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Eleven new studies suggest 'power poses' don't work

Wave of scientific studies suggest that power poses do not improve your life

EAST LANSING, Mich. - The claim that holding a "power pose" can improve your life became wildly popular several years ago, fueling the second most-watched TED talk ever but also casting doubts about the science behind the assertion.

Now comes the most definitive evidence to date - a wave of scientific studies spearheaded by a Michigan State University researcher - suggesting that power poses do not improve your life.

"This new evidence joins an existing body of research questioning the claim by power pose advocates that making your body more physically expansive - such as standing with your legs spread and your hands on your hips - can actually make you more likely to succeed in life," said Joseph Cesario, MSU associate professor of psychology.

Cesario co-edits a scientific journal, Comprehensive Results in Social Psychology, that recently published seven studies, all of which attempted - unsuccessfully - to replicate and extend the effects of power pose research. In other words, none of the studies showed positive effects of power poses on any behavioral measure, such as how well you perform in a job interview. The studies were even reviewed by Dana Carney, a University of California Berkeley professor who was one of the authors of the original power pose research.

In addition, Cesario and MSU graduate student David Johnson recently published four new studies testing whether holding power poses impacted important behaviors such as how well you do in a business negotiation. The work, published in the journal Social Psychological and Personality Science, again found no evidence that making yourself expansive mattered at all.

"There is currently little reason to continue to strongly believe," Cesario said, "that holding these expansive poses will meaningfully affect people's lives, especially the lives of the low-status or powerless people."

Led by Carney and Amy Cuddy from Harvard University, the original power pose study, in 2010, suggested that holding such poses can make you more likely to succeed in life, especially if you are "chronically powerless because of lack of resources, low hierarchical rank or membership in a low-power social group."

Cuddy's June 2012 TED talk, now with more than 42 million views, argued that "power posing" - or standing in a posture of confidence, even when we don't feel confident - will boost feelings of confidence and will have an impact on one's chances for success, such as in a job interview.

When you're alone before the interview, Cuddy recommends, hold a power pose for two minutes - whether that's standing with hands on hips, leaning over a table with your fingertips on the surface, or perhaps seated with your feet on the table and your arms folded behind your head.

"Share this science with people, because the people who can use it the most are the ones with no resources and no technology and no status and no power," Cuddy concludes the TED talk. "Give it to them because they can do it in private. They need their bodies, privacy and two minutes, and it can significantly change the outcomes of their life."

But the new research stands in stark contrast to Cuddy's claim. Cesario's research and the findings from the journal he co-edits do find that holding power poses makes people feel more powerful, but that's where the effect ends.

"Feeling powerful may feel good, but on its own does not translate into powerful or effective behaviors," Cesario said. "These new studies, with more total participants than nearly every other study on

the topic, show - unequivocally - that power poses have no effects on any behavioral or cognitive measure."

In several of the experiments by MSU's Cesario and Johnson, for example, participants watched Cuddy's TED talk, held a power pose and then completed a negotiation task with another participant. The participants who held the power poses did no better than their partners. In addition, the seven studies that appear in a special issue of Comprehensive Results in Social Psychology also fail to replicate the power pose effects.

"Based on the papers in the special issue, and prior replication attempts, one could conclude that the power pose effect on behavioral outcomes does not replicate," the researchers, including Cesario and Dana Carney, write in the journal.

Carney puts it even more bluntly in a previously posted statement on her website: "As evidence has come in over these past 2-plus years, my views have updated to reflect the evidence. As such, I do not believe that power pose effects are real."

http://bit.ly/2h2watn

Incidence of acute myocardial infarction may increase the day after Asian dust exposure

Epidemiological study by Japanese researchers shows that Asian desert sand is associated with the onset of myocardial infarction

A recent environmental epidemiological study by Japanese researchers has shown that Asian sand particles blown to Japan from desert areas of the Asian continent are associated with the onset of myocardial infarction. In particular, the research reveals an increased likelihood that patients with chronic kidney disease are susceptible to myocardial infarction when influenced by Asian dust. The accumulation of knowledge on health aspects susceptible to the influence of Asian dust is expected to lead to the prevention of adverse health effects.

Background

The yellow sand in the desert area of the Asian continent (ex: Gobi Desert, Takla Makan Desert) is sometimes picked up and transported long distances with the seasonal wind. Since air pollutants and microorganisms adhere to the yellow sand during transportation, adverse health effects from dust exposure is a great concern. In Japan, allergies, respiratory diseases, and cardiovascular diseases are reported to increase as the dust passes over the nation. Cardiovascular diseases in particular are associated with an increase in Asian dust in Japan.

For this reason, a Japanese research group focused on acute myocardial infarction among cardiovascular diseases. In the southwestern region of Japan, on the island of Kyushu, Asian dust is observed relatively often. At Kumamoto University Hospital, in the middle of Kyushu, cases of acute myocardial infarction are comprehensively registered in a medical database. Since background factors (i.e., age, sex, hypertension, diabetes, dyslipidemia, smoking, chronic kidney disease, etc.) of patients with acute myocardial infarction are also registered in the database, it is possible to determine what factors are most susceptible to Asian dust. The researchers used this database to analyze the relationship between the dust and acute myocardial infarction.

Research Data

The Japan Meteorological Agency announces incidents of Asian dust when an observer visually confirms that the air is turbid with Asian dust particles and the distance visible with the naked eye becomes less than 10 km. During the research period from April 2010 to March 2015, there were 41 days in the Kumamoto district meteorological observatory that observed Asian dust.

During the study period, there were 4,509 acute myocardial infarction patients registered in the database with clear onset dates. After excluding those who lived outside Kumamoto Prefecture, those who developed acute myocardial infarction during hospitalization or on holidays, or those who lacked patient background information, 3,713

people were analyzed for an association between exposure to Asian dust and the onset of acute myocardial infarction. The research design ignored risk factors for acute myocardial infarction, including, but not limited to, age, gender, hypertension, diabetes, dyslipidemia, smoking, and chronic kidney disease. The statistical model was also adjusted for weather factors (temperature and humidity) which varied depending on the day.

Results: Acute myocardial infarction increases the day after incidents of Asian dust.

The odds ratio (approximate value of relative risk) of developing acute myocardial infarction the day after an Asian dust incident was 1.46, with a 95% confidence interval of 1.09 - 1.95. Therefore, the association between the increased numbers of acute myocardial infarction patients after an observation of Asian dust is clear. This association is not changed even when considering the influence of air pollutants such as microparticulate materials (PM 2.5), photochemical oxidants, nitrogen dioxide, or sulfur dioxide.

Next, researchers examined the relationship between Asian dust and myocardial infarction after grouping by patient background factors (age, sex, hypertension, diabetes, dyslipidemia, smoking, and chronic kidney disease). It was found that the association between Asian dust and acute myocardial infarction was most prevalent in nonsmoking* male patients older than 75 years old with hypertension, diabetes, and chronic kidney disease. Among that cohort, it was clear that patients with chronic kidney disease were significantly more likely to suffer from acute myocardial infarction after being influenced by dust than those without chronic kidney disease.

To investigate whether there were more background factors susceptible to Asian dust, the researchers assigned 1 point for each of several categories: over 75 years of age, sex (1 point for being male), high blood pressure, diabetes, non-smoker, and chronic kidney disease. Patients with higher group scores (5 to 6 points) were shown to be more susceptible to Asian dust.

Discussion and Future Prospects

It is not yet known how much (or even how) yellow dust exposure is involved in the process of developing myocardial infarction. Even though adjustments were made to the concentration of air pollutants such as photochemical oxidants, nitrogen dioxide, and sulfur dioxide to eliminate their effects on the statistical model, the relationship between Asian dust and acute myocardial infarction remained. Asian dust consists of both relatively large particles and PM 2.5, which has been associated with acute myocardial infarction. Since the concentration of PM 2.5 was already high at the time of arrival of the Asian dust, researchers also analyzed its effects by excluding the influence of PM 2.5. The association was seen there as well meaning that particles with larger diameter than PM 2.5 may also be affected. Additionally, in patients with chronic kidney disease, adverse reactions such as oxidative stress or inflammation are progressing in the body so exposure to the Asian dust may bolster these reactions thereby causing acute myocardial infarction.

"Our research suggests that exposure to Asian dust may trigger the onset of acute myocardial infarction. As far as we know, this is the first report showing that patients with chronic kidney disease may more easily develop acute myocardial infarction when influenced by Asian dust," said Associate Professor Sunao Kojima of Kumamoto University, leader of the study. "This time, we assessed patients only on the days when the Japan Meteorological Agency reported Asian dust in our region. In the future, it will be necessary to estimate the concentration of Asian dust in the air and examine whether acute myocardial infarctions increase as the concentration increases. We also intend to accumulate knowledge on background factors that are susceptible to the influence of Asian dust at various concentrations to try and prevent the adverse health effects of Asian dust."

This research result was presented at the Hot Line of the European Cardiology Society held in Barcelona, Spain, at 11:30 AM (local time) on 29 Aug. 2017, and posted online in the European Heart Journal 2017 on 29 Aug. 2017.

(The views expressed in this research are those of researchers, not of the Japan Ministry of the Environment.)

**This study investigated background factors that make it easy for acute myocardial infarction to occur under the influence of Asian dust and showed that nonsmokers may be more susceptible. However, smoking is not recommended to prevent the occurrence of acute myocardial infarction caused by dust since it is clear that smoking itself is a risk factor for acute myocardial infarction from many other epidemiological studies. The researchers believe that people should first avoid smoking to avoid the risk of acute myocardial infarction rather than being concerned with exposure to Asian dust.*

Resource

Kojima, S.; Michikawa, T.; Ueda, K.; Sakamoto, T.; Matsui, K.; Kojima, T.; Tsujita, K.; Ogawa, H.; Nitta, H. & Takami, A., Asian dust exposure triggers acute myocardial infarction, European Heart Journal, Oxford University Press (OUP), 2017.

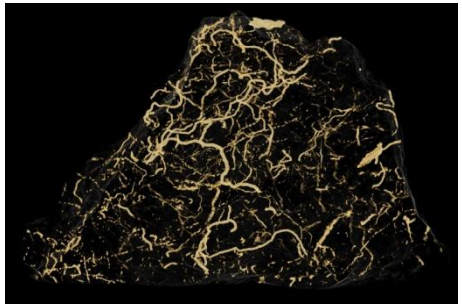
DOI: 10.1093/eurheartj/ehx509

http://bit.ly/2x19Nhb

Half-a-billion-year-old fossils shed light animal evolution on earth

Scientists have discovered traces of life more than half-a-billion years old that could change the way we think about how all animals evolved on earth.

The international team, including palaeontologist from The University of Manchester, found a new set of trace fossils left by some of the first ever organisms capable of active movement. Trace fossils are the tracks and burrows left by living organisms, not physical remains such as bones or body parts.



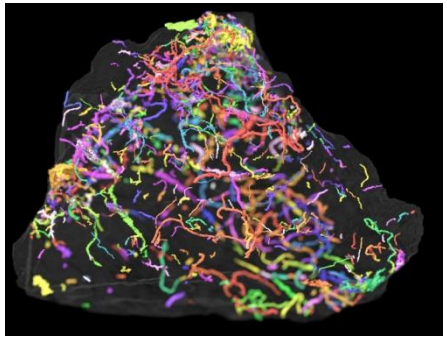
A 3-D X-ray image of trace fossil in sediment. **University of Bristol**

The fossils were discovered in sediment in the Corumbá region of western Brazil, near the border with Bolivia. The burrows measure from under 50 to 600 micrometres or microns (μm) in diameter, meaning the creatures that made them were similar in size to a human hair which can range from 40 to 300 microns in width. One micrometre is just one thousandth of a millimetre.

Dr Russell Garwood, from Manchester's School of Earth and Environmental Sciences, said: 'This is an especially exciting find due to the age of the rocks - these fossils are found in rock layers which actually pre-date the oldest fossils of complex animals - at least that is what all current fossil records would suggest.'

The fossils found date back to a geological and evolutionary period known as the Ediacaran-Cambrian transition. This was when the Ediacaran Period, which spanned 94 million years from the end of the Cryogenian Period, 635 million years ago, moved into the Cambrian Period around 541 million years ago. To put that into context, dinosaurs lived between 230 and 65 million years ago in the Mesozoic Era.

The Ediacaran-Cambrian transition is seen as extremely important period in evolutionary science and theory. Dr Garwood explains: 'The evolutionary events during the Ediacaran-Cambrian transition are unparalleled in Earth history. That's because current fossil records suggests that many animal groups alive today appeared in a really short time interval.'



X-ray microtomography image of trace fossil in sediment. **Luke Parry - University of Bristol**

However, the team suggest these burrows were created by 'nematoid-like organisms', similar to a modern-day roundworm, that used an undulating locomotion to move through the sediment, leaving these trace fossils behind. This is important because current DNA studies, known as 'molecular clocks', which are used to estimate how long ago a group animals originated, suggests the first animals appeared before these burrows. But this research, which has been published in Nature Ecology and Evolution, shows these trace fossils pre-date similar animals currently found in the fossil record.

Luke Parry, lead author from the University of Bristol, added: 'Our new fossils show that complex animals with muscle control were around approximately 550 million years ago, and they may have been overlooked previously because they are so tiny'.

'The fossils that we describe were made by quite complex animals that we call bilaterians. These are all animals that are more closely related to humans, rather than to simple creatures like jellyfish. Most fossils of bilaterian animals are younger, first appearing in the Cambrian period.'

To find such tiny fossils the team used X-ray microtomography, a special technique that uses X-rays to create a virtual, 3D model of something without destroying the original object.

Luke added: 'Our discovery highlights an unexplored window for tracking animal evolution in deep time.'

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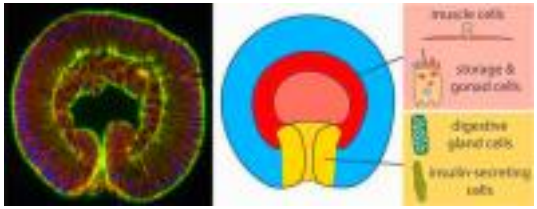
The evolutionary origin of the gut

How did the gut, the skin and musculature evolve? This question concerns scientists for more than a century.

