a significant advance in the hunt for environmental factors behind autism and lends new insights into the disorder's genetic causes.

"Our study shows the magnitude of what can happen if topoisomerases are impaired," said senior study author Mark Zylka, PhD, associate professor in the Neuroscience Center and the Department of Cell Biology and Physiology at UNC. "Inhibiting these enzymes has the potential to profoundly affect neurodevelopment -- perhaps even more so than having a mutation in any one of the genes that have been linked to autism." The study could have important implications for ASD detection and prevention.

Topoisomerase inhibitors reduce the expression of long genes in neurons, including a remarkable number of genes implicated in Autism Spectrum Disorders -- 200 kb is four times longer than the average gene.
Credit: Concept: Mark Zylka. Illustration: Janet Iwasa.

"This could point to an environmental component to autism," said Zylka. "A temporary exposure to a topoisomerase inhibitor in utero has the potential to have a long-lasting effect on the brain, by affecting critical periods of brain development. "

This study could also explain why some people with mutations in topoisomerases develop autism and other neurodevelopmental disorders.

Topiosomerases are enzymes found in all human cells. Their main function is to untangle DNA when it becomes overwound, a common occurrence that can interfere with key biological processes.

Most of the known topoisomerase-inhibiting chemicals are used as chemotherapy drugs. Zylka said his team is searching for other compounds that have similar effects in nerve cells. "If there are additional compounds like this in the environment, then it becomes important to identify them," said Zylka. "That's really motivating us to move quickly to identify other drugs or environmental compounds that have similar effects -- so that pregnant women can avoid being exposed to these compounds."

Zylka and his colleagues stumbled upon the discovery quite by accident while studying topotecan, a topoisomerase-inhibiting drug that is used in chemotherapy. Investigating the drug's effects in mouse and human-derived nerve cells, they noticed that the drug tended to interfere with the proper functioning of genes that were exceptionally long -- composed of many DNA base pairs. The group then made the serendipitous connection that many autism-linked genes are extremely long.

"That's when we had the 'Eureka moment,'" said Zylka. "We realized that a lot of the genes that were suppressed were incredibly long autism genes."

Of the more than 300 genes that are linked to autism, nearly 50 were suppressed by topotecan. Suppressing that many genes across the board -- even to a small extent -- means a person who is exposed to a topoisomerase inhibitor during brain development could experience neurological effects equivalent to those seen in a person who gets ASD because of a single faulty gene.

The study's findings could also help lead to a unified theory of how autism-linked genes work. About 20 percent of such genes are connected to synapses -- the connections between brain cells. Another 20 percent are related to gene transcription -- the process of translating genetic information into biological functions. Zylka said this study bridges those two groups, because it shows that having problems transcribing long synapse genes could impair a person's ability to construct synapses.

"Our discovery has the potential to unite these two classes of genes -- synaptic genes and transcriptional regulators," said Zylka. "It could ultimately explain the biological mechanisms behind a large number of autism cases."

The study's coauthors include Benjamin Philpot (co-senior author), Terry Magnuson, Ian King, Chandri Yandava, Angela Mabb, Hsien-Sung Huang, Brandon Pearson, J. Mauro Calabrese, Joshua Starmer and Joel Parker from UNC and Jack S. Hsiao and Stormy Chamberlain of the University of Connecticut Health Center.

http://www.eurekalert.org/pub_releases/2013-08/jhu-rat082813.php

Researchers aim to use light -- not electric jolts -- to restore healthy heartbeats

When a beating heart slips into an irregular, life-threatening rhythm, the treatment is well known: deliver a burst of electric current from a pacemaker or defibrillator.

But because the electricity itself can cause pain, tissue damage and other serious side-effects, a Johns Hopkins-led research team wants to replace these jolts with a kinder, gentler remedy: light.

In a paper published Aug. 28 in the online journal Nature Communications, five biomedical engineers from Johns Hopkins and Stony Brook universities described their plan to use biological lab data and an intricate computer model to devise a better way to heal ailing hearts. Other scientists are already using light-sensitive cells to control certain activities in the brain. The Johns Hopkins-Stony Brook researchers say they plan to give this technique a cardiac twist so that doctors in the near future will be able to use low-energy light to solve serious heart problems such as arrhythmia.

"Applying electricity to the heart has its drawbacks," said the project's supervisor, Natalia Trayanova, the Murray B. Sachs Professor of Biomedical Engineering at Johns Hopkins. "When we use a defibrillator, it's like blasting open a door because we don't have the key. It applies too much force and too little finesse. We want to control this treatment in a more intelligent way. We think it's possible to use light to reshape the behavior of the heart without blasting it."

To achieve this, Trayanova's team is diving into the field of optogenetics, which is only about a decade old. Pioneered by scientists at Stanford, optogenetics refers to the insertion of light-responsive proteins called opsins into cells. When exposed to light, these proteins become tiny portals within the target cells, allowing a stream of ions—an electric charge—to pass through. Early researchers have begun using this tactic to control the bioelectric behavior of certain brain cells, forming a first step toward treating psychiatric disorders with light.

In the Nature Communications paper, the researchers reported that they had successfully tested this same technique on a heart -- one that "beats" inside a computer. Trayanova has spent many years developing highly detailed computer models of the heart that can simulate cardiac behavior from the molecular and cellular levels all the way up to that of the heart as a whole. At Johns Hopkins, she directs the Computational Cardiology Lab within the Institute for Computational Medicine.

As detailed in the journal article, the Johns Hopkins computer model for treating the heart with light incorporates biological data from the Stony Brook lab of Emilia Entcheva, an associate professor of biomedical engineering. The Stony Brook collaborators are working on techniques to make heart tissue light-sensitive by inserting opsins into some cells. They also will test how these cells respond when illuminated.

"Experiments from this lab generated the data we used to build our computer model for this project," Trayanova said. "As the Stony Brook lab generates new data, we will use it to refine our model."

In Trayanova's own lab, her team members will use this model to conduct virtual experiments. They will try to determine how to position and control the light-sensitive cells to help the heart maintain a healthy rhythm and pumping activity. They will also try to gauge how much light is needed to activate the healing process. The overall goal is to use the computer model to push the research closer to the day when doctors can begin treating their heart patients with gentle light beams. The researchers say it could happen within a decade.

"The most promising thing about having a digital framework that is so accurate and reliable is that we can anticipate which experiments are really worth doing to move this technology along more quickly," said Patrick M. Boyle, a postdoctoral fellow in Trayanova's lab and lead author of the Nature Communications paper. "One of the great things about using light is that it can be directed at very specific areas. It also involves very little energy. In many cases, it's less harmful and more efficient than electricity."

After the technology is honed through the computer modeling tests, it could be incorporated into light-based pacemakers and defibrillators. It is interesting to note that it was a Johns Hopkins electrical engineering researcher, William B. Kouwenhoven, who developed the closed-chest electric cardiac defibrillator, which has been used since was the 1950s to save lives.

Trayanova was senior author of the Nature Communications paper. The co-authors were Entcheva and two members of Entcheva's lab team: graduate student John C. Williams and postdoctoral fellow Christina M. Ambrosi.

Lead author Boyle, who earned his Ph.D. at the University of Calgary, is supported by a fellowship from the Natural Sciences and Engineering Research Council of Canada. This research was also supported by National Institutes of Health grants R01 HL111649 and R01 HL103428, and by National Science Foundation grants NSF-CDI-1124804 and NSF-OCI-108849.

http://www.eurekalert.org/pub_releases/2013-08/uob-nte082813.php

Not the end of the world: Why Earth's greatest mass extinction was the making of modern mammals

The first mammals arose in the Triassic period, over 225 million years ago. These early furballs include small shrew-like animals such as Morganucodon from England, Megazostrodon from South Africa, and Bienotherium from China.

They had differentiated teeth (incisors, canines, molars) and large brains and were probably warm-blooded and covered in fur – all characteristics that make them stand apart from their reptile ancestors, and which contribute to their huge success today.

However, new research from the University of Lincoln, the National Museum in Bloemfontein, South Africa, and the University of Bristol suggests that this array of unique features arose step-wise over a long span of time, and that the first mammals may have arisen as a result of the end-Permian mass extinction which wiped out 90 per cent of marine organisms and 70 per cent of terrestrial species.

Dr Marcello Ruta of the University of Lincoln, lead author of the study, said: "Mass extinctions are seen as entirely negative. However, in this case, cynodont therapsids, which included a very small number of species before the extinction, really took off afterwards and was able to adapt to fill many very different niches in the Triassic – from carnivores to herbivores."

Co-author Dr Jennifer Botha-Brink of the National Museum in Bloemfontein, South Africa said: "During the Triassic, the cynodonts split into two groups, the cynognathians and the probainognathians. The first were mainly plant-eaters, the second mainly flesh-eaters, and the two groups seemed to rise and fall at random, first one expanding, and then the other. In the end, the probainognathians became the most diverse and most varied in adaptations, and they gave rise to the first mammals some 25 million years after the mass extinction."

Co-author Professor Michael Benton of the University of Bristol said: "We saw that when a major group, such as cynodonts, diversifies it is the body shape or range of adaptations that expands first. The diversity, or number of species, rises after all the morphologies available to the group have been tried out."

The researchers concluded that cynodont diversity rose steadily during the recovery of life following the mass extinction with their range of form rising rapidly at first before hitting a plateau. This suggests there is no particular difference in morphological diversity between the very first mammals and their immediate cynodont predecessors.

'The radiation of cynodonts and the ground plan of mammalian morphological diversity' by Marcello Ruta, Jennifer Botha-Brink, Steve Mitchell and Michael J. Benton in Proceedings of the Royal Society B

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Randomized Treatments May Be More Effective at Stopping Disease Outbreaks

Mathematicians have found that by varying the timing of treatments, doctors may be able to increase the odds that a disease outbreak will die off suddenly

By Calla Cofield | Wednesday, August 28, 2013 | 5

Herding cats is a cakewalk compared with getting people to take flu vaccine shots in the last weeks of summer—work, school, limited pharmacy hours, beach days and countless other factors conspire to interfere. As a result, vaccinations tend to trickle in over many months. Rather than resisting this tendency, some mathematicians now think that public health officials may one day embrace it. A bit of randomness in treatment schedules may actually help manage a disease outbreak.