Through the investigation of the embryonic development of sea anemones, a very old animal lineage, researchers from the University of Vienna have now come to conclusions which challenge the 150 year-old hypothesis of the homology (common evolutionary origin) of the germ layers that form all later organs and tissues.



Early embryonic stage of Nematostella vectensis. **Sabrina Kaul-Strehlow, Patrick Steinmetz**

According to a 150 year-old hypothesis, all tissues and organs in our body derive from one of three germ layers that are established during early embryogenesis. This "germ layer hypothesis" states that skin and nervous system derive from the outer ectoderm layer, the gut and some inner organs, like the pancreas, derive from the inner endoderm layer, while muscles and gonads stem from the middle layer, the mesoderm. Early on, researchers noted a fundamental difference in the number of germ layers in different animal groups.

While most animals, like humans, insects and worms, develop from three germ layers, the cnidarians (corals, sea anemones or jellyfish) lack the intermediate layer and present only two cell layers during development and throughout life. The emergence of mesoderm as the third intermediate germ layer is considered a key event during the evolution of complex animals. So far, however, it was controversial how mesoderm has evolved, and how the two cnidarian germ layers relate to the three layers in most other animals. A new publication from the laboratory of Ulrich Technau at the Department for Molecular Evolution and Development of the University of Vienna presents a fundamentally new view of the evolution of germ layers.

The inner-most, gut-forming endoderm has always been considered as evolutionary related between cnidarians and other animals. In their study, Technau and colleagues have now tested this hypothesis by tracing the embryonic origin of digestive enzyme-producing cells as well as their developmental regulator genes typical of the gut and pancreas in a sea anemone. The authors show that in sea anemones, against all previous beliefs, digestive enzyme- and insulin-producing gland cells do not develop from endoderm but from the ectodermal part of the mouth, the pharynx. "I was puzzled when I first saw that all endoderm derivatives of sea anemones are totally devoid of digestive gland cells. That was not what is taught in biology textbooks" explains Patrick Steinmetz, who contributed most of the experiments and is now a group leader at the University of Bergen in Norway.

"The results completely change the way we think of the origin of germ layers. It means that 'endoderm' in sea anemones and vertebrates, although they are called the same, are actually not evolutionary related" adds Ulrich Technau. If the mouth ectoderm of the sea anemone and not the endoderm corresponds to the vertebrate gut and pancreas, then what is the vertebrate correlate of the sea anemone

endoderm? When Steinmetz and Technau dwelled deeper into this question, they found strong similarities between the cnidarian endoderm and the intermediate mesoderm layer: both share a large number of regulatory genes, and both give rise to similar cell types such as muscle or gonad cells. The sea anemone thus shows a clear correlate of mesoderm, but not in an intermediate position as found in three-layered animals. Positioning, and not novel emergence, of tissue in-between the gut and skin was thus the key event that led to the evolution of three-layered animals.

"An overwhelming majority of animals nowadays develop three germ layers, and we have taken a big step towards the understanding of one of the most crucial events underlying this evolutionary success story" concludes Steinmetz.

Publication in Nature Ecology & Evolution: Steinmetz, P.R.H., Aman, A., Kraus, J.E.M., Technau, U. Gut-like ectodermal tissue in a sea anemone challenges germ layer homology. Nature Ecology & Evolution DOI: 10.1038/s41559-017-0285-5.

http://bit.ly/2xYAhqS

Scientists list 50 terms you may be confusing

Envy vs. jealousy, disease vs. illness and 48 more terms that seem to be the same but aren't

Should you punish a disobedient child, or try negative reinforcement? Is your shy new colleague antisocial or asocial? And which is worse: a prejudiced boss or a discriminatory one?

These are just three examples of psychological terms that are commonly assumed to be similar, if not identical, but which in fact refer to very different concepts. The confusion extends from television shows and science writing to textbooks and even scholarly articles.

A new paper published in open-access journal Frontiers in Education defines 50 such "term pairs" related to psychology. As the most comprehensive list of its kind, the paper aims to improve the psychological literacy of psychology students as well as the broader public.

Other examples of frequently confused terms include race/ethnicity, envy/jealousy, serial killer/mass murderer, and disease/illness.

"Words matter, and science is no exception," says Scott O. Lilienfeld, professor of psychology at Emory University, USA, and one of the paper's authors. "All sciences rely on specialized terminology which must be correctly understood to master the field's core concepts."

"In psychology, many terms are confused not only by new students but also by advanced students, psychology instructors, and science journalists. These misunderstandings can impede the learning of other psychological ideas."

The paper, "50 Differences That Make a Difference: A Compendium of Frequently Confused Term Pairs in Psychology", follows an earlier list of 50 widely used psychological terms that should generally be avoided.

Here's a short definition of the term pairs above:

1. *Negative reinforcement* involves the withdrawal of a stimulus and increases the likelihood of a previous behavior, while *punishment* involves the presentation of a stimulus and decreases the likelihood of a previous behavior. So if you want to lower the likelihood of further disobedience, punishment is the way to go (although most psychological research suggests that punishment works well in the short-term, but not in the long-term).

2. Your new colleague is most likely *asocial*. *Antisocial* people perform actions against others, frequently engaging in reckless, irresponsible, and at times illegal behaviors. In contrast, asocial people chronically withdraw from others due to shyness or not being interested in interpersonal contact.

3. *Prejudice* refers to a belief, discrimination to a behavior. Specifically, prejudice means arriving at a premature - and usually negative - judgment of others based on their membership in one or more categories (e.g., African-American, Jew, obese, Republican), whereas *discrimination* refers to the act of treating others poorly as a function of this membership. While both are bad, you'd probably prefer that your boss be prejudiced.

4. *Race* refers to a class, such as Caucasian or African-American, that is defined by biological differences such as white versus brown or black skin. *Ethnicity* is a broader concept, such as German or Chinese-American, that includes race as well as cultural variables such as country of origin, customs, and preferred language.

5. *Envy* and *jealousy* are so frequently confused (e.g., "I'm jealous that you're going to Hawaii next week!") that few people are aware they differ. Yet the distinction is typically simple: *Envy* involves two people, whereas *jealousy* involves three or more people. So you are envious, not jealous, that your friend is headed to Hawaii -- unless they are going with another friend as well.

6. A *serial killer* kills multiple people in a string of incidents that are separated by "cooling off" periods, whereas a *mass murderer* kills a large number of people in a single incident. Serial killers are also different from *spree killers*, whose homicidal episodes are not separated by clear-cut cooling-off periods.

7. According to most sociologists and cultural anthropologists, disease is the specific pathology or malfunctioning of a body part, and illness is the afflicted individual's reactions to the disease. **Read more!**

http://bit.ly/2wWBlow

Clinical trials often unregistered, unpublished

An analysis of more than 100 clinical trials found that they were often unregistered, unpublished and had discrepancies in the reporting of primary outcomes, according to a study published by JAMA.

The study is being released to coincide with its presentation at the Eighth International Congress on Peer Review and Scientific Publication.

A major aim of trial registration is to help identify and deter the selective reporting of outcomes based on the results. However, it is unclear whether registered outcomes accurately reflect the trial protocol and whether registration improves the reporting of primary outcomes in publications.

An-Wen Chan, M.D., D.Phil., of the Women's College Research Institute, University of Toronto, and colleagues examined adherence to trial registration and its association with subsequent publication and reporting of primary outcomes in 113 clinical trial protocols approved in 2007 by the research ethics committee for the region of Helsinki and Uusimaa, Finland.

Among the trials, 61 percent were prospectively registered (defined as within one month after the trial start date to allow for incomplete start dates and processing delays in the registry) and 57 percent were published.

A primary outcome was not defined in 20 percent. Discrepancies between the protocol and publication were more common in unregistered trials (55 percent) than registered trials (6 percent).

Discrepancies were defined as (1) a new primary outcome being reported that was not specified as primary in the protocol; or (2) a protocol-defined primary outcome being omitted or downgraded (reported as secondary or unspecified) in the registry or publication.

Prospective registration was significantly associated with subsequent publication (68 percent of registered trials vs 39 percent of unregistered trials).

Registered trials were also significantly more likely than unregistered trials to be subsequently published with the same primary outcomes as defined in the protocol (64 percent of registered trials vs 25 percent of unregistered trials).

Limitations of the study include the unclear generalizability beyond the Finnish jurisdiction and the limited sample size.

"Journal editors, regulators, research ethics committees, funders, and sponsors should implement policies mandating prospective registration for all clinical trials. Only with accessible, complete information can interventions be adequately evaluated for patient care," the authors write.

http://jamanetwork.com/journals/jama/fullarticle/10.1001/jama.2017.13001

http://bit.ly/2x0qOGv

Expensive drug driving up Medicare expenditures without evidence of greater efficacy

Over $1 billion spent in 5 years on a drug not proven more effective than much less expensive corticosteroids

PORTLAND, Ore. - Medicare spent more than $1 billion over a five-year period on a high-priced drug that has not been proven more effective for a collection of inflammatory conditions than much less expensive corticosteroids, research by the OHSU/OSU College of Pharmacy shows.

The analysis also indicates that a comparatively small group of "frequent prescribers" combine to write prescriptions that lead to the bulk of Medicare's expenditures on the drug, repository adrenocorticotropin, or ACTH.

In 2015 alone, Medicare spending topped $500 million on the drug, the cost of which has soared to $36,000 per course of therapy.

Known by the trade name **H.P. Acthar Gel**, often shortened to just **Acthar**, the drug's primary use is to treat rare epileptic spasms in children under age 2.

"The drug has an interesting back story," said Dan Hartung, lead author on a research letter that was published today in JAMA Internal Medicine. "It's a fairly old drug, first approved in 1952, prior to many of the FDA rules about clinical efficacy. The bar for what constitutes approved indications was much different then, much lower; it has many indications that came before the current rules were set in stone in the 1960s."

The drug, classified as a "biologic," was initially approved for a broad range of corticosteroid-responsive inflammatory conditions.

"It's a hormone produced in the human body that signals the release of steroids," Hartung said. "It does the same job as low-cost corticosteroids. And it really wasn't much on anyone's radar until 2007."

Questcor Pharmaceuticals purchased the rights to the largely forgotten Acthar in 2001 for $100,000 and began steadily raising Acthar's price. In 2007 Questcor increased the price of the drug, which once sold for $40 for a vial, or course of therapy, from $1,650 to $23,000 overnight. Questcor, acquired by Mallinckrodt Pharmaceuticals in 2017, markets the drug aggressively for relatively common conditions such as rheumatoid arthritis, multiple sclerosis and nephrotic syndrome, Hartung said. The Food and Drug Administration approved Acthar for those types of conditions decades ago when requirements were less strict; no clinical trials were required.

"There are a variety of FDA-approved indications that lack a lot of evidence that Acthar is even effective, let alone better than inexpensive corticosteroids," Hartung said. "And what allows for this kind of pricing is that it's a fairly complex molecule and no competitors can exactly duplicate it; they have a monopoly on this particular molecule."

In 2015, Acthar generated gross revenue of about $1 billion - more than half of which came from Medicare, and much of the rest coming from Medicaid, Hartung said, meaning public expenditures likely accounted for almost all of the sales.

Hartung and the other collaborators found Medicare spending on the drug increased tenfold and totaled $1.3 billion from 2011 to 2015.

In 2014, a total of 1,621 prescribers were responsible for $391.2 million in Acthar spending; among those, 203 frequent prescribers - 94 rheumatologists, 55 neurologists and 54 nephrologists, each with more than 10 prescriptions - accounted for $165 million of the total.

"And in general these physicians are prescribing about the same number of other drugs compared to their peer specialty groups, so we suspect they are not treating more severely ill patients," Hartung said. "Mallinckrodt is really aggressively marketing in ways that possibly subject prescribers to conflicts of interest. From the payer side, there's really little that little justifies this drug and its exorbitant cost over

much cheaper alternatives. If Medicare were to take a firm stand on reimbursements, this wouldn't be happening."

Joining Hartrung on the study were Kirbee Johnston, Shelby Van Leuven, Atul Deodhar, David Cohen and Dennis Bourdette.

Related Journal Article http://dx.doi.org/10.11001/jamainternmed.2017.3631

http://bit.ly/2fiJIRq

Cold region 'tipping point' now inevitable

The decline of cold regions called periglacial zones is now inevitable due to climate change, researchers say.

Periglacial zones, where there is often a layer of frozen ground known as permafrost, make up about a quarter of the Earth's land surface and are mostly found in the far north and south, and at high altitudes.

Scientists from the universities of Exeter and Helsinki and the Finnish Meteorological Institute examined natural processes caused by frost and snow which take place in these zones.

Their findings suggest that - even with optimistic estimates of future carbon emissions - areas covered by periglacial zones will reduce dramatically by 2050, and they will "almost disappear" by 2100.

This would have a major impact on landscapes and biodiversity, and could trigger climate "feedbacks" - processes that can amplify or diminish the effects of climate change.

"The results suggest that profound changes can be expected in current periglacial zones regardless of climate change mitigation policies," said Dr Juha Aalto, of the University of Helsinki and the Finnish Meteorological Institute.

"Unfortunately, it seems that many of the frost-driven processes we studied are already at the margin of the climate in which they can exist."

The scientists studied four processes which take place in periglacial zones, including snow accumulation sites and "frost churning" - which refers to mixing of materials caused by freezing and thawing.

"Our results forecast a future tipping point in the operation of these processes, and predict fundamental changes in ground conditions and related atmospheric feedbacks," Dr Aalto added.

Dr Stephan Harrison, of the University of Exeter's Penryn Campus in Cornwall, said: "The project used very high-resolution climate and land surface models to demonstrate that geological processes and ecosystems in high latitudes (the far north and south) will be fundamentally altered by climate change during this century."

Even based on the optimistic RCP2.6 estimate for future carbon emissions, the researchers predict a 72% reduction in the current periglacial zone in the area of northern Europe they studied.

By 2100, periglacial zones in will only exist in high mountain regions, they say.

Professor Miska Luoto, of the University of Helsinki, said: "The anticipated changes in land surface processes can feedback to the regional climate system via alterations in carbon cycle and ground surface reflectance (light reflected by snow and ice) caused by the increase of shrub vegetation to alpine tundra.

"Our results indicate significant changes in Northern European plant life. Many rare species can only be sustained in areas of intense frost activity or late-lying snow packs, so the disappearance of such unique environments will reduce biodiversity."

The research is part of the INFRAHAZARD project, funded by the Academy of Finland. The study was also funded by the EU's Seventh Framework Programme for Research and Technological Development and by the EU HELIX programme.

The paper, published in the journal Nature Communications, is entitled: "Statistical modelling predicts almost complete loss of major periglacial processes in Northern Europe by 2100."

http://bit.ly/2jqFSu6

How liver cancer develops

Discovery of a major mechanism in the development of liver cancer

Liver cancer is the second-leading cause of cancer-related death and represents the fastest rising cancer worldwide. In most cases, the tumor develops in patients with chronic liver disease. Such diseases include chronic infections with hepatitis viruses or a so-called fatty liver due to nutritional or genetically caused lipometabolic disorders or an excessive consumption of alcohol.

An international team of researchers headed up by UZH Professor Achim Weber from the Institute of Pathology and Molecular Pathology of the University Hospital Zurich and Mathias Heikenwälder, professor at the German Cancer Research Center in Heidelberg, Germany, has discovered a major mechanism in the development of liver cancer. One of the main players in this process is enzyme caspase-8, which assumes an important dual role.

Short-term protection at the price of long-term development of cancer

This protein is therefore jointly responsible for triggering programmed cell death, apoptosis, in diseased liver cells. If the liver is permanently damaged, increased activation of cell death in hepatocytes occurs first, as the scientists demonstrated using patient samples and various mouse models. In reaction, the liver cells divide faster to regenerate the tissue. This causes lasting stress: Over a period of years, damaged liver cells die off and new ones grow in their place.

Since the hereditary material doubles at each cell division, more and more errors are constantly stealing into the DNA. The rising number of mutations leads to genetic instability and increases the probability that a liver cell will become a tumor cell. Ultimately, the chronically increased cell death activity results in the development of liver cancer. The elimination of damaged cancer cells, while sensible in itself, therefore raises the risk of tumors in the long term. "We have observed this mechanism in all the various liver diseases and examined mouse models - it appears to be remarkably universal," Weber adds.

Enzyme caspase-8 has an important dual function

In their investigation, the researchers discovered an important second function of caspase-8: In a complex with additional proteins, the enzyme detects DNA damage in the remaining liver cells and initiates their repair. This reveals another mechanism by means of which caspase-8 protects liver cells. For Achim Weber, these results are relevant not only for basic research: "Our results have important implications for the clinic - for the treatment of patients with chronic liver diseases on the one hand and for the application of cancer medications that induce cell death on the other."

Related Journal Article http://dx.doi.org/10.1016/j.ccell.2017.08.010

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Body's own defense against ALS actually drives disease progression at later stages

Findings in mice underscore complexity of deadly neurological disease; lay foundation for therapies that could eventually prevent onset of ALS

Credit: Tom Maniatis/Columbia University's Zuckerman Institute

NEW YORK -- Columbia scientists have discovered that one of the body's natural defenses against amyotrophic lateral sclerosis (ALS) -- a cellular 'clean-up process' called autophagy -- suppresses disease progression early on, but in later stages advances the disease's deadly spread through the spinal cord. These findings in mice provide a window into ALS's earliest stages, as well as new insights into its complexity, namely the differing roles that autophagy plays in its progression. In addition, this study can help scientists search for ways to detect and even treat the disease before the onset of devastating symptoms that gradually rob patients of movement, speech and life.

The study is publishing this week in the Proceedings of the National Academy of Sciences.

"One of the biggest barriers to treating ALS is that its progression is dynamic -- many different cell types and mechanisms are involved -- so treating it at one stage of the disease might have very different, and potentially harmful, consequences at a different stage," said Tom Maniatis, PhD, a principal investigator at Columbia's Mortimer B. Zuckerman Mind Brain Behavior Institute and the study's senior author. "Here, we've identified a cellular process that likely plays a central role at the very beginnings of the disease, which could open the door to treatments that stop ALS before it has a chance to gain a foothold in the body."

ALS, also referred to as Lou Gehrig's disease, is a deadly disease of the central nervous system for which there is no effective treatment. It first attacks motor neurons, the type of nerve cells that guide muscle movement. As motor neurons die, disease spreads to other types of cells in the spinal cord. Over time, patients increasingly lose their ability to move, to speak and even to breathe on their own. In nearly all instances, patients succumb to ALS within five years of being diagnosed.

Despite the lack of effective therapies, however, much progress has been made in uncovering some of ALS's underlying mechanisms. For example, studies have shown that a common feature of all ALS patients is the abnormal accumulation, or aggregation, of protein clumps inside motor neurons. This accumulation kick starts autophagy, a critical cellular process in which such protein clumps, as well as other damaged parts of the cell, are broken down and removed. In addition, recent studies of ALS led by Columbia geneticist David Goldstein, PhD, revealed mutations in the genes that drives autophagy can cause ALS.

To more precisely explore the role of autophagy in ALS, Dr. Maniatis and his team developed two different groups of ALS mouse models. The first group was genetically modified to mimic the signs of ALS, but were otherwise normal. The second group was identical to the first but with one significant difference: autophagy in their motor neurons was suppressed. The researchers then compared how the disease progressed in these two groups.

The differences they observed were unexpected. They found that, in the absence of autophagy, ALS symptoms in the second group of mice advanced more quickly early in the disease, but later on the spread of disease was slower. Remarkably, the mice with suppressed autophagy lived longer than the first group of ALS mice.

"This strongly suggested that even though autophagy may initially stave off disease by suppressing protein aggregation, it eventually hastens the spread of ALS and its devastating symptoms to the rest of the spinal cord," said Dr. Maniatis, who also directs Columbia's Precision Medicine Initiative and is the Isidore S. Edelman Professor and Chair of biochemistry & molecular biophysics at Columbia University Medical Center.

The authors argue that when autophagy is intact, other cell types that surround motor neurons undergo an inflammatory reaction, which soon spreads throughout the spinal cord, and contributes to the progression of ALS.

However, in the absence of autophagy this spread occurs more slowly. They speculate that this may be due to the release of disease-causing protein aggregates that escape from dying motor neurons during the normal autophagy process. In the absence of autophagy this spread may be diminished.

Autophagy is governed by many genes working in concert across every cell in the body, so Dr. Maniatis and his team are now studying how mutations in these genes affect disease progression in their ALS mouse model.

"By the time ALS symptoms are noticeable, the disease is very far along so drugs aren't likely to work unless we can diagnose ALS much earlier -- which will be helped by understanding how mutations in autophagy genes cause ALS and affect disease progression," said Dr. Maniatis. "If we can find ways of treating the earlier stages of disease, rather than trying to stop it after it's full blown, it may be possible to develop more effective therapies."

This paper is titled: "Distinct roles for motor neuron autophagy early and late in the SOD1G93A mouse model of ALS." Additional contributors include first author Noam D. Rudnick, MD, PhD, Christopher J. Griffey, Paolo Guarnieri, MD, Valeria Gerbino, PhD, Xueyong Wang, PhD, Jason A. Piersaint, Juan Carlos Tapia, PhD, and Mark M. Rich, MD, PhD.

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The authors report no financial or other conflicts of interest.

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First research to suggest scratching may have evolved as a communication tool to help social cohesion

Looking stressed can help keep the peace

Scratching is more than an itch—when it is sparked by stress, it appears to reduce aggression from others and lessen the chance of conflict.

Scratching can be a sign of stress in many primates, including humans. Research by Jamie Whitehouse from the University of Portsmouth, is the first to suggest that these stress behaviours can be responded to by others, and that they might have evolved as a communication tool to help social cohesion.

The research, published in Scientific Reports, raises the question whether human scratching and similar self-directed stress behaviours serve a similar function.

Jamie said: "Observable stress behaviours could have evolved as a way of reducing aggression in socially complex species of primates. Showing others you are stressed could benefit both the scratcher and those watching, because both parties can then avoid conflict."

The research team conducted behavioural observations of 45 rhesus macaques from a group of 200, on the 35-acre island of Cayo Santiago, Puerto Rico. The team monitored the naturally occurring social interactions between these animals over a period of eight months.

The researchers found that scratching in the monkeys was more likely to occur in times of heightened stress, such as being close to high-ranking individuals or to non-friends.

Looking stressed can help keep the peace

Stress scratching significantly lowered the likelihood of a scratching monkey being attacked.

The likelihood of aggression when a high ranking monkey approached a lower ranking monkey was 75 per cent if no scratching took place, and only 50 per cent when the lower ranking monkey scratched.

Scratching also reduced the chance of aggression between individuals who did not have a strong social bond.

Jamie said: "As scratching can be a sign of social stress, potential attackers might be avoiding attacking obviously stressed individuals because such individuals could behave unpredictably or be weakened by their stress, meaning an attack could be either risky or unnecessary. "By revealing stress to others, we are helping them predict what we might do, so the situation becomes more transparent. Transparency ultimately reduces the need for conflict, which benefits everyone and promotes a more socially cohesive group."

The researchers expect the findings will lead to a better understanding of stress and the evolution of stress in humans as well as how we manage stress in captive animals.

http://nyti.ms/2x1mPLj

What Does It Cost to Create a Cancer Drug? Less Than You'd Think

What does it really cost to bring a drug to market?

By GINA KOLATA SEPT. 11, 2017

The question is central to the debate over rising health care costs and appropriate drug pricing. President Trump campaigned on promises to lower the costs of drugs.

But numbers have been hard to come by. For years, the standard figure has been supplied by researchers at the Tufts Center for the Study of Drug Development: $2.7 billion each, in 2017 dollars.

Yet a new study looking at 10 cancer medications, among the most expensive of new drugs, has arrived at a much lower figure: a median cost of $757 million per drug. (Half cost less, and half more.)

Following approval, the 10 drugs together brought in $67 billion, the researchers also concluded — a more than sevenfold return on investment. Nine out of 10 companies made money, but revenues varied enormously. One drug had not yet earned back its development costs. The study, published Monday in JAMA Internal Medicine,

relied on company filings with the Securities and Exchange Commission to determine research and development costs.

"It seems like they have done a thoughtful and rigorous job," said Dr. Aaron Kesselheim, director of the program on regulation, therapeutics and the law at Brigham and Women's Hospital.

"It provides at least something of a reality check," he added.

The figures were met with swift criticism, however, by other experts and by representatives of the biotech industry, who said that the research did not adequately take into account the costs of the many experimental drugs that fail.

"It's a bit like saying it's a good business to go out and buy winning lottery tickets," Daniel Seaton, a spokesman for the Biotechnology Innovation Organization, said in an email.

Dr. Jerry Avorn, chief of the division of pharmacoepidemiology and pharmacoeconomics at Brigham and Women's Hospital, predicted that the paper would help fuel the debate over the prices of cancer drugs, which have soared so high "that we are getting into areas that are almost unimaginable economically," he said.

A leukemia treatment approved recently by the Food and Drug Administration, for example, will cost $475,000 for a single treatment. It is the first of a wave of gene therapy treatments likely to carry staggering price tags. "This is an important brick in the wall of this developing concern," he said.

Dr. Vinay Prasad, an oncologist at Oregon Health and Science University, and Dr. Sham Mailankody, of Memorial Sloan Kettering Cancer Center, arrived at their figures after reviewing data on 10 companies that brought a cancer drug to market in the past decade.

Since the companies also were developing other drugs that did not receive approval from the F.D.A., the researchers were able to include the companies' total spending on research and development, not just what they spent on the drugs that succeeded.

One striking example was ibrutinib, made by Pharmacyclics. It was approved in 2013 for patients with certain blood cancers who did not respond to conventional therapy.

Ibrutinib was the only drug out of four the company was developing to receive F.D.A. approval. The company's research and development costs for their four drugs were $388 million, the company's S.E.C. filings indicated. After it was approved, Janssen Biotech acquired the drug for $21 billion. "That is a 50-fold difference between revenue post-approval and cost to develop," Dr. Prasad said.

Accurate figures on drug development are difficult to find and often disputed. Although it is widely cited, the Tufts study also was fiercely criticized.

One objection was that the researchers, led by Joseph A. DiMasi, did not disclose the companies' data on development costs. The study involved ten large companies, which were not named, and 106 investigational drugs, also not named.

But Dr. DiMasi found the new study "irredeemably flawed at a fundamental level." "The sample consists of relatively small companies that have gotten only one drug approved, with few other drugs of any type in development," he said. The result is "substantial selection bias," meaning that the estimates do not accurately reflect the industry as a whole.

Ninety-five percent of cancer drugs that enter clinical trials fail, said Mr. Seaton, of the biotech industry group. "The small handful of successful drugs — those looked at by this paper — must be profitable enough to finance all of the many failures this analysis leaves unexamined."

"When the rare event occurs that a company does win approval," he added, "the reward must be commensurate with taking on the multiple levels of risk not seen in any other industry if drug development is to remain economically viable for prospective investors."

Cancer drugs remain among the most expensive medications, with prices reaching the hundreds of thousands of dollars per patient.

Although the new study was small, its estimates are so much lower than previous figures, and the return on investment so great, that experts say they raise questions about whether soaring drug prices really are needed to encourage investment.

”That seems hard to swallow when they make seven times what they invested in the first four years,” Dr. Prasad said.

The new study has limitations, noted Patricia Danzon, an economist at the University of Pennsylvania’s Wharton School.

It involved just ten small biotech companies whose cancer drugs were aimed at limited groups of patients with less common diseases.

For such drugs, the F.D.A. often permits clinical trials to be very small and sometimes without control groups. Therefore development costs may have been lower for this group than for drugs that require longer and larger studies.

But, Dr. Danzon said, most new cancer drugs today are developed this way: by small companies and for small groups of patients. The companies often license or sell successful drugs to the larger companies. The new study, she said, “is shining a light on a sector of the industry that is becoming important now.” The evidence, she added, is “irrefutable” that the cost of research and development “is small relative to the revenues.”