This conclusion comes from an analysis of treatment options in infectious disease outbreaks through the lens of complexity theory, which attempts to make sense of systems that are fundamentally unpredictable. Researchers using complexity theory to study disease outbreaks have identified rare instances when the outbreak will die out suddenly. Say, for instance, health workers administer antibiotics to fight an outbreak of bacterial meningitis, causing infections to decline. A classic disease model would suggest that every infected person must be isolated and treated before the disease can die out. But complexity theory shows that occasionally, the disease will die out due to random and unpredictable factors.

Such a “random extinction event” is impossible to predict, but new research shows that judicious timing of treatments can increase the odds of one occurring. Knowing how to vary them to make random extinction events more likely could be particularly helpful in developing nations, where pharmaceutical supplies are often limited and treatments are not available year-round, but are given in bursts a certain number of times per year. This is often the case when an aid organization administers treatments remotely.

Ira Schwartz, an applied mathematician and physicist at the U.S. Naval Research Laboratory, and his colleagues utilized a computer simulation that models the general behavior of infectious diseases in a population of 8,000 people. The simulation took into account the element of randomness and compared the

outcome of two different scenarios: one in which treatment is delivered at regular intervals in time and another at random intervals. They compared these two scenarios for infectious diseases such as bacterial meningitis, venereal disease and plague, which are treated largely with antibiotics.
The results show that in cases where treatment bursts could only be administered between two and eight times per year, the random schedule created an exponential decrease in the time to a random extinction event: in other words, a disease died out faster. "The research demonstrates why randomized treatment schedules work," says Schwartz, a co-author on the paper, which was published in PLoS ONE in August.
In 2008 Schwartz co-authored another paper that used similar models to test the effect of random vaccination on incoming members of the population (infants), and showed similar decreases in disease extinction time.
In the new paper the researchers speculate that if disease treatments are delivered twice per year, six months apart, a disease may have time to regain strength between doses. In a random schedule, however, those doses might come closer together, increasing the likelihood that the second dose would attack the disease while the latter is in a weakened state. Such a one–two punch increases the possibility that a random extinction event will occur. (Although researchers can calculate the odds of such an event, they remain ultimately unpredictable.) For this reason, the researchers conclude that when resources are limited, treatment should be distributed to a larger percentage of the population in a few random, closely distributed pulses, rather than many smaller pulses distributed to fewer people.
With more research into the random interplay between treatment and disease, it is possible scientists will provide more suggestions for how to best administer treatments, particularly in locations where supplies and manpower are limited.
Charles Doering, acting director of the Center for the Study of Complex Systems at the University of Michigan, says Schwartz's team is one of few groups exploring how randomness in treatment schedules can affect infectious disease progress. Although the researchers used well-established models of how diseases spread and survive in human populations, their mathematical techniques for taking randomness into account, developed from quantum mechanics, is difficult to apply to disease models. "You never quite know," he says. "If you changed any of the structure of the model, maybe the conclusions would change." But the work may inspire further investigation with larger computer simulations or laboratory experiments that test these theories on live populations of microorganisms. "This gives a starting point; a working hypothesis to investigate," he adds.

http://scitechdaily.com/scientists-pinpoint-lowest-temperature-limit-life-earth/

Scientists Pinpoint Lowest Temperature Limit for Life on Earth

In a new study, scientists reveal that -20°C is the lowest temperature at which simple life can live and grow on Earth.

The study, which is published in PLoS One, reveals that below -20°C, single-celled organisms dehydrate, sending them into a vitrified – glass-like – state during which they are unable to complete their life cycle.
The researchers propose that, since the organisms cannot reproduce below this temperature, -20°C is the lowest temperature limit for life on Earth.
Scientists placed single-celled organisms in a watery medium, and lowered the temperature. As the temperature fell, the medium started to turn into ice and as the ice crystals grew, the water inside the organisms seeped out to form more ice. This left the cells first dehydrated, and then vitrified. Once a cell has vitrified, scientists no longer consider it living as it cannot reproduce, but cells can be brought back to life when temperatures rise again. This vitrification phase is similar to the state plant seeds enter when they dry out.
'The interesting thing about vitrification is that in general a cell will survive, where it wouldn't survive freezing, if you freeze internally you die. But if you can do a controlled vitrification you can survive,' says Professor Andrew Clarke of NERC's British Antarctic Survey, lead author of the study. 'Once a cell is vitrified it can continue to survive right down to incredibly low temperatures. It just can't do much until it warms up.'
More complex organisms are able to survive at lower temperatures because they are able to control the medium the cells sit in to some extent.
'Bacteria, unicellular algae and unicellular fungi – of which there are a huge amount in the world-are free-living because they don't rely on other organisms,' Clarke explains.
'Everything else, like trees and animals and insects, has the ability to control the fluid that surrounds their internal cells. In our case it's blood and lymph. In a complicated organism the cells sit in an environment that the organism can control. Free-living organisms don't have this; if ice forms in the environment they are subject to all the stresses that implies.'
If a free-living cell cools too quickly it would be unable to dehydrate and vitrify; instead it would freeze and wouldn't survive.

This goes some way towards explaining why preserving food using deep freezing works. Most fridge freezers operate at a temperature of nearly -20°C . This study shows that this temperature works because molds and bacteria are unable to multiply and spoil food. 'We were really pleased that we had a result which had a wider relevance, as it provided a mechanism for why domestic freezers are as successful as they are,' Clarke says.
The scientists believe that the temperature limit they have discovered is universal, and below -20°C simple forms of unicellular life can't grow on Earth. During the study they looked at a wide range of single-celled organisms that use a variety of different energy sources, from light to minerals, to metabolize. Every single type vitrified below this temperature.
'When you have a single-celled organism and cool it until ice forms in the external medium, in every case we looked at the cells dehydrated and then vitrified between -10°C and -25°C. There were no exceptions,' explains Clarke.

This study was supported by funding from NERC, the European Research Council, and the National de la Recherche Agronomique.
Publication: Andrew Clarke, et al., "A Low Temperature Limit for Life on Earth," 2013, PLoS ONE, 8(6): e66207; doi:10.1371/journal.pone.0066207

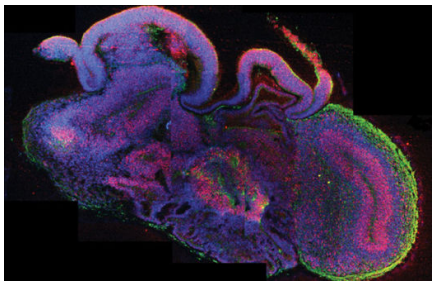
http://www.sciencenews.org/view/generic/id/352830/title/Tiny_human_almost-brains_made_in_lab

Tiny human almost-brains made in lab | Genes & Cells

Stem cells arrange themselves into a version of the most complex human organ

By Laura Sanders

Largely left to their own devices, human stem cells knitted themselves into tissue with a multitude of brain structures and specialized cadres of neurons in a form reminiscent of the brain of a nine-week-old fetus, scientists report August 28 in *Nature*.
The tissue doesn't approach the dizzying complexity of the human brain. Yet these tiny neural balls, each no bigger than a BB pellet, represent the most complex brain structure grown in a lab to date, researchers say.
The new work could provide an unprecedented window into the early stages of human brain development, a simple way to test pharmaceuticals on human brain tissue and a way to study the brain defects of individual patients, the study authors suggest.



A cross section of a lab-grown approximation of a human brain reveals several features, including neurons (green) and neuron-producing stem cells (red). **Madeline A. Lancaster**

"They've done something very remarkable," says Flora Vaccarino of Yale University.
After about two months of growing in a nutrient broth, the cells specialized into neurons that populated distinct, recognizable parts of the developing brain, such as the hippocampus, retina and choroid plexus, which produces cerebrospinal fluid in the brain.
The tissue clumps also had discrete parts of the cerebral cortex, the outer sheet of the human brain that's responsible for advanced thought processes. Other properties of the human brain held true, too: Many of the neurons were actively firing off electrical messages, experiments revealed. Select groups of young neurons seemed to have migrated to a different part of the organoid, a process that helps populate the brain with neurons. And like the brain, the tissue had a rich population of a specialized stem cell called radial glial stem cells. These cells kept neuron numbers growing.
Called "cerebral organoids" by study coauthors Madeline Lancaster and Jürgen Knoblich of the Austrian Academy of Science in Vienna, the tiny lab-grown tissues could have big implications for brain science. Already, by growing a personalized organoid with cells from a patient, the researchers have learned about microcephaly, a developmental disorder marked by a small brain. "There is enormous potential there," says neuroscientist Ed Lein of the Allen Institute for Brain Science in Seattle.
The organoid-growing process begins with human stem cells, taken either directly from an embryo or from adult skin samples that have been reprogrammed to an embryo-like state. These cells can grow into any tissue in the human body.
To make them into a cerebral organoid, the researchers let the cells grow for a few days in a dish, and then moved them into a broth that encourages the growth of neuroectoderm tissue, the kind that ultimately creates the brain. After that, the researchers injected these cells into a drop of gel that serves as a scaffold for the cells to grow on. In the final move, the gel droplets were transferred to spinning flasks that held nutrients.
This last step was crucial, the researchers found: The spinning motion distributed oxygen and nutrients to all of the cells in the organoid. Without it, cells, especially those in the center, would starve and die.