When it comes to drug prices, it does not matter what companies spend on research and development, Dr. Kesselheim said.

“They are based on what the market will bear.”

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When ancient fossil DNA isn't available, ancient glycans may help trace human evolution

Ancient DNA recovered from fossils is a valuable tool to study evolution and anthropology.

Yet ancient fossil DNA from earlier geological ages has not been found yet in any part of Africa, where it's destroyed by extreme heat and humidity. In a potential first step at overcoming this hurdle, researchers at University of California San Diego School of Medicine and Turkana Basin Institute in Kenya have discovered a new kind of glycan—a type of sugar chain—that survives even in a 4 million-year-old animal fossil from Kenya, under conditions where ancient DNA does not.

Partial upper jaw of Australopithecus anamensis, a primitive hominin, recovered from the bone bed excavated at the Allia Bay site. **Meave Leakey, PhD**

While ancient fossils from hominins (human ancestors and extinct relatives) are not yet available for glycan analysis, this proof-of-concept study, published September 11 in Proceedings of the National Academy of Sciences, may set the stage for unprecedented explorations of human origins and diet.

"In recent decades, many new hominin fossils were discovered and considered to be the ancestors of humans," said Ajit Varki, MD, Distinguished Professor of Medicine and Cellular and Molecular Medicine at UC San Diego School of Medicine. "But it's not possible that all gave rise to modern humans—it's more likely that there were many human-like species over time, only one from which we descended. This new type of glycan we found may give us a better way to investigate which lineage is ours, as well as answer many other questions about our evolution, and our propensity to consume red meat."

Glycans are complex sugar chains on the surfaces of all cells. They mediate interaction between cells and the environment, and often serve as docking sites for pathogens. For millions of years, the common ancestors of humans and other apes shared a particular glycan known as Neu5Gc. Then, for reasons possibly linked to a malarial parasite that exploited Neu5Gc as a means to establish infection, a mutation that probably occurred between 2 and 3 million years ago inactivated the human gene encoding the enzyme that makes the molecule. The loss of Neu5Gc amounted to a radical molecular

makeover of human ancestral cell surfaces and might have created a fertility barrier that expedited the divergence of the lineage leading to humans.

Today, chimpanzees and most other mammals still produce Neu5Gc. In contrast, only trace amounts can be detected in human blood and tissue—not because we make Neu5Gc, but, according to a previous study by Varki's team, because we accumulate the glycan when eating Neu5Gc rich red meat. Humans mount an immune response to this non-native Neu5Gc, possibly aggravating diseases such as cancer.

In their latest study, Varki and team found that, as part of its natural breakdown, a signature part of Neu5Gc is also incorporated into chondroitin sulfate (CS), an abundant component in bone. They detected this newly discovered molecule, called Gc-CS, in a variety of mammalian samples, including easily detectable amounts in chimpanzee bones and mouse tissues.

When ancient fossil DNA isn't available, ancient glycans may help trace human evolution

Excavation of the bone bed at the Allia Bay site, East Turkana, in 1996. A cross section of the bone bed can be seen passing diagonally from the center of the image to the right hand corner. This is the site where researchers collected a …more

Like Neu5Gc, they found that human cells and serum have only trace amounts of Gc-CS—again, likely from red meat consumption. The researchers backed up that assumption with the finding that mice engineered to lack Neu5Gc and Gc-Cs (similar to humans) had detectable Gc-CS only when fed Neu5Gc-containing chow.

Curious to see how stable and long-lasting Gc-CS might be, Varki bought a relatively inexpensive 50,000-year-old cave bear fossil at a public fossil show and took it back to the lab. Despite its age, the fossil indeed contained Gc-CS.

That's when Varki turned to a long-time collaborator—paleoanthropologist and famed fossil hunter Meave Leakey, PhD, of Turkana Basin Institute of Kenya and Stony Brook University. Knowing that researchers need to make a very strong case before they are given precious ancient hominin fossil samples, even for DNA analysis, Leakey recommended that the researchers first prove their method by detecting Gc-CS in even older animal fossils. To that end, with the permission of the National Museums of Kenya, she gave them a fragment of a 4-million-year-old fossil from a buffalo-like animal recovered in the excavation of a bone bed at Allia Bay, in the Turkana Basin of northern Kenya. Hominin fossils were also recovered from the same horizon in this bone bed.

Varki and team were still able to recover Gc-CS in these much older fossils. If they eventually find Gc-Cs in ancient hominin fossils as well, the researchers say it could open up all kinds of interesting possibilities.

"Once we've refined our technique to the point that we need smaller sample amounts and are able to obtain ancient hominin fossils from Africa, we may eventually be able to classify them into two groups—those that have Gc-CS and those that do not. Those that lack the molecule would mostly likely belong to the lineage that led to modern humans," said Varki, who is also adjunct professor at the Salk Institute for Biological Studies and co-director of the UC San Diego/Salk Center for Academic Research and Training in Anthropogeny (CARTA).

In a parallel line of inquiry, Varki hopes Gc-CS detection will also reveal the point in evolution when humans began consuming large amounts of red meat.

"It's possible we'll one day find three groups of hominin fossils—those with Gc-CS before the human lineage branched off, those without Gc-CS in our direct lineage, and then more recent fossils in which trace amounts of Gc-CS began to reappear when our ancestors began eating red meat," Varki said. "Or maybe our ancestors lost Gc-CS more gradually, or only after we began eating red meat. It will be interesting to see, and we can begin asking these questions now that we know we can reliably find Gc-CS in ancient fossils in Africa."

Leakey is also hopeful about the role Gc-CS could play in the future, as an alternative to current approaches.

"Because DNA rapidly degrades in the tropics, genetic studies are not possible in fossils of human ancestors older than only a few thousand years," she said. "Therefore such ancient glycan studies have the potential to provide a new and important method for the investigation of human origins."

Co-authors of this study also include: Anne K. Bergfeld, Roger Lawrence, Sandra L. Diaz, Oliver M.T. Pearce, Darius Ghaderi, and Pascal Gagneux, all at UC San Diego.

Anne K. Bergfeld el al., "N-glycolyl groups of nonhuman chondroitin sulfates survive in ancient fossils," PNAS (2017). www.pnas.org/cgi/doi/10.1073/pnas.1706306114

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Ethnic diversity in schools may be good for students' grades, study suggests

Early adolescents' grades were higher when they socialized with peers from other ethnicities, according to the findings of a University of California, Davis, study that looked at the lunching habits of more than 800 sixth-graders in three states.

Karen Nikos-Rose

The findings suggest that schools might look for ways to provide cross-ethnic interaction among students—outside of lunch—to take advantage of ethnic diversity, researchers said. "The great part about these findings is that the results were just as true for white students as ethnic minority students (African American, Asian, Latino/a, and multiethnic)," said Adrienne Nishina, associate professor in the Department of Human Ecology and study co-author.

Even white and Asian students, who had significantly higher GPAs than members of other ethnic groups, appeared to benefit from daily cross-ethnic interactions, the study found.

Students who spent lunchtime with at least one cross-ethnic peer received higher GPAs in academic courses as well as higher teacher expectations for their educational attainment at the end of sixth grade, Nishina said. She said teacher expectations are a factor that can influence how students remain engaged in school long term.

Students reported an average jump in GPA of one-third of a point, or the equivalent of going from a B-plus average to an A-minus average. And, the study said, the social skills gained in interaction among peers of other ethnicities might enhance students' problem-solving skills, which can transfer into academic success. "It may also help later in life with career success, as individuals become increasingly comfortable and skilled at interacting with ethnically diverse peers," said Jakeem Lewis, the study's lead author and a doctoral student in human ecology.

The data was collected from students who self-reported their interactions at the end of five separate school days during a two-week period at six public middle schools in California, Oregon and Wisconsin. The sampling was ethnically diverse, with none of the schools having an ethnic majority of students, and many students at each of the schools reported having cross-ethnic friends.

The study, "Early Adolescents' Peer Experiences With Ethnic Diversity in Middle School: Implications for Academic Outcomes" appears in the Journal of Youth and Adolescence.

More information: Jakeem Amir Lewis et al. Early Adolescents' Peer Experiences with Ethnic Diversity in Middle School: Implications for Academic Outcomes, Journal of Youth and Adolescence (2017). DOI: 10.1007/s10964-017-0697-1

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Western researchers reverse the negative effects of adolescent marijuana use

Researchers at Western University have found a way to use pharmaceuticals to reverse the negative psychiatric effects of THC, the psychoactive chemical found in marijuana.

Chronic adolescent marijuana use has previously been linked to the development of psychiatric diseases, such as schizophrenia, in adulthood. But until now, researchers were unsure of what exactly was happening in the brain to cause this to occur.

"What is important about this study is that not only have we identified a specific mechanism in the prefrontal cortex for some of the mental health risks associated with adolescent marijuana use, but we have

also identified a mechanism to reverse those risks," said Steven Laviolette, professor at Western's Schulich School of Medicine & Dentistry.

In a study published online today in Scientific Reports the researchers demonstrate that adolescent THC exposure modulates the activity of a neurotransmitter called GABA in the prefrontal cortex region of the brain. The team, led by Laviolette and post-doctoral fellow Justine Renard, looked specifically at GABA because of its previously shown clinical association with schizophrenia.

"GABA is an inhibitory neurotransmitter and plays a crucial role in regulating the excitatory activity in the frontal cortex, so if you have less GABA, your neuronal systems become hyperactive leading to behavioural changes consistent with schizophrenia," said Renard.

The study showed that the reduction of GABA as a result of THC exposure in adolescence caused the neurons in adulthood to not only be hyperactive in this part of the brain, but also to be out of synch with each other, demonstrated by abnormal oscillations called 'gamma' waves. This loss of GABA in the cortex caused a corresponding hyperactive state in the brain's dopamine system, which is commonly observed in schizophrenia.

By using drugs to activate GABA in a rat model of schizophrenia, the team was able to reverse the neuronal and behavioural effects of the THC and eliminate the schizophrenia-like symptoms.

Laviolette says this finding is especially important given the impending legalization of marijuana in Canada. "What this could mean is that if you are going to be using marijuana, in a recreational or medicinal way, you can potentially combine it with compounds that boost GABA to block the negative effects of THC."

The research team says the next steps will examine how combinations of cannabinoid chemicals with compounds that can boost the brains GABA system may serve as more effective and safer treatments for a variety of mental health disorders, such as addiction, depression and anxiety.

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'Superbug' bacteria gang up on us, fueled by antibiotic use, nursing home study suggests

Understanding the ecosystem of multidrug-resistant bacteria, and how antibiotics affect them, could lead to better infection prevention

ANN ARBOR, Mich. ¬ What's worse than getting exposed to a kind of bacteria that modern antibiotics can't kill? Getting exposed to more than one - because they may work together to cause an infection, new research suggests.

And trying different antibiotics to control one such "superbug" may only encourage others lurking nearby, according to new findings made in hundreds of nursing home patients by a team from the University of Michigan.

In fact, the researchers say it's time to think about such bacteria as members of an antibiotic-resistant ecosystem in healthcare environments - not as single species that act and respond alone.

Forty percent of the 234 frail elderly patients in their study had more than one multidrug-resistant organism, or MDRO, living on their bodies. Patients who had specific pairs of MDROs were more likely to develop a urinary tract infection involving an MDRO.

The researchers created a map of interactions among bacteria and classes of antibiotics, which they've published with their findings in the Proceedings of the National Academy of Sciences.

Eventually, that kind of mapping could help healthcare providers. For instance, they could choose to treat a patient with a specific antibiotic not just because of its ability to kill one MDRO, but also for its potential downstream impact on other MDROs that may be lurking on the patient, or nearby.

But that will take time, and more research in the laboratory and in healthcare facilities, say the researchers, led by systems biologist Evan Snitkin, Ph.D. of the U-M Medical School Department of Microbiology and Immunology.

So in the meantime, they hope their new findings will give healthcare providers and patients even more reason to avoid using antibiotics in the first place unless they're truly necessary - because "superbugs" evolve in response to them.

An ecosystem of resistance

The researchers used detailed data from a long-term study of nursing home patients led by U-M geriatrician Lona Mody, M.D., M.Sc., who studies infection transmission and prevention in nursing homes. The team also included Betsy Foxman, Ph.D., a longtime researcher in the epidemiology of antibiotic resistance and urinary tract infections.

Nearly two-thirds of the patients studied were treated with one or more of 50 different antibiotics during the study period. All the patients in the study used a urinary catheter to empty their bladders for at least three days during the study period. This allowed the researchers to look at patterns of urinary tract infections, which in nursing home and hospital patients often arise from bacteria entering the bladder along a catheter.

The findings showed that colonization of such patients' skin, noses and throats with common MDROs was not random.

"We observed a complex network of interactions, with acquisition of each of six different MDRO species being influenced by different sets of antibiotics, and primary MDRO colonization in turn increasing the risk of acquisition and infection by other MDROs," says lead author Joyce Wang, Ph.D., a postdoctoral fellow in Snitkin's lab who led the analysis.

Colonization with one MDRO increased the risk of acquiring other MDROs - but not all others. It was as if they were interacting very specifically with other species. And treatment of a patient with any given antibiotic increased their chances of being colonized with an MDRO - which in turn altered their risk of becoming colonized with another MDRO later.

Superbug cooperation

The researchers focused on two of the most dangerous MDROs -- vancomycin resistant Enterococcus (VRE), and methicillin-resistant Staphylococcus aureus (MRSA) - as well as four Gram-negative bacteria that have evolved resistance to two powerful antibiotics.

One of the four, Proteus mirabilis, causes many catheter-associated UTIs and can form biofilms that involve many bacteria. It's known to release a compound called urease, which acts as a means of communication among bacteria.

The other three species of MDRO studied were Acinetobacter baumannii, Escherichia coli and Pseudomonas aeruginosa.

These same species are known to cause many infections in hospitals, which have poured major effort into fighting them and preventing their spread.

But, says Snitkin, "A lot of the attention in infection prevention is paid to large academic hospitals - but this is a fruitless endeavor if you're not controlling the same organisms in all the connected healthcare facilities and nursing homes," where patients go after a hospital stay, or live long-term. "We need to understand what clinical practices drive the spread of MDROs in healthcare facilities, and counterintuitively, it appears that a key factor is the use of certain antibiotics used against an individual organism that may impact other circulating organisms."

In short, every nursing home and likely every hospital in America is home to a natural experiment in the evolution of bacteria strains, to become resistant to drugs and to survive on a host patient or travel between hosts.

The people who work to prevent infections in healthcare facilities could someday harness advanced DNA sequencing techniques to help them combat superbugs, Snitkin says.

These tools, which he and his colleagues have been using in their research labs for a decade, help pinpoint exactly which strains of different bacteria are present, and how they're evolving.

That, combined with knowledge about how different MDRO strains interact with one another and how specific antibiotics affect them, could help steer doctors' decisions in future.

Wang, Snitkin and Mody are affiliated with the U-M Medical School, which is part of the Michigan Medicine academic medical center; Foxman is a professor in the U-M School of Public Health. The research was funded by the Centers for Disease Control and Prevention, and by a pilot grant from the U-M Claude D. Pepper Older Americans Independence Center, a research division of the U-M Geriatrics Center funded by the National Institute on Aging of the National Institutes of Health. Mody is a member of the U-M Institute for Healthcare Policy and Innovation. Snitkin is part of the U-M Host Microbiome Initiative and Center for Microbial Systems. *Reference: PNAS Early Edition, doi:10.1073/pnas.1710235114*

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Kawasaki Disease: High- or Low-Dose Aspirin?

High- vs Low-Dose Aspirin for Treatment of Kawasaki Disease

William T. Basco, Jr., MD, MS

Given that 15%-25% of children with untreated Kawasaki disease will develop coronary artery aneurysms or dilation, intravenous immunoglobulin (IVIg) and aspirin are now considered standards of care for the management of this disorder. It is unclear, however, whether higher-dose aspirin should be given to achieve anti-inflammatory effects beyond the antithrombotic effects of lower-dose aspirin. Higher-dose aspirin may shorten the duration of fever, but it is unclear whether it reduces cardiovascular morbidity.

A study by Dallaire and colleagues[1] analyzed data from patients with Kawasaki disease admitted to one of five Canadian institutions from 2004 to 2015. Study children were aged 0 to 10 years, and those with structural heart disease were excluded. The investigators retrospectively compared the outcomes of children prescribed only low-dose aspirin with those who received high-dose aspirin as part of their treatment. Two of the study institutions typically dosed patients at 3-5 mg/kg/day (low-dose aspirin), whereas the other institutions typically dosed at 80 mg/kg/day (high-dose aspirin). All children, who were experiencing their first episode of Kawasaki disease, received treatment within the first 10 days of fever onset, and all received IVIg. The investigators were able to recreate the visit history for all children through 12 months after being diagnosed with Kawasaki disease. The main outcome of interest was any coronary artery abnormality (eg, coronary artery diameter greater than a predetermined cut-off). The study took a noninferiority approach in that the two treatment doses would be considered noninferior if the difference in the risk for coronary artery abnormalities was ≤5%. The analysis cohort included 1213 children, 848 of whom were treated at high-dose aspirin institutions. In general, the treatment groups were not different at enrollment for age, sex, or duration of fever before treatment.

Study Findings

Overall, 21% of the children experienced a coronary artery abnormality. However, about half of those changes were considered transient because they were no longer present at the 6-week follow-up evaluation. Coronary artery abnormalities persisted at follow-up in 12.9% of the children. The frequency of any coronary abnormality was similar between the two groups (20.5% of the high-dose aspirin patients vs 22.2% of the low-dose aspirin children). The adjusted difference was 0.3%, with a 95% confidence interval of -4.5% to 5.0%. Similarly, coronary artery abnormalities persisted in 13.2% of high-dose patients compared with 12.3% of low-dose patients, a difference that did not reach statistical significance in the adjusted risk models. Additional analyses, including looking at the sizes of the coronary artery abnormalities, did not show any differences. Retreatment frequency was also similar (24.4% in the high-dose group and 27.4% in the low-dose group, a difference that was not statistically significant in adjusted models). Finally, duration of fever was 7.8 days in both groups.

The investigators concluded that with respect to coronary artery abnormalities or secondary outcomes, low-dose aspirin is not inferior to high-dose aspirin treatment of Kawasaki disease.

Viewpoint

In 20 years of practice at my institution, we have gradually shifted from using high-dose to low-dose aspirin, making me wonder what our data might show! As the study authors acknowledge, data to suggest that aspirin adds anything to treatment with IVIg are limited, and no prospective, randomized, double-blind trials have been conducted. Although this is a single study, combining data from five institutions strengthens the findings, and the investigators attempted to control for important clinical covariates, including some measures of disease severity. For now, I have to agree that despite our lack of randomized, prospective clinical trials, their data suggest that low-dose aspirin can be considered noninferior to high-dose aspirin for the treatment of Kawasaki disease in children.

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http://bit.ly/2x3WBGt

Oysters Can Get Herpes, And It's Killing Them

A deadly virus threatens to decimate oyster populations around the world

By Colleen Burge, The Conversation

Oysters, a delicacy eaten on most coastlines of the world, are a multi-billion-dollar industry. They also are intriguing to study from a health perspective. Oysters feed by filtering tiny plankton from the surrounding water, processing up to 50 gallons per oyster daily. In doing so, they improve water quality and make their ecosystems healthier. But the water that they grow can be filled with disease-causing microorganisms that can affect both oysters and humans.

Today a deadly herpes virus, Ostreid herpesvirus 1 (OsHV-1), is threatening Pacific oysters (Crassostrea gigas), the world's most popular and valuable oyster species. It is almost certain to spread more widely in our globally connected world.

I know what you're thinking: "Oysters get herpes??" Yes, and they can also can get sick from other types of pathogens and stresses. But you won't contract this virus from eating an oyster, whether you enjoy them on the half-shell or cooked. OsHV-1 can infect other bivalve species, like some animal herpes viruses that can cross species barriers, but it is genetically distinct from other animal herpes viruses and does not infect humans.

With support from the NOAA Sea Grant aquaculture program, I'm working with a diverse team that includes researchers, regulators and outreach specialists in the United States and abroad to better prepare the U.S. oyster industry for the spread of this virus.

Pacific oysters are native to Asia and are the most popular and valued oyster for aquaculture globally. Humans transferred them from their native range to multiple grow-out areas globally, including France, the United States and Australia. They are the primary species grown on the U.S. West Coast, whereas both wild and cultured Eastern oysters grow on the East and Gulf coasts. In contrast to Eastern oysters, Pacific oysters were relatively resistant to infectious diseases until OsHV-1 emerged in the early 1990s.

Herpes is often fatal to Pacific oysters. That's especially true for OsHV-1 microvariants – mutant variants of OsHV-1 which are more virulent than the original reference strain. These viruses are spreading globally, causing mass mortalities of Pacific oysters.

An OsHV-1 microvariant was first detected in France in 2008, where it killed 80 to 100 percent of affected oyster beds. Since then, similar variants have caused mass mortalities of oysters in many European countries. A 2010 outbreak in England killed over eight million oysters.

OsHV-1 microvariants also infect Pacific oysters in New Zealand and Australia. Their spread in Australia, in particular to Tasmania, has crippled the Australian Pacific oyster aquaculture industry.

U.S. oyster growers are strongly concerned about the spread of OsHV-1 microvariants globally. I was part of the team that first detected OsHV-1 in Tomales Bay, California. To date the virus has been detected only in oysters in Tomales Bay and an adjacent bay, and no

microvariants have been found yet in U.S. waters. The California OsHV-1 causes mortalities of young Pacific oysters, but is thought to be less virulent than OsHV-1 microvariants.

Given the spread of the OsHV-1 microvariants elsewhere around the world, it may only be a matter of time until they reach U.S. coastal bays or other nonimpacted oyster growing areas. We spent the summer of 2017 conducting experiments in Tomales Bay to determine whether any cultured U.S. oysters species are resistant to OsHV-1, and soon will also conduct laboratory challenges with OsHV-1 microvariants.

Once OsHV-1 is established within a bay, mass oyster deaths typically occur each year during the summer when water temperatures are warm. The situation is analogous to a human who is infected with herpes and periodically get cold sores. Normally the virus is latent (present at a low level) and does not cause cold sores. But after a stressful situation, the virus replicates and cold sores emerge.

Not all oysters die of herpes, and if OsHV-1 behaves like other herpes viruses, it probably remains present latently within infected oysters' tissues and is reactivated after a stressful event. For oysters, most of the evidence for virus reactivation points to warm summer water conditions.

We can't vaccinate oysters, and even if antibiotics were effective against viruses, they are not permitted for treating oysters in the United States. Though oysters have an innate immune system that destroys foreign invaders, it lacks an adaptive response, including cells that "remember," recognize and destroy specific pathogens, as human B or T lymphocytes do. Most vaccines rely on this "immune memory" to be effective. Recent research indicates that oysters' innate immune systems can be stimulated by a virus mimic, but we do not know whether this effect is long-lasting.

The most effective strategy to date has been developing disease-resistant oyster lines, which can limit both mortalities and oysters' susceptibility to infection. But this approach involves exposing healthy oysters to the virus – and moving oysters infected with OsHV-1 to naive (disease-free) areas could spread the virus. This means that we can use this approach only in places where OsHV-1 already exists.

Toward that end, breeding programs in locations including France, New Zealand and Australia are working to develop OsHV-1-resistant Pacific oysters. A complementary approach is to expose oysters and determine genes involved in OsHV-1 resistance. I am currently working with two strains of OsHV-1 – the California virus and a microvariant in France – to determine OsHV-1 resistance genes, including a collaboration with the Ifremer station in La Tremblade, France.

The most effective way to limit damage in new locations from OsHV-1 is to limit its spread. However, we also want to be ready in case OsHV-1 microvariants spread to the United States. Beyond their cash value and the benefits that oysters provide by filtering water, oyster reefs provide food and habitat for many commercial fish species. Oysters can't move themselves out of harm's way, nor can we move all susceptible oysters, so we need to protect them where they grow.

http://bbc.in/2wuRKwf

More pregnant women to get Group B Strep treatment

All pregnant women who go into labour too soon should be given antibiotics to protect their baby from a potentially deadly infection called Group B Strep (GBS), say new guidelines.

By Michelle Roberts Health editor, BBC News online

Hundreds of newborn babies a year in the UK catch it. With prompt treatment, most can make a full recovery. Currently, two in every 20 infected babies develops a disability and one in every 20 dies.

The Royal College of Obstetricians and Gynaecologists wants to change this. It says any woman who goes into labour before 37 weeks should be offered antibiotics as a precaution, even if her waters have not broken and the protective amniotic sac surrounding the baby in the womb is still intact.

Group B Strep bacteria can live harmlessly in the lower vaginal tract - about one in four women has it - and it can be passed on to the baby during delivery. Most women will not realise they are a carrier.

The updated guidelines from the RCOG say pregnant women should be given information about the condition to raise awareness.

They also say women who have tested positive for GBS in a previous pregnancy can be tested at 35 to 37 weeks in subsequent pregnancies to see if they also need antibiotics in labour.

But they do not go as far as recommending routine screening of mothers-to-be.

The RCOG says there is no clear evidence that this would be beneficial, as previously stated by the government's National Screening Committee but campaigners disagree.

Group B Strep Support would like every pregnant woman to be offered the opportunity to be tested for the bacteria.

Chief executive Jane Plumb said: "The RCOG guideline is a significant improvement on previous editions, however, the UK National Screening Committee still recommends against offering GBS screening to all pregnant women, ignoring international evidence that shows such screening reduces GBS infection, disability and death in newborn babies."

Rebecca Gunn, 32 and from Wakefield, had GBS during her second pregnancy.

"I had gone in to hospital after experiencing some bleeding at 17 weeks, and that is when they picked up that I was a GBS carrier.

"The diagnosis came out of the blue. I was really surprised, as GBS hadn't even crossed my mind."

Rebecca went into labour at 38 weeks and was given intravenous antibiotics after her waters broke.

She gave birth to her son, Alistair, who was fortunately unaffected by GBS.

"I knew nothing about GBS. I'm not saying this to scare people, but it's important they are informed and aware of the risks," she said.

Group B Strep facts

GBS is not a sexually transmitted disease. Treating a woman carrying GBS does not prevent these normal bacteria that many adults carry from returning

A woman who has it will not usually have symptoms or side-effects

Testing is the only way to know if you are carrying GBS

If you are pregnant and found to have it, steps can be taken to reduce the risk of GBS to your baby

http://bit.ly/2fowzpK

Type 2 diabetes is a reversible condition

A body of research putting people with Type 2 diabetes on a low calorie diet has confirmed the underlying causes of the condition and established that it is reversible.

Professor Roy Taylor at Newcastle University, UK has spent almost four decades studying the condition and will present an overview of his findings at the European Association For The Study Of Diabetes (EASD 2017) in Lisbon. In the talk he will be highlighting how his research has revealed that for people with Type 2 diabetes:

- ***Excess calories leads to excess fat in the liver***
- ***As a result, the liver responds poorly to insulin and produces too much glucose***
- ***Excess fat in the liver is passed on to the pancreas, causing the insulin producing cells to fail***
- ***Losing less than 1 gram of fat from the pancreas through diet can re-start the normal production of insulin, reversing Type 2 diabetes***
- ***This reversal of diabetes remains possible for at least 10 years after the onset of the condition***

"I think the real importance of this work is for the patients themselves," Professor Taylor says. "Many have described to me how embarking on the low calorie diet has been the only option to prevent what they thought - or had been told - was an inevitable decline into further medication and further ill health because of their diabetes. By studying the underlying mechanisms we have been able to demonstrate the simplicity of type 2 diabetes."

Get rid of the fat and reverse Type 2 diabetes

The body of research by Professor Roy Taylor now confirms his Twin Cycle Hypothesis - that Type 2 diabetes is caused by excess fat actually within both liver and pancreas.

This causes the liver to respond poorly to insulin. As insulin controls the normal process of making glucose, the liver then produces too much glucose. Simultaneously, excess fat in the liver increases the normal process of export of fat to all tissues. In the pancreas, this excess fat causes the insulin producing cells to fail.