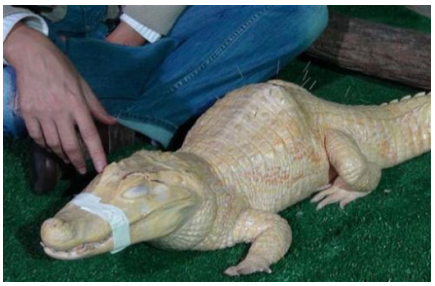
After about two months, the organoids had pushed past the boundary of their gel droplets, reaching a diameter of about 4 millimeters.
So far, the researchers have grown hundreds of these cerebral organoids and the oldest is about a year old. In the oldest ones, the cells are still alive but have stopped dividing, Lancaster says. The organoids reach maximum size after about two months; any larger and the cells on the interior would not get enough nutrients and oxygen, she says.
One of the most remarkable aspects of the work is that the organoids formed these complex, brainlike structures with little from researchers, Lein says. “The biggest thing for me is realizing that most of the information for generating a brain is intrinsic,” he says. “These cells carry enough information to generate a brain.”
That means that cells from different people can easily be used to grow very different sorts of brains.
As part of their study, Lancaster, Knoblich and colleagues grew a personalized organoid using cells from the skin of a patient with microcephaly. Lancaster says she immediately saw that the organoid was smaller than usual.
Microcephaly has been difficult to study. But with the microcephaly organoid, the researchers figured out why the brains were smaller.
Neuron-producing radial glial cells were stopping their job too early and disappearing, the researchers found. This early termination could ultimately result in too few neurons, a situation that might also happen in microcephaly. These organoids could offer insight into more complex disorders rooted in brain development, too, such as schizophrenia and autism, says Knoblich.
Of course, these organoids differ from the brain in many ways. Unlike the brain’s organized structure, regions in the organoids were arranged haphazardly. The neurons made connections, but probably not meaningful ones like those in the human brain. And important support systems, such as blood vessels, were absent.
“If you look at our organoid as a whole, it is not a brain,” Knoblich says. Nonetheless, the system is a useful approximation.
M. Lancaster et al. Cerebral organoids model human brain development and microcephaly. Nature. Published online August 28, 2013. doi:10.1038/nature12517. Available online: [Go to]

http://phys.org/news/2013-08-acupuncture-ailing-alligator-brazil.html

Acupuncture helps ailing alligator in Brazil (Update)

Bino's back was killing him. He was suffering from scoliosis. He couldn't move his legs, two of them anyway, and his tail just wouldn't swish.

What's an albino alligator in that sort of health bind to do? Acupuncture, naturally. Bino the albino alligator lives at the Sao Paulo Aquarium, where he's been since 2007. Veterinarians said Wednesday that he was born eight years ago with his ailments, and nothing seemed to alleviate them.
So, in early 2011 veterinarians decided to see if acupuncture might help Bino, as it has other animals living at the aquarium.
"The acupuncture will ... alleviate his pain and keep all his vital functions going," said Rafael Gutierrez, a biologist at the aquarium of Sao Paulo, adding that the 30-minute weekly treatments would continue indefinitely, as long as they kept showing solid results.



Bino, the albino alligator, receives acupuncture treatment in Sao Paulo, Brazil, Tuesday, Aug 27, 2013. Veterinarians at the Sao Paulo aquarium have found a novel treatment for Bino, who suffers from hunchback and scoliosis: acupuncture. Once a week, several needles are inserted into Bino's back and the treatment is working. He's already able to twitch his tail again and move his back legs, which until recently he was unable to do. **(AP Photo/Ana Pereira)**

Acupuncture on animals is becoming increasingly common around the globe, the biologists at the Sao Paulo aquarium said, especially with pets such as cats, dogs and horses. The use of acupuncture on animals began thousands of years ago in China.
In the U.S., the number of veterinarians who hold membership in the American Academy of Veterinary Acupuncture has jumped 50 percent in the last few years to 900 doctors, said Simon Flynn, the executive director of the academy that's based in Glastonbury, Connecticut.
"There are many zoo veterinarians who use acupuncture, a number of equine practitioners who treat race horses with acupuncture, it's proven to be a useful treatment," Flynn said. "It's common with dogs and it's becoming increasingly common with cats. More veterinarians are seeing the worth of the treatment."
Typical ailments treated by acupuncture include neck and back issues, skin problems and pain in general, among other complaints, said Flynn.

Bino the Sao Paulo alligator requires a few precautions not needed with your average house cat. Inserting the needles into Bino's back requires the important first step of taping shut his lock-tight jaws full of sharp teeth. Bino wrestles around a bit as the tape is applied, but soon calms down.
Veterinarian Daniela Cervaletti then slides behind Bino, firmly pressing the needles into his leathery white and yellow hide. The needles are inserted along his spine and around the area where the animal developed a hunchback.
Bino doesn't move at all as nearly a dozen needles go in. Cervaletti gently strokes the side of Bino's neck after she applies them all, then waits several minutes before removing them.
The treatment complete, handlers help Bino back into a display pool, his white skin stark against brown fake rocks painted with foliage.
He moves easily and swishes his tail, gliding along the water as a gaggle of young schoolchildren in matching blue and gray uniforms squeal in delight, faces pressed up against the glass separating them from Bino.

http://www.sciencedaily.com/releases/2013/08/130828172821.htm

Promising Chronic Pain Drug Developed

A team of researchers led by Andrew Coop, PhD, professor and chair of the Department of Pharmaceutical Sciences (PSC) at the University of Maryland School of Pharmacy (UMSOP), has developed a new opioid drug that shows great potential to advance treatment and improve quality of life for individuals living with chronic pain.

Spotlighted in a recent issue of ACS Chemical Neuroscience, the compound, known as UMB 425, is as strong as morphine, but displays diminished tolerance over time with no obvious toxic effects.
"UMB 425 is a breakthrough in the development of therapeutics to treat chronic pain," says Coop. "Unlike other drugs developed to act on only one biological target, UMB 425 acts on two different opioid receptors in the body. When activated at the same time, these receptors work together to provide pain relief and slow the body's development of tolerance to the drug. This diminished tolerance allows a lower dose of the opioid to be administered for a longer time period, while still achieving the same level of pain relief."
For individuals living with chronic pain, either as a result of injury or disease such as arthritis, opioids are the standard treatment. But as the dosage increases to offset the body's tolerance to their effects, opioids cause a number of adverse effects, including constipation, nausea, drowsiness, and dizziness.
The unique dual-profile of UMB 425 -- made possible through Coop's collaborations with Alexander MacKerell, PhD, professor in PSC and director of the School's Computer Aided Drug Design Center, and Maureen Kane, PhD, assistant professor in PSC and co-director of the School's Mass Spectrometry Facility -- provides both pain relief as well as diminished tolerance in one drug.
"Historically, medicinal chemists have developed drugs aimed at only one biological target," says Coop. "However, two drugs administered together have the potential to metabolize differently in different individuals, as well as affect patients' adherence to both drugs. A single compound that is able to provide both pain relief and diminished tolerance has the advantage of a defined ratio that we can optimize to ensure patients receive the maximum pain relief, while experiencing minimum adverse effects."
Coop and his team conducted several in vitro and in vivo studies to determine the drug's effectiveness in alleviating pain and diminishing tolerance over time. If future research and clinical trials are successful, UMB 425 could have a significant impact on the treatment and quality of life for individuals living with chronic pain.
"The clinical implication of this research has the potential to be tremendous," says Mary Lynn McPherson, PharmD, BCPS, CPE, professor and vice chair for academic affairs in the Department of Pharmacy Practice and Science, and an international authority in the fields of pain management and palliative care.
"If clinicians can prescribe lower doses of opioids, they will not have to raise a patient's dose because of tolerance to the analgesic effects. Using lower doses will result in less severe adverse effects for the patient, both short-term effects such as nausea and constipation, as well as long-term adverse effects on the endocrine and immunologic systems. This would be a highly significant advance in pain management."
Coop and his team will continue to test UMB 425 to determine an optimal ratio at which it acts on the targeted opioid receptors to maximize pain relief, while minimizing tolerance. The team's ultimate goal is to develop two compounds derived from UMB 425 that will lead to Phase I clinical trials.

Jason R. Healy, Padmavani Bezawada, Jihyun Shim, Jace W. Jones, Maureen A. Kane, Alexander D. MacKerell, Andrew Coop, Rae R. Matsumoto. Synthesis, Modeling, and Pharmacological Evaluation of UMB 425, a Mixed μ Agonist/δ Antagonist Opioid Analgesic with Reduced Tolerance Liabilities. ACS Chemical Neuroscience, 2013; : 130611155052001 DOI: 10.1021/cn4000428

http://www.eurekalert.org/pub_releases/2013-08/ehs-pc082613.php

'1 pill can kill': Effects of unintentional opioid exposure in young children

Medication poisonings among children are an important public health problem.

During 2010-2011, an average of 1500 children under 6 years of age was evaluated in emergency departments each year due to unintentional exposure to buprenorphine. Ingestion of strong opioids, such as buprenorphine, can cause central nervous system depression, respiratory depression, and death in young children. In a new study scheduled for publication in The Journal of Pediatrics, researchers study how young children are gaining access to buprenorphine, as well as the effects of unintentional exposure to its different formulations.

Buprenorphine (or the buprenorphine-naloxone combination form), usually sold as a tablet or film strip, is used to treat adults who are addicted to opioids, such as prescription pain medication and heroin. Tablets typically are dispensed in 30-day supply bottles with child-resistant caps, and film strips are dispensed in single-dose, child-resistant foil packs. Dr. Eric Lavonas and colleagues from the Rocky Mountain Poison and Drug Center, the University of Colorado School of Medicine, the University of Oklahoma, Integris Baptist Medical Center, Degge Group, and Venebio Group studied 2380 cases of unintentional exposure to buprenorphine in any form involving children under 6 years of age. The average age of the children was 2 years. Common effects of buprenorphine exposure were lethargy, respiratory depression, miosis (small pupils), and vomiting. Although most children had good outcomes, 587 children were admitted to the intensive care unit and 4 children died.

The researchers found that children were 3.5 to 8.8 times more likely to accidentally ingest the tablets as have unintentional exposure to film strips; 95% of cases involved tablets. In 57% of the cases, at least one root cause for the exposure was identified: 415 cases involved medication stored in sight, in 110 cases the child accessed the medication from a bag or purse, and in 75 cases the medication was not stored in the original packaging. Although most exposures were in the child's own home, 5% of exposures occurred while the child was being watched by another caregiver.