The Counterpoint study which was published in 2011, confirmed that if excess food intake was sharply decreased through a very low calorie diet, all these abnormal factors would be reversed.

The study showed a profound fall in liver fat content resulting in normalisation of hepatic insulin sensitivity within 7 days of starting a very low calorie diet in people with type 2 diabetes. Fasting plasma glucose became normal in 7 days. Over 8 weeks, the raised pancreas fat content fell and normal first phase insulin secretion became re-established, with normal plasma glucose control.

Keep the weight off and keep the diabetes at bay

"The good news for people with Type 2 diabetes is that our work shows that even if you have had the condition for 10 years, you are likely to be able to reverse it by moving that all important tiny amount of fat out of the pancreas. At present, this can only be done through substantial weight loss", Professor Taylor adds.

The Counterbalance study published in 2016, demonstrated that Type 2 diabetes remains reversible for up to 10 years in most people, and also that the normal metabolism persists long term, as long as the person doesn't regain the weight.

Professor Taylor explained the science behind the mechanisms: "Work in the lab has shown that the excess fat in the insulin producing cell causes loss of specialised function. The cells go into a survival mode, merely existing and not contributing to whole body wellbeing. Removal of the excess fat allows resumption of the specialised function of producing insulin. The observations of the clinical studies can now be fully explained."

He added: "Surprisingly, it was observed that the diet devised as an experimental tool was actually liked by research participants. It was associated with no hunger and no tiredness in most people, but with rapidly increased wellbeing. The 'One, Two' approach used in the Counterbalance study was a defined two phase programme. The Phase 1 is the period of weight loss - calorie restriction without additional exercise. A carefully planned transition period leads to Phase 2 - long term supported weight maintenance by modest calorie restriction with increased daily physical activity." This approach consistently brings about 15kg of weight loss on average.

After the details were posted on the Newcastle University, UK website, this has been applied clinically and people who were highly motivated have reported that they have reversed their type 2 diabetes and continued to have normal glucose levels (normoglycaemic) over years.

A further study in general practice, the Diabetes Remission Clinical Trial (DiRECT) funded by Diabetes UK is now underway to determine the applicability of this general approach to routine Primary Care practice with findings due before the end of the year.

Patients or GPs who would like more information about the diet that reverses Type 2 diabetes see the Magnetic Resonance Centre website.

http://bit.ly/2fau2Tu

Asthma drug from the garden center

Researchers at the University of Bonn test a substance from the leaves of a common ornamental plant

The coralberry could offer new hope for asthmatics: researchers at the University of Bonn have extracted a new kind of active pharmaceutical ingredient from its leaves to combat this widespread respiratory disease. In mice, it almost completely inhibits the characteristic contraction of the airways. The plant itself is not exotic:

it can be found in any well-stocked garden center. The study is published in the renowned journal Science Translational Medicine.

The coralberry is no outstanding beauty most of the year. This however changes in the winter months: it then forms striking, bright red berries, which make it a popular ornamental plant during this time. Nevertheless, the scientists involved in the study are interested in the plant for another reason: the leaves of the coralberry contain a substance with the cryptic name FR900359. It is assumed that this could be suitable as a medication against certain diseases, despite the fact that Ardisia crenata (its botanical name) has so far been largely disregarded by science.

The leaves of the coralberry (Ardisia crenata) contain the natural substance FR900359. **Raphael Reher/Daniela Wenzel/Uni Bonn**

Researchers at the Institutes of Physiology I, Pharmaceutical Biology and Pharmaceutical Chemistry at the University of Bonn, together with asthma specialists from Nottingham (United Kingdom), have now published a study that could change this. They found that FR900359 is very effective at preventing the bronchial muscles from contracting. Asthmatics regularly suffer from these pronounced contractions preventing adequate ventilation of the lungs. The resulting shortness of breath can be life-threatening.

More effective than common medicines

The new compound relieves these spasms - and is supposedly more effective and has a more prolonged action than the most common asthma drug salbutamol. "However, we have so far only tested the substance in asthmatic mice," explains junior professor Dr. Daniela Wenzel. Wenzel is doing research in respiratory diseases at the Institute of Physiology I at the University of Bonn; she was the leader of the study.

The idea to test FR900359 came from the Institute of Pharmaceutical Biology: there, the scientists managed to isolate and characterize the active pharmaceutical substance from the leaves of the coralberry. "This compound inhibits critical signaling molecules in our cells, the Gq proteins," explains Wenzel. Gq proteins exert key functions in many processes in the body - including control of the airway tone.

Normally, interaction of various signaling pathways induces narrowing of the airways. Inhibition of individual signaling pathways can reduce the contraction of the respiratory tract. However, this does not make it possible to completely prevent such contractions in patients with severe asthma. The various contracting signals converge on Gq proteins and trigger airway spasm. "When we inhibit the activation of Gq proteins with FR900359, we achieve a much greater effect," emphasizes Dr. Michaela Matthey from the Institute of Physiology I.

This worked exceptionally well in asthmatic mice in the study. "We were able to prevent the animals from reacting to allergens such as house dust mite with a narrowing of the bronchia," Wenzel is pleased to report. There were hardly any side effects, as the active pharmaceutical ingredient could be applied via inhalation to the respiratory tract and thus only reached the systemic circulation in small quantities. However, it is not known whether the substance is also suitable for use in people. Although the scientists have already been able to show that human bronchial muscle cells in a petri dish and isolated human airways react in a similarly promising manner, further tests, which could take years, are required prior to its application in people.

Nevertheless, the work is already a great success. This is no coincidence: the German Research Foundation (DFG) funds the research group "G protein signal cascades: creating new pharmaceutical concepts with molecular probes and active pharmaceutical ingredients" at the University of Bonn. The aim is to pharmaceutically influence central signaling molecules such as the Gq

proteins to identify novel substances for the treatment of certain diseases. Physiologists and pharmacists at the University collaborate closely within the research group; the current study is the result of this successful scientific interaction.

Publication: Michaela Matthey, Richard Roberts, Alexander Seidinger, Annika Simon, Ralf Schröder, Markus Kuschak, Suvi Annala, Gabriele M König, Christa E Müller, Ian P Hall, Evi Kostenis, Bernd K Fleischmann, Daniela Wenzel: Targeted inhibition of Gq signaling induces airway relaxation in mouse models of asthma; Science Translational Medicine; DOI: 10.1126/scitranslmed.aag2288

http://bit.ly/2xpGAwN

Brain rewiring in Parkinson's disease may contribute to abnormal movement

The brain's own mechanisms for dealing with the loss of dopamine neurons in Parkinson's disease may be a source of the disorder's abnormal movement, according to a Northwestern Medicine study published in Neuron.

The study suggests the loss of dopamine may cause the brain to rewire in a maladaptive manner, contributing to impaired movement in Parkinson's disease. These findings also suggest that there are fundamental problems with scientists' traditional model of Parkinson's disease, said senior author Mark Bevan, PhD, professor of Physiology at Northwestern University Feinberg School of Medicine.

The prevailing consensus was that excessive patterning of the subthalamic nucleus (STN), a component of the basal ganglia, by the cerebral cortex was linked to the symptomatic expression of Parkinson's disease, including muscle rigidity and slowness of movement, according to Bevan. "When one saw a burst of activity in the cortex that was consistently followed by an abnormal burst of activity in the STN, scientists assumed that the direct connection between the two was responsible," Bevan said.

Thus, Bevan and his colleagues, including lead author Hong-Yuan Chu, PhD, a post-doctoral fellow in the Bevan Lab, expected to see transmission in the cortex-to-STN pathway increase as dopamine levels dropped. Instead, they found the opposite: the strength of the pathway decreased massively. "Like most scientists who come across something unexpected, we thought we'd done something wrong," Bevan said. "So, we used multiple, complementary approaches but everything pointed to the same conclusion."

Further investigation suggested abnormal activity in a more indirect pathway from the cortex to the STN, involving the globus pallidus, was responsible. Abnormal activity in the indirect pathway leaves the STN vulnerable to excessive excitation, triggering compensatory plasticity that ultimately proved to be harmful, according to the study.

When the scientists prevented this maladaptive plasticity in late-stage Parkinson's models, they found the symptoms improved, pointing to a link between compensation and motor dysfunction.

"According to the classic model, these adaptations should be homeostatic and preserve STN function," Bevan said. "Preventing them should make the symptoms much worse -- but it made them better instead."

While the compensatory mechanisms may initially keep the brain operating normally under conditions of moderate dopamine neuron loss, as the disease progresses and more dopamine neurons die, the adaptations may become so extreme that they impair movement, according to the study. These results suggest that there are fundamental flaws in our traditional understanding of brain dysfunction in Parkinson's disease, Bevan said.

For Bevan, the unexpected results in this study served as a reminder that scientists must remain open-minded. "It's easy to be emotional and cling to your hypothesis," Bevan said. "You have to be dispassionate, open-minded, and look at the data -- if the data is not consistent with the hypothesis then you have to reject it and come up with a new one."

This study was funded by the National Institutes of Health's National Institute of Neurological Disorders and Stroke grants 2R37 NS041280, P50 NS047085, 5T32 NS041234, and F31 NS090845. Confocal imaging work was performed at the Northwestern University Center for Advanced Microscopy, which was supported by National Cancer Institute Cancer Center Support grant P30 CA060553.

http://bit.ly/2x4bPhr

Ebola, Zika & More: How Many Viruses Can Get into Men's Semen?

At least 27 viruses can make their way into human semen

By Rachael Rettner, Senior Writer

During recent outbreaks of the Zika virus, researchers discovered that the virus could find its way into men's semen and stay there for months. But how many other viruses can get into semen?

To find out, researchers at the University of Oxford in the United Kingdom searched the scientific literature for reports of "viremic" viruses — ones that get into the blood — that have also been found in semen.

The results showed that at least 27 viruses can make their way into human semen. "The presence of viruses in semen is probably more widespread than currently appreciated," the researchers wrote in the October issue of the journal Emerging Infectious Diseases.

The list includes a number of well-known viruses, such as Ebola, HIV, hepatitis C, chickenpox, herpes, mumps and chikungunya (a mosquito-borne virus), as well as some lesser-known viruses, such as JC virus, simian foamy virus and Rift Valley fever.

In addition, some of these viruses, such as HIV and herpes, are known to spread sexually. But for many of the viruses on the list, it's unclear whether they can be spread through sex, the researchers said.

The results raise a number of questions, including how long the viruses remain in semen, at what concentrations they are present, and whether the viruses remain "viable" or capable of causing disease, the researchers said. The answers to these questions will help researchers better understand the risk for sexual spread of these viruses, the study said.

More research is also needed on whether these viruses can infect sperm, the researchers said. (Sperm are men's reproductive cells, whereas semen is usually a mixture of sperm and fluids.) This is an important question, because infections in sperm could cause mutations in the sperm DNA that might be passed on to the next generation, and possibly increase the risk of conditions such as cancer, the researchers said.

It's thought that some viruses persist in semen — even when they've been cleared from the rest of the body — because the testes are an "immunologically privileged" site in the body, meaning they are protected from attack by the body's immune system.

The findings also highlight the need for researchers to consider whether treatments being developed for viral diseases can be effective against viruses in all parts of the body, including the male reproductive tract, the researchers said.

http://nyti.ms/2f1zrZ5

Climate Change Threatens the World's Parasites (That's Not Good)

As many as one in three parasite species may go extinct in the next century, a new study finds, which is not cause for celebration.

Carl Zimmer

Animals around the world are on the move. So are their parasites.

Recently, scientists carried out the first large-scale study of what climate change may do to the world's much-loathed parasites. The team came to a startling conclusion: as many as one in three parasite species may face extinction in the next century.

As global warming raises the planet's temperature, the researchers found, many species will lose territory in which to survive. Some of their hosts will be lost, too.

"It still absolutely blows me away," said Colin J. Carlson, lead author of the study and a graduate student at the University of California, Berkeley.

He knows many people may react to the news with a round of applause. "Parasites are obviously a hard sell," Mr. Carlson said.

But as much as a tapeworm or a blood fluke may disgust us, parasites are crucial to the world's ecosystems. Their extinction may effect entire food webs, perhaps even harming human health.

Parasites deserve some of the respect that top predators have earned in recent decades. Wolves were once considered vermin, for example — but as they disappeared, ecosystems changed.

Scientists realized that as top predators, wolves kept populations of prey in check, which allowed plants to thrive. When wolves were restored to places like Yellowstone local ecosystems revived, as well.

Researchers have begun carefully studying the roles that parasites play. They make up the majority of the biomass in some ecosystems outweighing predators sharing their environments by a factor of 20 to 1.

Specimens from the National Parasite Collection, which holds more more than 20 million parasites of all varieties. Though reviled, parasites play a significant role in maintaining the world's ecosystems. **Paul Fetters for the Smithsonian Institution**

For decades, scientists who studied food webs drew lines between species — between wildebeest and the grass they grazed on, for example, and between the wildebeest and the lions that ate them.

In a major oversight, they didn't factor in the extent to which parasites feed on hosts. As it turns out, as much as 80 percent of the lines in a given food web are links to parasites. They are big players in the food supply.

Parasites can control populations of their hosts. Some are killed outright; other hosts, once infected, cannot reproduce, which would divert resources that the parasite craves to eggs or sperm. Some parasites move from host to host by making prey species easier for predators to kill.

So if these horrendous pests are major players in ecosystems that we want to save — what then? "This view requires that parasites be protected alongside their hosts," said Kevin D. Lafferty, an ecologist at the University of California, Santa Barbara, who was not involved in the new study.

A warming climate complicates the picture. Some researchers had already investigated the fate of a few parasite species, but Mr. Carlson and his colleagues wanted to get a global view of the impact of climate change.

They began their work with the National Parasite Collection, founded in 1892 and now maintained by the Smithsonian Institution. One of the world's biggest, it includes 20 million specimens, some preserved in jars of alcohol and some mounted on slides.

By determining the present range of each parasite species, Mr. Carlson and his colleagues were able to estimate the kind of climate in which it can survive and how it might fare in a hotter world.

Building this global geographic database took five years. The researchers often relied on the old tags and cards stored with the specimens to figure out where they lived — often a difficult task.