Buprenorphine can be helpful in adult patients who are struggling with addiction issues, but it should not be accessible by children because even a single dose can be life-threatening. Therefore, it is important for all caregivers to be especially vigilant in keeping medications in their original packaging and up, away, and out of sight of children. Although this study focused on just one medication used in a specific population, other more widely used medications, such as those used to treat high blood pressure or diabetes, can be as harmful in young children. According to Dr. Lavonas, "This study underscores the value of providing medications that are particularly dangerous when taken by children, in single dose, child resistant packaging." This approach is likely to be more effective at reducing unintentional exposure than additional efforts at education.

http://nyti.ms/17ogNPt

Human Microbiome May Be Seeded Before Birth

We are each home to about 100 trillion bacteria, which we carry with us from birth till death.

By CARL ZIMMER

But when Juliette C. Madan was trained as a neonatologist in the mid-2000s, her teachers told her in no uncertain terms that we only acquire those bacteria after we are born. “It was clear as day, we were told, that fetuses were sterile,” she said. Dr. Madan is now an assistant professor of pediatrics at the Geisel School of Medicine at Dartmouth, and she’s come to a decidedly different view on the matter. “I think that the tenet that healthy fetuses are sterile is insane,” she said.

Dr. Madan and a number of other researchers are now convinced mothers seed their fetuses with microbes during pregnancy. They argue that this early inoculation may be important to the long-term health of babies. And manipulating these fetal microbes could open up new ways to treat medical conditions ranging from pre-term labor to allergies.

In 1900, the French pediatrician Henry Tissier declared unborn babies bacteria-free. Only when they started their journey down through the birth canal did they begin to get covered with microbes. The newborns then acquired more as they were handled and nursed. “This was considered a kind of scientific dogma,” said Esther Jiménez Quintana of Complutense University of Madrid.

This dogma gained strength from studies on babies born prematurely. Infections are a major risk factor in early labor. Many researchers saw this as evidence that the only bacteria in the uterus were dangerous ones.

But scientists came to this conclusion without finding out whether healthy fetuses had bacteria, too. “It became a self-fulfilling prophecy,” said Dr. Madan.

That has started to change in the past few years. In 2010, Josef Neu, a University of Florida pediatrician, examined the first stool from newborn babies, before they had their first meal. He found a diversity of bacteria in the stool, whether the babies were born on time or born prematurely.

"When we first saw this, we though it was an artifact," said Dr. Neu. If the fetuses were indeed sterile, their stool should have been germ-free. But in follow-up studies, he has gotten the same results.
Other scientists have also found evidence indicating that healthy fetuses pick up bacteria in the womb. Dr. Quintana and her colleagues have found bacteria in the amniotic fluid of healthy babies, as well as in umbilical cord blood and placentas.
If other animals are any guide, we shouldn't be surprised if human fetuses are laced with bacteria. In an essay published last week in the journal PLOS Biology, Seth R. Bordenstein and Lisa J. Funkhouser of Vanderbilt University observed that mothers transmitting bacteria to their offspring is the rule rather than the exception in the animal kingdom. Studying other species may give scientists clues about how human mothers inoculate their unborn children.
One open question is the route that bacteria take from mothers to their fetuses. A number of researchers suspect that immune cells in the mother's intestines swallow up bacteria there and ferry them into the bloodstream, where they eventually wind up in the uterus.
It's also not clear whether mothers deliver a random collection of species or a special set that are beneficial to them. Studies on children and adults have shown that our resident bacteria — collectively known as the microbiome — help us in many ways. They digest compounds in our food that would otherwise be indigestible. Beneficial bacteria also help tutor the immune system, so that it attacks pathogens without overreacting and damaging the body itself. The microbiome can even fend off disease-causing bacteria.
Dr. Neu and other pediatricians are now investigating whether the microbiome helps fetuses before birth. He speculates that a healthy supply of bacteria in a fetus can reduce the chances of premature birth. If harmful bacteria manage to slip past those defenses, they may trigger an immune reaction that is sensed by the mother, prompting her to go into labor.
As scientists investigate the microbiome, they are also exploring ways of manipulating it to treat disorders ranging from gut infections to autoimmune disorders. Dr. Neu hopes it may be possible someday to bring the same medical help to fetuses.
"We might provide mothers with a microbial cocktail," he said. The bacteria would pass from a mother to her fetus. Doctors might prescribe certain species to protect the fetus from infections, warding off early labor. Nurturing the fetal microbiome could help babies in other ways, like boosting their immune system.
Some scientists don't think the evidence supports these ideas, though. Bacteria in fetuses may not have any special role to play in their health. "It could just be part of the vulnerabilities that pregnancy poses on the maternal body," said Maria Dominguez-Bello, an associate professor at N.Y.U. Langone Medical Center.
But figuring out which explanation is right will demand the careful study of healthy fetuses — something that has only barely begun. "The frontier is ahead of us," said Dr. Bordenstein.

http://www.sciencedaily.com/releases/2013/08/130829092648.htm

First Large Scale Study Links Autism and Autoimmunity

A new, large-scale study of more than 2,700 mothers of children with autism shows that about one in 10 mothers have antibodies in their bloodstream that react with proteins in the brain of their babies.

The research, published in Molecular Psychology (August 20, 2013) indicates that while the blood-brain barrier in the adult women prevents them from being harmed by the antibodies, that same filter in the fetuses is not well-developed enough and so may allow the "anti-brain" antibodies to pass through to the babies' brains, possibly causing autism.
The study was led by Dr. Betty Diamond, head of the Center for Autoimmune and Musculoskeletal Disorders at The Feinstein Institute for Medical Research in Long Island, New York, who said the very large sample size "gives a clearer impression of the prevalence of these antibodies."
"We at AARDA applaud Dr. Diamond's research into an area that concerns all parents," said Virginia T. Ladd, President of American Autoimmune Related Diseases Association, Inc. (AARDA).
According to AARDA, in healthy people, when a foreign invader, such as a virus or bacteria, enters the body, the immune system produces antibodies to attack those foreign substances. In people with autoimmunity, the immune system mistakenly recognizes the body's own healthy tissues and organs as foreign invaders and produces antibodies to attack them. These auto-antibodies -- or antibodies produced against the self -- then cause disease. The disease that results depends upon which tissues and/or organs the antibodies are attacking.
Some 50 million Americans live and cope with autoimmune disease (AD), 75 percent of whom are women. AD is one of the top 10 leading causes of death of women under the age of 65. It encompasses more than 100 diseases, including psoriasis, Graves' disease, Sjogren's syndrome, multiple sclerosis, rheumatoid arthritis, Crohn's disease and lupus. It is responsible for more than $100 billion in direct health care costs annually.

http://www.sciencedaily.com/releases/2013/08/130829110430.htm

Doubling the Daily Allowance of Protein Intake With Diet and Exercise Protects Muscle Loss

A new report appearing in the September issue of The FASEB Journal challenges the long-held adage that significant muscle loss is unavoidable when losing weight through exercise and diet.

In the report, scientists show that consuming twice the recommended daily allowance (RDA) of protein while adhering to a diet and exercise plan prevents the loss of muscle mass and promotes fat loss. Tripling the RDA of protein, however, failed to provide additional benefits.

"It is our hope that the findings from this well-controlled study will be discussed and cited by the Institute of Medicine for the updated Dietary Reference Intakes on protein," said Stefan M. Pasiakos, Ph.D., a researcher involved in the work from the Military Nutrition Division at the U.S. Army Research Institute of Environmental Medicine in Natick, MA. "We believe that the RDA for protein should be based on a level to optimize health, as well as prevent deficiencies, and our data demonstrate a potential inadequacy of the current RDA for sparing muscle mass during weight loss, which may affect a significant portion of the population."

To make this discovery, Pasiakos and colleagues assigned young men and women controlled diets for 31 days that provided dietary protein at three different levels: 1) the U.S. RDA, 2) twice the U.S. RDA, and 3) three times the U.S. RDA. Volunteers were given adequate total calories to maintain constant body weight for the first 10 days to allow their metabolism to adapt to the dietary protein level, and then for the following three weeks, weight loss was induced by restricting the total calories and increasing daily exercise sufficiently to elicit an average two-pound weight loss per week. All meals were prepared and administered by research staff and exercise was highly controlled. Body composition and measurements of muscle protein metabolism were performed at the end of both the stable weight maintenance and weight loss phases of the study. Results of this study demonstrated that there are limits to the protective effect of extra protein. As such, these data suggest an optimal, and perhaps maximal, level of protein for young, active adults who may undergo short-term periods of intentional or unintentional weight loss.

"This study essentially confirms what body builders have shown us for a long time -- a high protein diet helps prevent muscle loss when trying to lose fat," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal. "Although eating a well balanced diet is still necessary for health and weight maintenance, upping one's protein intake when dieting might be a useful tool in the short term."

S. M. Pasiakos, J. J. Cao, L. M. Margolis, E. R. Sauter, L. D. Whigham, J. P. McClung, J. C. Rood, J. W. Carbone, G. F. Combs, A. J. Young. Effects of high-protein diets on fat-free mass and muscle protein synthesis following weight loss: a randomized controlled trial. The FASEB Journal, 2013; 27 (9): 3837 DOI: 10.1096/fj.13-230227

http://www.medscape.com/viewarticle/810193?src=rs

Higher Depression Rates in Women a Myth?

Women have long been thought to have much higher rates of depression than men, but when alternative and traditional symptoms of depression are considered, these sex disparities disappear, new research shows.

Fran Lowry

"The sex differences framework is rooted in the idea that the construct of depression is the same in men and women and seeks to investigate sex differences in a range of related variables, including symptoms," investigators led by Lisa A. Martin, PhD, from the University of Michigan, Dearborn, write.

"Although this has been a popular approach to date, it is often critiqued for relying on oppositional binaries that understand 'male depression' only as it is contrasted with 'female depression,' which fails to acknowledge the heterogeneity that exists within these groups."

The study is published online August 28 in *JAMA Psychiatry*.

More Anger, Aggression in Men

The aim of the study was to explore whether sex disparities in depression rates disappear when other symptoms besides conventional depression symptoms are considered.

The researchers used data from the National Comorbidity Survey Replication (NCS-R), a nationally representative survey of the incidence and prevalence of mental disorders among English-speaking adults in the United States.

The survey included 3310 women and 2382 men. Their mean age was 45.2 years, 73.4% were non-Hispanic white, and 51.6% had some education beyond high school. The mean annual household income was $59,575. The mean income for men was $63,365, and for women, it was $49,327.

The researchers developed 2 scales. The first, the Male Symptoms Scale (MSS), included alternative male-type symptoms of depression, including irritability, anger attacks/aggression, sleep disturbance, alcohol or drug abuse, risk-taking behavior, hyperactivity, stress, and loss of interest in pleasurable activities.

The second scale, the Gender Inclusive Depression Scale (GIDS), included all of the MSS symptoms, plus 7 traditional symptoms of depression, including sad/depressed mood, loss of vitality, tiredness, ambivalence, anxiety/uneasiness, and complaintiveness or feeling pathetic.
Using the MSS scale that included alternative, male-type symptoms of depression, the researchers found a higher prevalence of depression in men (26.3%) than in women (21.9%) (P = .007).
The researchers also found that men reported significantly higher rates of anger attacks/aggression, substance abuse, and risk-taking behavior compared with women.

More Stress, Irritability in Women

Women, on the other hand, reported significantly greater rates of stress, irritability, sleep problems, and loss of interest in things they usually enjoyed, such as work, hobbies, and personal relationships. No sex difference in the prevalence of depression as assessed by the GIDS that included alternative and traditional depression symptoms was found. According to that scale, 30.6% of men and 33.3% of women met criteria for depression.
In terms of severity of depression, the researchers found that 63.2% of men and 62.0% of women fell into the mild category, meaning that they had 1 to 4 symptoms; 28.3% of men and 28.9% of women fell into the moderate category, with 5 to 9 symptoms; and 8.5% of men and 9.1% of women fell into the severe category, with 10 to 15 symptoms. No significant sex differences were demonstrated at any severity level, they report.
"These results suggest that relying only on men's disclosure of traditional symptoms could lead to an underdiagnosis of depression in men and that clinicians should consider other clues when assessing depression in men," the authors write.
They also point out that "despite the significant findings reported in this study, there are noteworthy limitations." One limitation was that the study did not include symptoms among men such as overworking, overexercising, changing their sexual behavior, or gambling. Also, items that assessed taking chances or reckless behavior were not linked to an emotional condition. Future studies should include items that assess the excluded behaviors, the authors suggest.
They conclude that the results of their study have the potential to bring "significant advances to the field in terms of the perception and measurement of depression. These findings could lead to important changes in the way depression is conceptualized and measured." *The investigators have disclosed no relevant financial relationships.*
JAMA Psychiatry. Published online August 28, 2013. Full text

http://phys.org/news/2013-08-soil-beneath-ocean-harbor-bacteria.html

Soil beneath ocean found to harbor long lived bacteria, fungi and viruses

Researchers with the Integrated Ocean Drilling Program (IODP) have presented findings at this year's Goldschmidt conference.

Phys.org - They report having found bacteria, fungi and viruses living a mile and a half beneath the ocean floor—such specimens, they report, appear to be millions of years old and reproduce only every 10,000 years.
The IODP is an international effort with participants from 22 countries. Its goal is to study the history of the ocean basins, which it does by drilling (from the scientific drill ship JOIDES) deep into the ocean floor and retrieving samples of what is found.
In addition to being old, the specimens found in the soil are also sparse, at least when compared to microorganisms found in soil on the surface of the planet. The team reports that they found just 10,000 bacteria specimens in a teaspoon-sized sample of dirt retrieved from deep below the ocean floor. That contrasts with the billions or even trillions of bacteria normally found when looking at soil found on land. The team also reports finding fungi and viruses, which were less sparse (they found ten times as many viruses as bacteria) but still well below what is found in normal soil.
The researchers report that they've found many interesting characteristics of the microorganisms. Not only are they able to somehow find an energy source so far below ground level, but their metabolism is extremely slow—likely accounting for their longevity. Some of the researchers on the team aren't sure they're even willing to classify the organisms as live creatures—suggesting they exist in a sort of zombie-like state. All of the specimens found, the team reports, exist in sediment that is approximately 100 million years old, which suggests that they too may be nearly the same age.
In addition to wondering how the microbes find an energy source, the researchers also appear perplexed as to how they reproduce with such great distances between others of their kind. The team plans to dig deeper, clearly unsure how far down they will have to go to find the limits to where life exists.
Other researchers at the conference, which attracts approximately 4,000 geochemists each year, wondered whether microorganisms living at such depths might be having an impact on the amount of carbon sequestrated and if as a result they may have a bigger impact on the carbon life cycle than scientists have realized.
More information: Goldschmidt conference: goldschmidt.info/2013/index

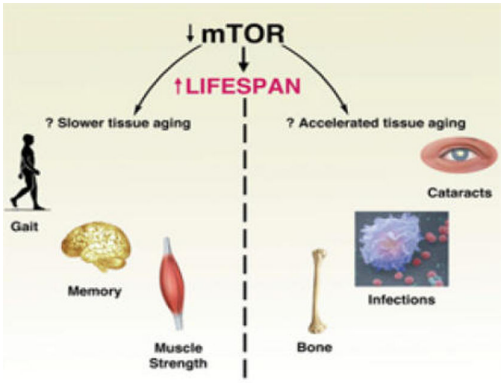
http://www.sciencedaily.com/releases/2013/08/130829124011.htm

Single Gene Change Increases Mouse Lifespan by 20 Percent

Lowering the expression of a single gene, researchers have extended the average lifespan of a group of mice by about 20 percent

By lowering the expression of a single gene, researchers at the National Institutes of Health have extended the average lifespan of a group of mice by about 20 percent -- the equivalent of raising the average human lifespan by 16 years, from 79 to 95. The research team targeted a gene called mTOR, which is involved in metabolism and energy balance, and may be connected with the increased lifespan associated with caloric restriction.

A detailed study of these mice revealed that gene-influenced lifespan extension did not affect every tissue and organ the same way. For example, the mice retained better memory and balance as they aged, but their bones deteriorated more quickly than normal. This study appears in the Aug. 29 edition of Cell Reports.



By lowering the expression of a single gene, researchers at the National Institutes of Health have extended the average lifespan of a group of mice by about 20 percent -- the equivalent of raising the average human lifespan by 16 years, from 79 to 95. **(Credit: Image courtesy of NIH/National Heart, Lung and Blood Institute)**

"While the high extension in lifespan is noteworthy, this study reinforces an important facet of aging; it is not uniform," said lead researcher Toren Finkel, M.D., Ph.D., at NIH's National Heart, Lung, and Blood Institute (NHLBI). "Rather, similar to circadian rhythms, an animal might have several organ-specific aging clocks that generally work together to govern the aging of the whole organism."

Finkel, who heads the NHLBI's Laboratory of Molecular Biology in the Division of Intramural Research, noted that these results may help guide therapies for aging-related diseases that target specific organs, like Alzheimer's. However, further studies in these mice as well as human cells are needed to identify exactly how aging in these different tissues is connected at the molecular level.

The researchers engineered mice that produce about 25 percent of the normal amount of the mTOR protein, or about the minimum needed for survival. The engineered mTOR mice were a bit smaller than average, but they otherwise appeared normal.

The median lifespan for the mTOR mice was 28.0 months for males and 31.5 months for females, compared to 22.9 months and 26.5 months for normal males and females, respectively. The mTOR mice also had a longer maximal lifespan; seven of the eight longest-lived mice in this study were mTOR mice. This lifespan increase is one of the largest observed in mice so far.

While the genetically modified mTOR mice aged better overall, they showed only selective improvement in specific organs. They generally outperformed normal mice of equivalent age in maze and balance tests, indicating better retention of memory and coordination. Older mTOR mice also retained more muscle strength and posture. However, mTOR mice had a greater loss in bone volume as they aged, and they were more susceptible to infections at old age, suggesting a loss of immune function.

In addition to the NHLBI, this study was carried out by intramural researchers at the NIH's National Cancer Institute; National Institute of Diabetes and Digestive and Kidney Diseases; and National Institute on Aging.

J. Julie Wu, Jie Liu, Edmund B. Chen, Jennifer J. Wang, Liu Cao, Nisha Narayan, Marie M. Fergusson, Ilsa I. Rovira, Michele Allen, Danielle A. Springer, Cory U. Lago, Shuling Zhang, Wendy DuBois, Theresa Ward, Rafael deCabo, Oksana Gavrilova, Beverly Mock, Toren Finkel. Increased Mammalian Lifespan and a Segmental and Tissue-Specific Slowing of Aging after Genetic Reduction of mTOR Expression. Cell Reports, 2013; DOI: 10.1016/j.celrep.2013.07.030

http://nyti.ms/17ogNPt

Why your brain may work like a dictionary

DOES your brain work like a dictionary? A mathematical analysis of the connections between definitions of English words has uncovered hidden structures that may resemble the way words and their meanings are represented in our heads.

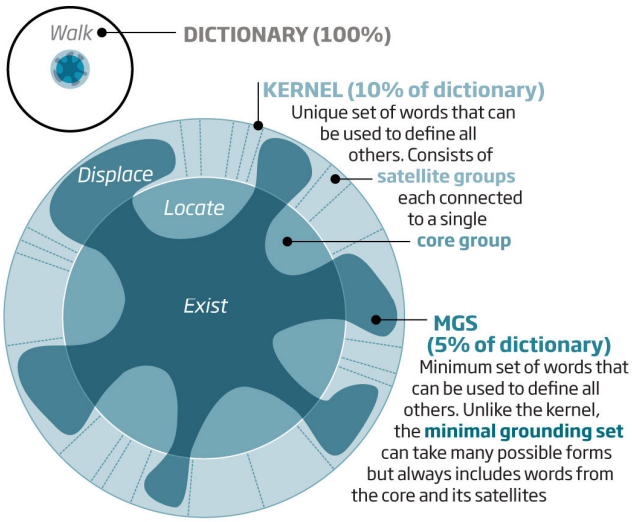
29 August 2013 by Jacob Aron

"We want to know how the mental lexicon is represented in the brain," says Stevan Harnad of the University of Quebec in Montreal, Canada. As every word in a dictionary is defined in terms of others, the knowledge needed to understand the entire lexicon is there, as long as you first know the meanings of an initial set of starter, or "grounding", words. Harnad's team reasoned that finding this minimal set of words and pinning down its structure might shed light on how human brains put language together.