"Sometimes you'd just get, 'Island, Ocean,'" Mr. Carlson said. "You can imagine the stress that caused."

After he and his colleagues were done sifting through the collection, they ended up with 53,133 parasites they felt confident enough to use in their study. The records come from 457 species of tapeworms, ticks, fleas and other animals.

Parasites typically live in or on their hosts, but that does not protect them from climate change. Rising air temperatures can harm them. Ticks, for instance, risk baking in the heat as they wait in the grass for their next victim. Hookworm larvae require damp soil to survive before slipping into someone's foot.

And parasites need their hosts — if they go extinct, their parasites probably will, too. So Mr. Carlson and his colleagues also evaluated how hosts are expected to fare in response to climate change.

The researchers combined all these factors to estimate the risk that each kind of parasite faced. Some kinds won't lose much in a warming world, the study found. For instance, thorny-headed worms

are likely to be protected because their hosts, fish and birds, are common and widespread. But other types, such as fleas and tapeworms, may not be able to tolerate much change in temperature; many others infect only hosts that are facing extinction, as well.

In all, roughly 30 percent of parasitic species could disappear, Mr. Carlson concluded. The impact of climate change will be as great or greater for these species as for any others studied so far.

Dr. Lafferty said the new results challenged those of much smaller studies, which had come to opposite conclusions. “Our natural tendency is to assume that parasites and the disease they cause will increase as the rest of biodiversity declines,” he said.

Mr. Carlson said that climate change would do more than just drive some species extinct. Some parasites would move into new territory.

Deer ticks, for example, spread Lyme disease, and climate change models suggest they have a rosy future as they expand northward. “We’re not worried about them going extinct,” said Mr. Carlson.

Migrating parasites like these will arrive in ecosystems where other parasitic species are disappearing. With less competition, they may be able to wreak more havoc — and not just on animal hosts. Many human diseases are the result of parasites and pathogens jumping from animal species to our own. “If parasites are keeping disease down in wildlife, they might also be indirectly keeping them down in humans,” Mr. Carlson said. “And we might lose that.”

http://bit.ly/2wktMc0

Could interstellar ice provide the answer to birth of DNA?

Researchers at the University of York have shown that molecules brought to earth in meteorite strikes could potentially be converted into the building blocks of DNA.

They found that organic compounds, called amino nitriles, the molecular precursors to amino acids, were able to use molecules present in interstellar ice to trigger the formation of the backbone molecule, 2-deoxy-D-ribose, of DNA. It has long been assumed that amino acids were present on earth before DNA, and may have been responsible for the formation of one of the building blocks of DNA, but this new research throws fresh doubt on this theory.

Dr Paul Clarke, from the University of York's Department of Chemistry, said: "The origin of important biological molecules is one of the key fundamental questions in science. The molecules that form the building blocks of DNA had to come from somewhere; either they were present on Earth when it formed or they came from space, hitting earth in a meteor shower.

"Scientists had already shown that there were particular molecules present in space that came to Earth in an ice comet; this made our team at York think about investigating whether they could be used to make one of the building blocks of DNA. If this was possible, then it could mean that a building block of DNA was present before amino acids."

In order for cellular life to emerge and then evolve on earth, the fundamental building blocks of life needed to be synthesised from appropriate starting materials - a process sometimes described as 'chemical evolution'.

The research team showed that amino nitriles could have been the catalyst for bringing together the interstellar molecules, formaldehyde, acetaldehyde, glycolaldehyde, before life on Earth began. Combined, these molecules produce carbohydrates, including 2-deoxy-D-ribose, the building blocks of DNA. DNA is one of the most important molecules in living systems, yet the origin 2-deoxy-D-ribose, before life on earth began, has remained a mystery.

Dr Clarke said: "We have demonstrated that the interstellar building blocks formaldehyde, acetaldehyde and glycolaldehyde can be converted in 'one-pot' to biologically relevant carbohydrates - the ingredients for life. "This research therefore outlines a plausible mechanism by which molecules present in interstellar space, brought to earth by meteorite strikes, could potentially be converted into 2-deoxy-D-ribose, a molecule vital for all living systems."

The research is published in the journal Chemical Communications.

http://bit.ly/2f1asoM

Is the Alzheimer's gene the ring leader or the sidekick?

A lesser known gene, TOMM40, appears to have significant influence on late-life development of dementia and Alzheimer's

The notorious genetic marker of Alzheimer's disease and other forms of dementia, ApoE4, may not be a lone wolf.

Researchers from USC and the University of Manchester have found that another gene, TOMM40, complicates the picture. Although ApoE4 plays a greater role in some types of aging-related memory ability, TOMM40 may pose an even greater risk for other types.

TOMM40 and APOE genes are neighbors, adjacent to each other on chromosome 19, and they are sometimes used as proxies for one another in genetic studies. At times, scientific research has focused chiefly on one APOE variant, ApoE4, as the No. 1 suspect behind Alzheimer's and dementia-related memory decline. The literature also considers the more common variant of APOE, ApoE3, neutral in risk for Alzheimer's disease.

USC researchers believe their new findings raise a significant research question: Has TOMM40 been misunderstood as a sidekick to ApoE4 when it is really a mastermind, particularly when ApoE3 is present?

"Typically, ApoE4 has been considered the strongest known genetic risk factor for cognitive decline, memory decline, Alzheimer's disease or dementia-related onset," said T. Em Arpawong, the study's lead author and a post-doctoral fellow in the USC Dornsife College of Letters, Arts and Sciences Department of Psychology. "Although prior studies have found some variants of this other gene TOMM40 may heighten the risk for Alzheimer's disease, our study found that a TOMM40 variant was actually more influential than ApoE4 on the decline in immediate memory - the ability to hold onto new information."

Studies have shown that the influence of genes associated with memory and cognitive decline intensifies with age. That is why the scientists chose to examine immediate and delayed verbal test results over time in conjunction with genetic markers.

"An example of immediate recall is someone tells you a series of directions to get somewhere and you're able to repeat them back," explained Carol A. Prescott, the paper's senior author who is a professor of psychology at USC Dornsife College and professor of gerontology at the USC Davis School of Gerontology. "Delayed recall is being able to remember those directions a few minutes later, as you're on your way."

The study was published in the journal PLOS ONE on Aug. 11.

Prescott and Arpawong are among the more than 70 researchers at USC who are dedicated to the prevention, treatment and potential cure of Alzheimer's disease. The memory-erasing illness is one of the greatest health challenges of the century, affecting 1 in 3 seniors and costing $236 billion a year in health care services. USC researchers across a range of disciplines are examining the health, societal and political effects and implications of the disease.

In the past decade, the National Institute on Aging has nearly doubled its investment in USC research. The investments include an Alzheimer Disease Research Center.

Tracking memory loss

For the study, the team of researchers from USC and The University of Manchester utilized data from two surveys: the U.S. Health and Retirement Study and the English Longitudinal Study of Ageing. Both data sets are nationally representative samples and include results of verbal memory testing and genetic testing.

The research team used verbal test results from the U.S. Health and Retirement Survey, collected from 1996 to 2012, which interviewed participants via phone every two years. The researchers utilized the verbal memory test scores of 20,650 participants, aged 50 and older who were tested repeatedly to study how their memory changed over time.

To test immediate recall, an interviewer read a list of 10 nouns and then asked the participant to repeat the words back immediately. For delayed recall, the interviewer waited five minutes and then asked the participant to recall the list. Test scores ranged from 0 to 10.

The average score for immediate recall was 5.7 words out of 10, and the delayed recall scoring average was 4.5 words out of 10. A large gap between the two sets of scores can signal the development of Alzheimer's or some other form of dementia.

"There is usually a drop-off in scores between the immediate and the delayed recall tests," Prescott said. "In evaluating memory decline, it is important to look at both types of memory and the difference between them. You would be more worried about a person who has scores of 10 and 5 than a person with scores of 6 and 4."

The first person is worrisome because five minutes after reciting the 10 words perfectly, he or she can recall only half of them, Prescott said. The other person wasn't perfect on the immediate recall test, but five minutes later, was able to remember a greater proportion of words.

To prevent bias in the study's results, the researchers excluded participants who reported that they had received a likely diagnosis of dementia or a dementia-like condition, such as Alzheimer's. They also focused on participants identified as primarily European in heritage to minimize population bias. Results were adjusted for age and sex.

The researchers compared the U.S. data to the results of an independent replication sample of participants, age 50 and up, in the English Longitudinal Study of Aging from 2002 to 2012. Interviews and tests were conducted every two years.

Genetic markers of dementia

To investigate whether genes associated with immediate and delayed recall abilities, researchers utilized genetic data from 7,486 participants in the U.S. Health and Retirement Study and 6,898 participants in the English Longitudinal Study of Ageing.

The researchers examined the association between the immediate and delayed recall results with 1.2 million gene variations across the human genome. Only one, TOMM40, had a strong link to declines in immediate recall and level of delayed recall. ApoE4 also was linked but not as strongly.

"Our findings indicate that TOMM40 plays a larger role, specifically, in the decline of verbal learning after age 60," the scientists wrote. "Further, our analyses showed that there are unique effects of TOMM40 beyond ApoE4 effects on both the level of delayed recall prior to age 60 and decline in immediate recall after 60."

Unlike ApoE4, the ApoE3 variant is generally thought to have no influence on Alzheimer's disease or memory decline. However, the team of scientists found that adults who had ApoE3 and a risk variant of TOMM40, were more likely to have lower memory scores. The finding suggests that TOMM40 affects memory - even when ApoE4 is not a factor.

The team suggested that scientists should further examine the association between ApoE3 and TOMM40 variants and their combined influence on decline in different types of learning and memory.

"Other studies may not have detected the effects of TOMM40," Prescott said. "The results from this study provide more evidence that the causes of memory decline are even more complicated than we thought before, and they raise the question of how many findings in other studies have been attributed to ApoE4 that may be due to TOMM40 or a combination of TOMM40 and ApoE4."

Other study co-authors from USC were John J. McArdle (Dornsife College and Davis School); Margaret Gatz (Dornsife College, Davis School and Keck School of Medicine of USC); Chris Armoskus (Zilkha Neurogenetics Institute, Keck School of Medicine) and James A. Knowles (formerly of the Keck School of Medicine now at State University of New York Downstate Medical Center). Co-authors from the University of Manchester were Neil Pendleton and Krisztina Mekli.

Ninety percent of the data analysis for the study was covered by a National Institute on Aging grant (F32-AG-048681) of $158,374 to Arpawong and an NIA pilot award (P30-AG-017265) of $24,970 from the USC/UCLA Center on Biodemography and Population Health. The remaining support for the data analysis was covered by funds from USC and the University of Manchester.

http://bit.ly/2y5fmc1

SIDS research confirms changes in babies' brain chemistry

University of Adelaide researchers have confirmed that abnormalities in a common brain chemical are linked to sudden infant death syndrome (SIDS).

In the first study of its kind looking at babies outside the United States, researchers from the University of Adelaide's Adelaide Medical School investigated 41 cases of SIDS deaths and discovered striking abnormalities in chemical serotonin within the brain.

Serotonin, otherwise known as 5-HT, is a neurotransmitter found in different parts of the human body, including the central nervous system. Among its many roles, serotonin is involved in the regulation of sleep, and also control of the cardiovascular and respiratory systems.

This latest research, published in the Journal of Neuropathology & Experimental Neurology, confirms and supports the concept that brainstem dysfunction, resulting in significantly altered serotonin expression, is associated with some SIDS deaths.

SIDS is the sudden unexpected death of an infant under one year of age that cannot be explained after a thorough investigation, including an autopsy. It is the leading cause of death in infants between one month and one year of age in Australia and the developed world.

The research was conducted by PhD student Dr Fiona Bright under the supervision of University of Adelaide Professor of Pathology Roger Byard. Dr Bright today graduated with her PhD from the University of Adelaide.

Her work builds on research conducted in the United States at the Boston Children's Hospital and Harvard Medical School, where Dr Bright was based for 18 months during her combined studies.

"Our research is significant because it has confirmed that abnormalities in serotonin in the brain are most definitely linked to cases of SIDS. This helps to support the findings of the American research," Dr Bright says.

"Serotonin is a key neurochemical that plays an important role in the control and management of the complex respiratory, cardiovascular and autonomic systems within the human infant brainstem.

"Our research suggests that alterations in these neurochemicals may contribute to brainstem dysfunction during a critical postnatal developmental period. As a result, this could lead to an inability of a SIDS infant to appropriately respond to life-threatening events, such as lack of oxygen supply during sleep.

"Notably, the SIDS cases we studied were all linked to at least one major risk factor for SIDS, with more than half of the infants found in an adverse sleeping position and having had an illness one month prior to death," Dr Bright says.

Professor Byard says: "Better understanding of the complex role of these neurochemicals, and the exact causes of their dysfunction in the brain, will help future research to develop potential biomarkers for infants at increased risk of SIDS.

"Ultimately, we hope that this work will lead to improved prevention strategies, helping to save baby's lives and the emotional trauma experienced by many families."

This research was funded under a Fellowship established by the River's Gift SIDS charity.

"River's Gift's primary objective is to fund world-leading SIDS research to make a tangible contribution to the discovery of a cure for this heart-breaking loss of life," says River's Gift General Manager Karl Waddell.

"The University of Adelaide research is a significant step towards achieving that objective."

http://bit.ly/2yeUznd

New theory on origin of the asteroid belt

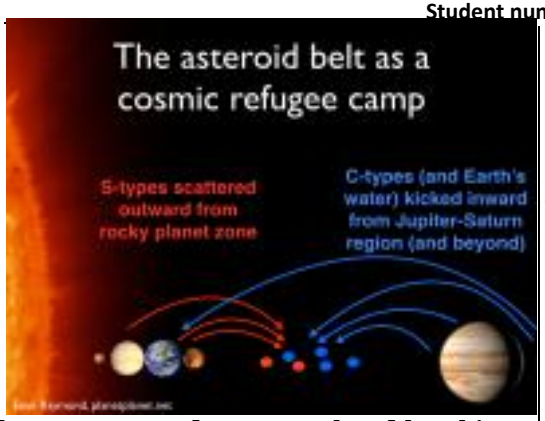
A pair of researchers with Université de Bordeaux has proposed a new theory to explain the origin of the asteroid belt.