The team converted each of four different English dictionaries into a mathematical structure of linked nodes known as a graph. Each node in this graph represents a word, which is linked to the other words used to define it – so "banana" might be connected to "long", "bendy", "yellow" and "fruit". These words then link to others that define them.

This enabled the team to remove all the words that don't define any others, leaving what they call a kernel. The kernel formed roughly 10 per cent of the full dictionary – though the exact percentages depended on the particular dictionary. In other words, 90 per cent of the dictionary can be defined using just the other 10 per cent.

But even this tiny set is not the smallest number of words you need to produce the whole dictionary, as many of these words can in turn be fully defined by others in the kernel. This is known as the minimal grounding set (MGS), which Harnad explores in his most recent work.



Link English words (*walk*, say) according to their dictionary definitions, and structures emerge that may resemble how our brains represent language

Unlike the kernel, which forms a unique set of words for each dictionary, there are many possible word combinations that can be used to create an MGS – though it is always about half the size of the kernel.

What's more, the kernel has a deeper structure. The team found that half of its words made up a core group in which every word connects to every other via a chain of definitions. The other half was divided into satellite groups that didn't link to each other, but did connect with the core (see diagram).

And this structure seems to relate to meaning: words in the satellites tend to be more abstract than those in the core, and an MGS is always made up of words from both the core and satellites, suggesting both abstract and concrete words are needed to capture the full range of meaning.

So what, if anything, can this tell us about how our brains represent words and concepts? To find out, Harnad's team looked at data on how children acquire words and found a pattern: as you move in from the full dictionary towards the kernel and finally the MGS, words tend to have been acquired at a younger age, be used more frequently, and refer to more concrete concepts (arxiv.org/abs/1308.2428). "The effect gets stronger as you go deeper into the kernel," Harnad says.

That doesn't mean children learn language in this way, at least not exactly. "I don't really believe you just have to ground a certain number of things and from then on close the book on the world and do the rest by words alone," says Harnad. But the correlation does suggest that our brains may structure language somewhat similarly to a dictionary. To learn more, the team has created an online game that asks players to define an initial word, then define the words in those definitions. The team then compares whether their mental dictionaries are similar in structure to actual ones.

Phil Blunsom at the University of Oxford isn't convinced word meanings can be reduced to a chain of definitions. "It's treating words in quite a symbolic fashion that is going to lose a lot of the meaning." But Mark Pagel of the University of Reading, UK, expects the approach to lead to new insights – at least for adult brains. "This will be most useful in giving us a sense of how our minds structure meaning," he says. For example, one question raised by the relatively small size of the MGS is why we burden ourselves with so much extraneous vocabulary.

http://www.sciencedaily.com/releases/2013/08/130829214354.htm

A Wine a Day ... Keeps the Psychiatrist Away?

Light Drinking Linked to Lower Risk of Depression

Drinking wine in moderation may be associated with a lower risk of developing depression, according to research published in Biomed Central's open access journal BMC Medicine. The reported findings by the PREDIMED research Network suggest that the moderate amounts of alcohol consumed may have similar protective effects on depression to those that have been observed for coronary heart disease.

Alcohol consumption around the world is increasing, and previous studies have shown that heavy alcohol intake is related to mental health problems, such as depression. Few studies have looked at the relationship between mental health and moderate alcohol intake. In a new article in BMC Medicine, researchers report on a cohort study that followed over 5,500 light-to-moderate drinkers for up to seven years. The results show an inverse relationship between alcohol intake and incidence of depression.

The study participants are from the PREDIMED study, aged between 55 and 80 years old, had never suffered from depression or had alcohol-related problems when the study started. Their alcohol consumption, mental health and lifestyles were followed for up to seven years through yearly visits, repeated medical exams, interviews with dieticians and questionnaires.
The main alcoholic beverage drunk by the study participants was wine. When analysed, it was shown that those who drank moderate amounts of wine each week were less likely to suffer from depression. The lowest rates of depression were seen in the group of individuals who drank two to seven small glasses of wine per week. These results remained significant even when the group adjusted them for lifestyle and social factors, such as smoking, diet and marital status.
Professor Miguel A. Martínez-González, from the University of Navarra (Spain), senior author of the paper, said, 'Lower amounts of alcohol intake might exert protection in a similar way to what has been observed for coronary heart disease. In fact, it is believed that depression and coronary heart disease share some common disease mechanisms.' Previous studies have indicated that non-alcoholic compounds in the wine, such as resveratrol and other phenolic compounds, may have protective effects on certain areas of the brain.
Geo et al. Alcohol intake, wine consumption and the development of depression: the PREDIMED study. BMC Medicine, 2013 [link]

http://www.eurekalert.org/pub_releases/2013-08/fi-ons082913.php

Oral nutritional supplements demonstrate significant health and cost benefits

Analysis of more than 1 million adult hospital cases revealed 21 percent reduction in length of hospital stay and cost with nutritional intervention

ABBOTT PARK, Ill., - Abbott (NYSE: ABT) A recent health economics and outcomes study, conducted by leading health economists and supported by Abbott, found that oral nutritional supplements provided to patients during hospitalization were associated with significant reductions in length of stay and hospitalization cost. Additionally, the 30-day readmission risk was significantly reduced for patients with at least one known subsequent readmission.
The study is being presented this weekend at the European Society for Clinical Nutrition and Metabolism (ESPEN) annual congress in Leipzig, Germany, where it will be highlighted as one of the conference's three "Best Abstracts." The meeting is a leading conference in clinical nutrition, bringing together participants from more than 80 countries.
The study analyzed more than 1 million adult inpatient cases in the U.S., and found that patients provided oral nutritional supplements during hospitalization benefited from:
21 percent, or 2.3 day, reduction in length of stay
21.6 percent, or $4,734, reduction in patient hospitalization cost
Additionally, there was a 6.7 percent reduction in the probability of a 30-day readmission in patients who had at least one known subsequent readmission and were provided oral nutritional supplements during the previous hospitalization.
The study, which also was recently published in the American Journal of Managed Care, provides insights into the economic benefits of prescribing oral nutritional supplements to adult patients in the hospital setting.
"Patients identified as having nutritional deficiencies often face a longer and more difficult recovery process, resulting in higher health care costs and an increase in complication rates," said Marinos Elia, MD, BSc Hon, FRCP, Professor of Clinical Nutrition and Metabolism at University of Southampton. "Research demonstrates that oral nutritional supplementation can lead to highly positive economic benefits and improved patient outcomes."
In the study, investigators were able to determine differences in length of stay and costs by comparing hospital stays where oral nutritional supplements were prescribed to patients with similar conditions where oral nutritional supplements weren't prescribed.
"Because oral nutritional supplements are formulated to provide advanced nutrition and calories for patients and are relatively inexpensive to provide, the sizeable savings they generate make supplementation a cost-effective therapy," said study co-author, Tomas Philipson Ph.D., Daniel Levin Chair of Public Policy at the University of Chicago.
"In today's outcome conscious hospital environment, Abbott is committed to delivering products that improve the quality of care for patients and also help reduce health care costs," said Robert H. Miller, Ph.D., divisional vice president, Global R&D and Scientific Affairs for Abbott Nutrition. "In addition to the numerous retrospective studies focused on health economics and outcomes research in our pipeline, nearly all of our clinical research studies now include an economic analysis to help demonstrate a nutritional therapy's total value proposition."

About the Study

The "Impact of Oral Nutritional Supplementation on Hospital Outcomes" study is a retrospective data analysis on the effect of oral nutritional supplements on hospital economic outcomes. The study compared hospital stays where oral nutritional supplements were provided with similar hospital stays that did not provide oral nutritional supplements. The difference between length of hospital stay and cost of treatment (including supplies, labor, depreciation of equipment, etc.) were measured. The probability of 30-day hospital readmission also was calculated.

The retrospective analysis utilized information from more than one million adult inpatient cases found in the Premier Research Database from 2000 – 2010, maintained by the Premier healthcare alliance – representing a total of 44 million hospital episodes from across the United States or approximately 20 percent of all inpatient admissions in the United States. The full sample consisted of adults 18 years and older and focused on oral feeding interventions only. The matched sample ultimately included: 1,160,088 total episodes (oral nutritional supplements episodes N= 580,044 and non-oral nutritional supplements episodes N=580,044), where propensity score matching and instrumental variables were used to address potential bias due to non-random selection.

http://www.medscape.com/viewarticle/810066?src=rss

'Do As I Do: Take Aspirin Daily'

Looking at aspirin as a preventive agent, in terms of primary and secondary prevention

David J. Kerr, CBE, MD, DSc, FRCP, FMedSci

Hello. I am David Kerr, Professor of Cancer Medicine at Oxford, United Kingdom, and Past President of the European Society of Medical Oncology. Great to talk to you all again.

Do you remember from childhood when Mother, or usually Father, said, "Don't do as I do; do as I say." How many of us have been imprinted with that from early childhood? I am going to turn this on its head.

I just returned from a fantastic roundtable discussion on aspirin. This was a selective multidisciplinary meeting with cancer biologists, clinicians, and epidemiologists. Across the spectrum of disease we had neurologists, cardiac specialists, and of course oncologists. We were looking at aspirin as a preventive agent, in terms of primary and secondary prevention. In particular, the data concerning colorectal cancer have become very compelling with regard to aspirin's capacity to prevent primary disease, and to reduce the risk for the disease happening in the first place.[1-3] For patients who have had the cancer resected, it appears from observational data and very large cohorts of study, such as those reported by Algra and Rothwell recently in the *Lancet*,[4] that aspirin can have a remarkable effect in reducing the incidence of subsequent metastasis.

Of interest, though, the improvement and divergence in survival rates and recurrence rates only occurs after 5 years.[5] For the first 5 years of observations, the survival rates and recurrence rates overlap following post-primary dissection of colorectal cancer. Then they start to diverge. That is when something remarkable happens.

There were 2 particular points of discussion at the meeting. One was, what do we do with these data? How do we promulgate them? We may be able to accomplish some important work with the Global Alliance for Chronic Diseases, with WHO (World Health Organization) promulgating the wider, safer use of low-dose aspirin.

Second, how do we respond to that as individuals? This is where I turn my father's missive on its head. "Don't do as I say. Do as I do." I came back from the meeting and I have now started to take low-dose aspirin, 100 mg daily, because the data were so compelling that as an individual I feel moved to do this. Of course I eat my greens. Of course I will try to do my 3 ×30 minutes of decent exercise a week. Of course I have a set of moderately complex reasons for wanting to live a bit longer. Aspirin will be part of my compendium for doing that.

If you want a better, healthier, longer life with a reduced risk for colorectal cancer, don't do as I say; do as I do. Perhaps I can convince you that it is worthwhile to take low-dose aspirin.

As always, thanks for listening. I would be very happy to answer any comments that you make here to me or to post. For now, Medscapers, ahoy! Thank you.

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High dose statins prevent dementia

Almost all the statins (except lovastatin) decreased the risk for new onset dementia when taken at higher daily doses

Dr Lin said: "Statins are widely used in the older population to reduce the risk of cardiovascular disease. But recent reports of statin-associated cognitive impairment have led the US Food and Drug Administration (FDA) to list statin-induced cognitive changes, especially for the older population, in its safety communications."

He added: "Previous studies had considered statin therapy to exert a beneficial effect on dementia. But few large-scale studies have focused on the impact of statins on new-onset, non-vascular dementia in the geriatric population."

Accordingly, the current study examined whether statin use was associated with new diagnoses of dementia. The researchers used a random sample of 1 million patients covered by Taiwan's National Health Insurance. From this they identified 57,669 patients aged >65 years who had no history of dementia in 1997 and 1998. The analysis included pre-senile and senile dementia but excluded vascular dementia.

There were 5,516 new diagnoses of dementia during approximately 4.5 years of follow-up. The remaining 52,153 patients aged >65 formed the control group. Subjects were divided into tertiles according to their mean daily equivalent1 dosage and total (across the entire follow up period) equivalent dosage.

The adjusted hazard ratios (HRs) for dementia were significantly inversely associated with increased daily or total equivalent statin dosage. The HRs for the three tertiles of mean equivalent daily dosage (lowest to highest) were 0.622, 0.697 and 0.419 vs control ($p<0.001$ for trend). The HRs for the three tertiles of total equivalent dosage (lowest to highest) were 0.773, 0.632 and 0.332 vs control ($p<0.001$ for trend). The protective effect of statins remained in different age, gender and cardiovascular risk subgroups.

Dr Lin said: "The adjusted risks for dementia were significantly inversely associated with increased total or daily equivalent statin dosage. Patients who received the highest total equivalent doses of statins had a 3-fold decrease in the risk of developing dementia. Similar results were found with the daily equivalent statin dosage."

He added: "It was the potency of the statins rather than their solubility (lipophilic or hydrophilic) which was a major determinant in reducing dementia. High potency statins such as atorvastatin and rosuvastatin showed a significant inverse association with developing dementia in a dose-response manner. Higher doses of high potency statins gave the strongest protective effects against dementia."

Dr Lin continued: "The results were consistent when analysing daily doses of different kinds of statins. Almost all the statins (except lovastatin) decreased the risk for new onset dementia when taken at higher daily doses. A high mean daily dosage of lovastatin was positively associated with the development of dementia, possibly because lovastatin is a lipophilic statin while the anti-inflammatory cholesterol lowering effect of lovastatin is not comparable to that of atorvastatin and simvastatin."

Dr Lin concluded: "To the best of our knowledge, this was the first large-scale, nation-wide study which examined the effect of different statins on new onset dementia (except vascular dementia) in an elderly population. We found that high doses of statins, particularly high potency statins, prevent dementia."

[1]Equivalent dosages are used when comparing the effects of different drugs. Each statin was assigned an appropriate equivalent dose according to the following formula: lovastatin 40mg = pravastatin 40mg = simvastatin 20mg = atorvastatin 10mg = fluvastatin 80mg = rosuvastatin 5mg.

http://www.eurekalert.org/pub_releases/2013-09/uou-mia082613.php

Move it and lose it: Every 'brisk' minute counts

University of Utah study shows higher-intensity activity impacts weight, even in short bouts

To win the war against weight gain, it turns out that every skirmish matters – as long as the physical activity puts your heart and lungs to work.

In a new study published today in the American Journal of Health Promotion, University of Utah researchers found that even brief episodes of physical activity that exceed a certain level of intensity can have as positive an effect on weight as does the current recommendation of 10 or more minutes at a time.

"What we learned is that for preventing weight gain, the intensity of the activity matters more than duration," says Jessie X. Fan, professor of family and consumer studies at the U. "This new understanding is important because fewer than 5 percent of American adults today achieve the recommended level of physical activity in a week according to the current physical activity guidelines. Knowing that even short bouts of 'brisk' activity can add up to a positive effect is an encouraging message for promoting better health."

The current physical activity guideline for Americans is to get at least 150 minutes of moderate to vigorous physical activity, MVPA, a week, which can be accumulated in eight to 10 minute periods. MVPA is defined as greater than 2,020 counts per minute measured with a tool called an accelerometer.
For an average person in an everyday setting without a fancy gadget to gauge the exertion, that would translate roughly to a walking speed of about three mph. But taking the stairs, parking at the far end of the lot, and walking to the store or between errands are choices that can add up and can make a positive health difference, the researchers note.
The study shows that higher-intensity activity was associated with a lower risk of obesity, whether in "bouts" of fewer or greater than 10 minutes.
This may be especially important news for women, who were on average less physically active than men. However, neither men nor women came close to the weekly 150-minute recommendation with bouts of eight to 10 minutes. However, when adding shorter bouts of higher-intensity activity, men exceeded the recommendation on average, accumulating 246 minutes per week, and women came close, at 144 minutes per week on average. The message is: a little more effort can have an important health payback.

How the Study was Conducted

Subjects for the study were drawn from the National Health and Nutrition Examination Survey, NHANES, a national program that has been collecting health and nutrition data from a representative sample of adults and children in the United States since 1999.
From 2003 to 2006, participants in the survey wore accelerometers for seven days, which captured data on their physical activity. This information was in addition to the broad range of demographic and health-related information collected in the NHANES program from interviews and physical examinations.
For this study, participants from 18 to 64 years of age were drawn from the database. There were some exclusions, including pregnancy or impairments that compromised participants' ability to walk, such as being wheelchair bound. The final sample size for the current study was 2,202 women and 2,309 men.
Researchers compared measurements of physical activity based on length of time and intensity. Four categories were created: higher-intensity bouts (greater than 10 minutes exertion at greater than 2,020 counts per minutes, or CPM), higher-intensity short bouts (less than 10 minutes at greater than 2,020 CPM), lower-intensity long bouts (greater than 10 minutes and less than 2,019 CPM), and lower-intensity short bouts (less than 10 minutes and less than 2,019 CPM).
The study used body mass index, BMI, to measure weight status. BMI is a standard formula calculated using an individual's weight adjusted for height, and is used as an indicator of healthy weight. A BMI between 18.5 and 24.9 is considered normal weight, whereas a BMI between 25 and 29.9 is overweight; and over 30 is obese.
Results show that for women, each daily minute spent in higher-intensity short bouts was related to a decrease of .07 BMI. Looking at it another way, each such minute offset the calorie equivalent of .41 pounds. This means that when comparing two women each 5-feet-5-inches tall, the woman who regularly adds a minute of brisk activity to her day will weigh nearly a half-pound less. Results were similar for men. Importantly for both, each daily minute of higher-intensity activity lowered the odds of obesity -- 5 percent for women, and 2 percent for men.

http://www.eurekalert.org/pub_releases/2013-09/stap-mto082813.php

Mycobacterium tuberculosis: Our African follower for over 70,000 years!

Tuberculosis (TB) remains one of deadliest infectious diseases of humans, killing 50% of individuals when left untreated.

Even today, TB causes 1-2 million deaths every year mainly in developing countries. Multidrug-resistance is a growing threat in the fight against the disease.
An international group of researchers led by Sebastien Gagneux from the Swiss Tropical and Public Health Institute (Swiss TPH) has now identified the origin in time and space of the disease. Using whole-genome sequencing of 259 Mycobacterium tuberculosis strains collected from different parts of the world, they determined the genetic pedigree of the deadly bugs. This genome comparison to be published September 1st in the journal Nature Genetics indicates that TB mycobacteria originated at least 70,000 years ago in Africa.
Stunningly close relationship between humans and M. tuberculosis
The researchers compared the genetic evolutionary trees of mycobacteria and humans side-by-side. And to the researcher's surprise, the phylogenetic trees of humans and the TB bacteria showed a very close match. "The evolutionary path of humans and the TB bacteria shows striking similarities," says Sebastien Gagneux.

This strongly points to a close relationship between the two, lasting tens of thousands of years. Humans and TB bacteria not only have emerged in the same region of the world, but have also migrated out of Africa together and expanded all over the globe.
The migratory behaviour of modern humans accompanied with changes in lifestyle has created favourable conditions for an increasingly deadly disease to evolve. "We see that the diversity of tuberculosis bacteria has increased markedly when human populations expanded," says evolutionary biologist Sebastien Gagneux.
Human expansion in the so called Neolithic Demographic Transition (NDT) period combined with new human lifestyles living in larger groups and in village-like structures may have created conditions for the efficient human-to-human transmission of the disease, Gagneux suggests. This may also have increased the virulence of the bacteria over time.
The results indicate further that TB is unlikely to have jumped from domesticated animals to humans, as seen for other infectious diseases. "Simply, because Mycobacteria tuberculosis emerged long before humans started to domesticate animals," says Swiss TPH's Sebastien Gagneux.

New strategies to defeat tuberculosis

Tuberculosis remains a global threat. New drugs and vaccines are urgently needed to fight this poverty-related disease. Multidrug-resistance against first-line treatments is a growing threat in many countries. Therefore, the exploration of the evolutionary patterns of TB bacteria may help predicting future patterns of the disease. This may contribute to future drug discovery and to the design of improved strategies for disease control.

http://www.eurekalert.org/pub_releases/2013-09/esoc-qsd083013.php

Quitting smoking drops heart attack risk to levels of never smokers

Quitting smoking reduces the risk of heart attack and death to the levels of non-smokers

Dr Min said: "Smoking is an established risk factor for cardiovascular disease. Studies have identified that quitting smoking can reduce heart attacks and death but have not examined the relationship of this salutary effect on the presence and severity of coronary artery disease (CAD). Our study aimed to find out what impact stopping smoking had on the risk of cardiovascular events, death and the severity of CAD."
The prospective CONFIRM (Coronary CT Evaluation for Clinical Outcomes: An International Multicenter Study) registry of 13,372 patients from 9 countries in Europe, North America and East Asia examined the risk of major adverse cardiac events in 2,853 active smokers, 3,175 past smokers and 7,344 never smokers.
Both active smokers and past smokers had a higher prevalence of severely blocked coronary arteries compared to non-smokers. This was determined using coronary computed tomographic angiography (CCTA), a non-invasive imaging technique that enables direct visualisation of the coronary arteries. Active and past smokers had a 1.5-fold higher probability of severe stenoses in 1 and 2 major heart arteries, and a 2-fold increased probability of severe stenoses in all 3 major heart arteries.
Dr Min, who is director of the Institute of Cardiovascular Imaging at the New York-Presbyterian Hospital and the Weill Cornell Medical College, said: "Our results show that quitting smoking does not reduce the amount of disease smoking causes in the coronary arteries, but it does reduce the risk of heart attack and death to the levels of non-smokers."
After 2.0 years of follow-up, 2.1% of the study patients experienced heart attacks or death. Rates of heart attack or death were almost 2-fold higher in active smokers compared to never smokers. Past smokers had the same rates or heart attack or death as never smokers, despite having a higher prevalence, extent and severity of CAD (see figure). The findings in both active and past smokers persisted even when they were matched with non smokers who were similar in age, gender and CAD risk factors.
Dr Min said: "Our study was the first to demonstrate that the presence and severity of coronary blockages do not go away with quitting smoking, but that the risk of heart attack and death does. Future studies are being pursued to determine how this protective effect may occur."
He continued: "Numerous questions remain and require further study. For example, will the severe blockages observed in patients who have quit smoking provoke adverse events after 2 years (the duration of the present study). Further, does the duration of smoking or the number of cigarettes smoked per day affect the severity of CAD or the prognosis related to quitting smoking. Our team and several others are pursuing such investigations."
Dr Min concluded: "It's never too late to quit smoking. This study clearly shows that stopping smoking lowers the risk of heart attacks and death to the level of never smokers."

http://www.sciencedaily.com/releases/2013/09/130901153919.htm

Administering Natural Substance Spermidin Stopped Dementia in Fruit Flies

Age-induced memory impairment can be suppressed by administration of the natural substance spermidin.

This was found in a recent study conducted by Prof. Dr. Stephan Sigrist from Freie Universität Berlin and the Neurocure Cluster of Excellence and Prof. Dr. Frank Madeo from Karl-Franzens-Universität Graz. Both biologists, they were able to show that the endogenous substance spermidine triggers a cellular cleansing process, which is followed by an improvement in the memory performance of older fruit flies.

At the molecular level, memory processes in animal organisms such as fruit flies and mice are similar to those in humans. The work by Sigrist and Madeo has potential for developing substances for treating age-related memory impairment. The study was first published in the online version of Nature Neuroscience.

Aggregated proteins are potential candidates for causing age-related dementia. With increasing age, the proteins accumulate in the brains of fruit flies, mice, and humans. In 2009 Madeo's group in Graz already found that the spermidin molecule has an anti-aging effect by setting off autophagy, a cleaning process at the cellular level. Protein aggregates and other cellular waste are delivered to lysosomes, the digestive apparatus in cells, and degraded.

Feeding the fruit flies spermidin significantly reduced the amount of protein aggregates in their brains, and their memories improved to juvenile levels. This can be measured because flies can learn under classical Pavovian conditioning and adjust their behavior accordingly.

In humans, memory capacity decreases beginning around the age of 50. This loss accelerates with increasing age. Due to increasing life expectancy, age-related memory impairment is expected to increase drastically. The spermidine concentration increases with age in flies as in humans. If it were possible to delay the onset of age-related dementia by giving individuals spermidin as a food supplement, it would be a great breakthrough for individuals and for society. Patient studies are the next step for Sigrist and Madeo.

NeuroCure is a Cluster of Excellence in the neurosciences at Charité – Universitätsmedizin Berlin working in collaboration with the departments of biology and biochemistry at Freie Universität Berlin and Humboldt-Universität zu Berlin as well as with three independent research institutions.

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http://www.bbc.co.uk/news/health-23901636

Shingles jab campaign for people in their 70s

People in their 70s across the UK will be offered a vaccine against shingles from this week.

The government-led programme will initially offer the vaccine to those aged 70, 78 and 79.

Shingles, or herpes zoster, is an infection of a nerve and the area of skin around it, and can cause a painful rash.

Around 800,000 people will be eligible for the vaccine in the first year of the programme. In England, Scotland and Northern Ireland, those aged 70 and 79 will initially be invited to take up the vaccination. Wales will target 78 and 79-year-olds. Over the next few years, the programme will expand to include more of the 70-to-79 age group across the UK until it is fully covered. After that, the jab should only need to be offered to people as they reach their 70th birthdays.

The Department of Health has said it will cost about £25m a year in England, but will save the NHS about £20m a year in fewer hospital stays, GP appointments and prescriptions.

Flare-up

Shingles is caused by the same virus that causes chickenpox. Around 14,000 people develop it each year.

After someone has had chickenpox most of the virus is destroyed but some survives and lies inactive in the body in the nervous system. It can then be reactivated later in life when the immune system is weakened by increasing age, stress or treatments that affect immunity. In severe cases it can cause complications such as hearing loss or brain swelling. Shingles is most common in the over-70s. Someone who has not had chickenpox can catch it from someone with shingles - but it is not possible to catch shingles itself from someone with the condition.

Dr Paul Cosford, director for health protection and medical director at Public Health England, said having the vaccine would reduce the chances of having shingles by a third.

Health minister Lord Howe said: "Shingles can be a nasty disease for older people and can lead to long-term health problems for around 14,000 people each year. "This new vaccine can prevent some of the most serious cases, giving people the chance to live without the discomfort and pain that shingles causes."

http://phys.org/news/2013-09-japan-nuclear-reactor-checkups.html

Japan heads back to nuclear zero for reactor checkups

Workers will switch off one of Japan's two working reactors Monday, with the other set for shutdown later this month and no restarts in sight amid continued public hostility to nuclear power.

Kansai Electric Power will start reducing generating power at its Unit No. 3 at the Oi plant, Fukui prefecture, western Japan, shortly before 5:00 pm (0800 GMT), a company spokesman said.

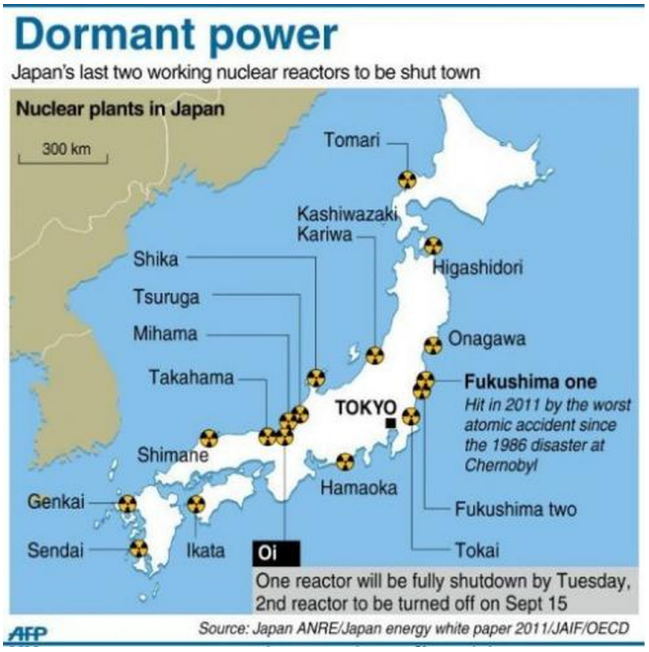
The reactor will be fully shut down by early Tuesday in readiness for inspections legally mandated within 13 months of the start of commercial operations, he said.

The reactor is one of the only two still generating power in Japan. The other one, Unit No. 4 at Oi, is to be switched off on September 15.

It is not known when they will resume operations because they will be assessed under a set of guidelines recently drawn up by the nuclear watchdog, according to Kansai Electric.

The two reactors were restarted—despite public opposition—in July last year after passing safety tests, ending a brief period in which no atomic power was generated in Japan. They were the only units to be brought back online after undergoing such tests in the aftermath of the disaster in March 2011 at Fukushima.

Dormant power



Graphic locating nuclear plants in Japan. The last two working reactors will be shutdown this month for testing.

There, a 9.0 magnitude earthquake and the tsunami it caused crippled reactor cooling systems, sparking meltdowns and spewing radioactive materials in the world's worst atomic disaster since Chernobyl in 1986.

Japan has turned to pricey fossil-fuel alternatives to fill the gap left by the shutdown of atomic plants, which had supplied about one-third of resource-poor Japan's electricity before the disaster.

Operator Tokyo Electric Power (TEPCO) has been struggling to contain the crisis at Fukushima, which has been hit by a series of mishaps that have cast doubt on the utility's ability to fix the crisis.

Recent months have brought a steady stream of news about leaks of water contaminated with radiation as well as a blackout caused by a gnawing rat that left cooling pools without power for more than a day.

The company said Sunday it had found highly radioactive water dripping from a pipe connecting two coolant tanks at one of four radiation hotspots.