September 14, 2017 by Bob Yirka

Phys.org - In their paper published in Science Advances, Sean Raymond and Andre Izidoro describe their theory and what they found when trying to model it.

The asteroid belt (sometimes referred to as the main asteroid belt) orbits between Mars and Jupiter.

It consists of asteroids and minor planets forming a disk around the sun. It also serves as a sort of dividing line between the inner rocky planets and outer gas giants.



The asteroid belt may be have started out empty and was populated by objects from across the Solar System. Sean Raymond, planetplanet.net

Current theory suggests that the asteroid belt was once much more heavily populated, but the gravitational pull of Jupiter flung approximately 99 percent of its former material to other parts of the solar system or beyond. Astronomers also assumed that Jupiter's gravity prevented the material in the belt from coalescing into larger planets. In this new effort, the researchers propose a completely different explanation of the asteroid belt's origin—suggesting that the belt started out as an empty space and was subsequently filled by material flung from the inner and outer planets.

The researchers note that asteroids closer to the rocky planets (called S-type asteroids) tend to contain silicate, similar to the inner planets. By contrast, asteroids in the belt closer to the gas giants (called C-type asteroids) tend to contain more carbon, making them more like the gas giants. This, the researchers note, suggests that the asteroids actually came from the planets as they were forming—excess material was essentially kicked away into the asteroid belt, where it remains today.

To test their theory, the researchers created a model mimicking the early solar system, during which the asteroid belt starts out as empty. Running the model forward, they report, showed that it was possible that material from the other planets could have made its way to the belt, resulting in the disk observed today. They plan to continue their research to see if they can find more evidence for their theory, or for the conventional view.

Explore further: Astronomers identify oldest known asteroid family

More information: Sean N. Raymond et al. The empty primordial asteroid belt, Science Advances (2017). DOI: 10.1126/sciadv.1701138

Abstract

The asteroid belt contains less than a thousandth of Earth's mass and is radially segregated, with S-types dominating the inner belt and C-types the outer belt. It is generally assumed that the belt formed with far more mass and was later strongly depleted. We show that the present-day asteroid belt is consistent with having formed empty, without any planetesimals between Mars and Jupiter's present-day orbits. This is consistent with models in which drifting dust is concentrated into an isolated annulus of terrestrial planetesimals. Gravitational scattering during terrestrial planet formation causes radial spreading, transporting planetesimals from inside 1 to 1.5 astronomical units out to the belt. Several times the total current mass in S-types is implanted, with a preference for the inner main belt. C-types are implanted from the outside, as the giant planets' gas accretion destabilizes nearby planetesimals and injects a fraction into the asteroid belt, preferentially in the outer main belt. These implantation mechanisms are simple by-products of terrestrial and giant planet formation. The asteroid belt may thus represent a repository for planetary leftovers that accreted across the solar system but not in the belt itself.

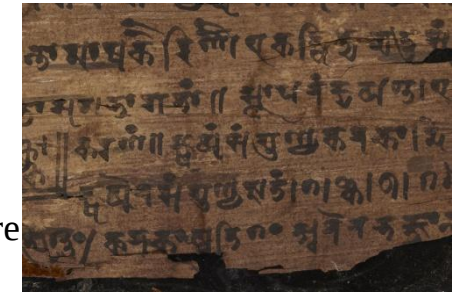
http://bit.ly/2h9CXSa

History of zero pushed back 500 years by ancient Indian text

The symbol "0" is a familiar sight, but its origins are far from certain.

By Timothy Revell

A recent batch of carbon dating is causing the history of mathematics to be rewritten, as it has discovered zeros dating back to a period 500 years before previously seen.



The earliest recorded use of zero **Bodleian Libraries, University of Oxford**

The numbers appear in an ancient Indian text called the Bakhshali manuscript, which consists of 70 leaves of birch bark, filled with

mathematics and text in the form of Sanskrit. “It seems to be a training manual for Buddhist monks,” says Marcus du Sautoy at the University of Oxford. The manuscript was first discovered by a local farmer in 1881, and was named after the village it was found in, in what is now Pakistan. It’s been housed by the University of Oxford’s Bodleian library since 1902.

Now, for the first time, the manuscript has been carbon dated – and this has immediately upturned some commonly held beliefs. It was originally thought that manuscript was from the 9th century, but the dating methods revealed that the oldest pages are from somewhere between 224 AD and 383 AD.

This means that the manuscript predates a 9th century inscription of zero on the wall of a temple in Gwalior, India, which was previously considered to be the oldest recorded example of a zero.

The 70 leaves of birch bark that make up the Bakhshali manuscript **Bodleian Libraries, University of Oxford**

Across the text there are hundreds of zeros denoted using a dot. It’s this dot that will later evolve to be the symbol with a hole in the middle that we know today. The dot was originally used as a placeholder, like how “0” is used in the number 505 to denote that there are no tens, but was not yet a number in its own right.

The use of zero as a placeholder appeared in several different ancient cultures, such as the ancient Mayans and Babylonians. But only the Indian dot that would eventually go on to gain true number status, first described in 628 AD by the Indian astronomer and mathematician Brahmagupta.

“Some of these ideas that we take for granted had to be dreamt up. Numbers were there to count things, so if there is nothing there why would you need a number?” says du Sautoy. The concept of zero, initially banned as heresy, was eventually allowed for the development of calculus, and underpins the digital age. “The whole of modern technology is built on the idea of something and nothing,” he says.

Dating it had always been tricky because not all of the pages come from the same date, with as many as 500 years between the oldest and youngest pages. “There’s still some mystery about how all of these leaves got collected together,” says du Sautoy.

http://bit.ly/2h6sn1S

AI spots Alzheimer’s brain changes years before symptoms emerge

MRI scans may help identify early signs of the disease

By Anil Ananthaswamy

Artificial intelligence can identify changes in the brains of people likely to get Alzheimer’s disease almost a decade before doctors can diagnose the disease from symptoms alone. The technique uses non-invasive MRI scans to identify alterations in how regions of the brain are connected.

Alzheimer’s is a neurodegenerative disease that is the leading cause of dementia for the elderly, eventually leading to loss of memory and cognitive functions. The race is on to diagnose the disease as early as possible. Although there is no cure, drugs in development are likely to work better the earlier they are given. An early diagnosis can also allow people to start making lifestyle changes to help slow the progression of the disease.

In an effort to enable earlier diagnosis, Nicola Amoroso and Marianna La Rocca at the University of Bari in Italy and their colleagues developed a machine-learning algorithm to discern structural changes in the brain caused by Alzheimer’s disease.

First, they trained the algorithm using 67 MRI scans, 38 of which were from people who had Alzheimer’s and 29 from healthy controls. The scans came from the Alzheimer’s Disease Neuroimaging

Initiative database at the University of Southern California in Los Angeles.

Positive discrimination

The idea was to teach the algorithm to correctly classify and discriminate between diseased and healthy brains. The researchers divided each brain scan into small regions and analysed the neuronal connectivity between them, without making any assumptions about the ideal size of these regions for diagnosis.

They found that the algorithm made the most accurate classification of Alzheimer's when the brain regions being compared were about 2250 to 3200 cubic millimetres. This was intriguing, says La Rocca, since this is similar to the size of the anatomical structures connected with the disease, such as the amygdala and hippocampus.

The team then tested the algorithm on a second set of scans from 148 subjects. Of these, 52 were healthy, 48 had Alzheimer's disease and 48 had mild cognitive impairment (MCI) but were known to have developed Alzheimer's disease 2.5 to nine years later.

The AI distinguished between a healthy brain and one with Alzheimer's with an accuracy of 86 per cent. Crucially, it could also tell the difference between healthy brains and those with MCI with an accuracy of 84 per cent.

This shows that the algorithm could identify changes in the brain that lead to Alzheimer's almost a decade before clinical symptoms appear. The researchers were limited by the scans available from the database, so they weren't able to test whether the algorithm could predict the onset of disease even earlier.

Early diagnosis

Alzheimer's disease has been linked to the formation of sticky beta-amyloid plaques and neurofibrillary tau tangles in the brain. "Nowadays, cerebrospinal fluid analyses and brain imaging using radioactive tracers can tell us to what extent the brain is covered with plaques and tangles, and are able to predict relatively accurately who is at high risk of developing Alzheimer's 10 years later," says La Rocca. "However, these methods are very invasive, expensive and only available at highly specialised centres."

In contrast, the new technique can distinguish with similar accuracy between brains that are normal and the brains of people with MCI who will go on to develop Alzheimer's disease in about a decade – but using a simpler, cheaper and non-invasive technique. More work will be needed to distinguish between people with MCI whose brains go on to age normally, or who might develop other kinds of dementia.

Blood tests that look for biomarkers of Alzheimer's could be even cheaper and simpler than the new technique, but none are on the market yet. "There are no blood tests for Alzheimer's disease," says Goran Šimić at the University of Zagreb in Croatia. "There have been some attempts, but without much success yet."

Next step

Patrick Hof at the Icahn School of Medicine at Mount Sinai in New York is intrigued by the new test. He says that a method that might predict the disease a decade before it is fully expressed would be "incredibly valuable" should preventative therapeutics emerge.

La Rocca says her team now intends to extend the technique to help with the early diagnosis of other neurodegenerative conditions such as Parkinson's disease. "It's a method that is very versatile," she says.

Reference: *arXiv, 1709.02369*

http://bbc.in/2xH5ybR

Every childhood vaccine may go into a single jab

A technology that could eventually see every childhood vaccine delivered in a single injection has been developed by US researchers.

By James Gallagher Health and science reporter, BBC News website

Their one-shot solution stores the vaccine in microscopic capsules that release the initial dose and then boosters at specific times.

The approach has been shown to work in mouse studies, described in the journal Science.

The researchers say the technology could help patients around the world.

Childhood immunisations come with tears and screams. And there are a lot of them.

- ***Diphtheria, tetanus, whooping cough, polio, Hib and hepatitis B at eight, 12 and 16 weeks.***
- ***Pneumococcal jab at eight weeks, 16 weeks and one year***
- ***Men B vaccine at eight weeks, 16 weeks and one year***
- ***Hib/Men C vaccine at one year***
- ***Measles, mumps and rubella at one year and three years and four months***

Source: NHS Choices

A team at Massachusetts Institute of Technology has designed a new type of micro-particle that could combine everything into a single jab.

The particles look like miniature coffee cups that are filled with vaccine and then sealed with a lid. Crucially, the design of the cups can be altered so they break down and spill their contents at just the right time. One set of tests showed the contents could be released at exactly nine, 20 and 41 days after they were injected into mice. Other particles that last for hundreds of days have also been developed, the researchers say. The approach has not yet been tested on patients.

'Significant impact'

Prof Robert Langer, from MIT, said: "We are very excited about this work. "For the first time, we can create a library of tiny, encased vaccine particles, each programmed to release at a precise, predictable time, so that people could potentially receive a single injection that, in effect, would have multiple boosters already built into it.

"This could have a significant impact on patients everywhere, especially in the developing world."

The work differs from previous attempts, which slowly released medicines over a long period of time. The idea is the short, sharp bursts of vaccine more closely mimic routine immunisation programmes.

Fellow researcher Dr Kevin McHugh said: "In the developing world, that might be the difference between not getting vaccinated and receiving all of your vaccines in one shot."

http://bit.ly/2x3IzqS

Retaining older teachers for secondary education

Not all teachers succeed in staying happy with their work until the end of their career.

Dissatisfied older teachers will tend to quit before reaching retirement age. Work overload, low status of the profession, disruptive student behaviour, and a poor relationship with students are reasons often mentioned for the declining job satisfaction of older teachers.

Shortage of teachers

In the Netherlands, like in many other Western countries, we face a shortage of teachers. In the public debate, much attention is paid to beginning teachers. How can we keep them for the profession? This is important. But it is equally important to keep older teachers for the profession. To this little attention is paid in the public debate, but also in research. The purpose of this dissertation was to gain insight into the relation between the job satisfaction of older teachers and the quality of their relationship with students.

Older teachers differ in the extent to which they are satisfied with their work and the relationship with their students. Unsatisfied older teachers name extrinsic factors as causes for their dissatisfaction, such as work overload and administrative burden. Satisfied older teachers often name intrinsic factors, such as a good relationship with students.

Older teachers also differ in how they estimate the relationship with their students: more positively or negatively than the students. In coaching older teachers, it is important to take into consideration the role that the relationship with students has for job satisfaction.

Coaching for satisfied teachers

Coaching should not only be aimed at dissatisfied older teachers; coaching of (still) satisfied older teachers may be important to maintain their job satisfaction. Older teachers often overestimate or underestimate themselves in their relationship with students. It is important to address this in coaching. In the case of underestimating,

this is in the interest of the teachers themselves. In the case of overestimating it may also be to the advantage of the students.

http://bit.ly/2hbxn1l

Memory decline after head injury may be prevented by slowing brain cell growth

Rutgers study questions traditional scientific view that neurogenesis aids recovery

The excessive burst of new brain cells after a traumatic head injury that scientists have traditionally believed helped in recovery could instead lead to epileptic seizures and long-term cognitive decline, according to a new Rutgers New Jersey Medical School study.

In the September issue of Stem Cell Reports, Viji Santhakumar, associate professor in the department of Pharmacology, Physiology and Neuroscience, and her colleagues, challenge the prevailing assumption by scientists in the field that excessive neurogenesis (the birth of new brain cells) after injury is advantageous.

"There is an initial increase in birth of new neurons after a brain injury but within weeks, there is a dramatic decrease in the normal rate at which neurons are born, depleting brain cells that under normal circumstances should be there to replace damaged cells and repair the brain's network," said Santhakumar. "The excess new neurons lead to epileptic seizures and could contribute to cognitive decline"

In the United States an estimated 1.7milllion people sustain a TBI each year, making the condition a major cause of death and disability. Symptoms can include impaired thinking or memory, personality changes and depression and vision and hearing problems as well as epilepsy. About 80 percent of those who develop epilepsy after a brain injury have seizures within the first two years after the damage occurs.

Santhakumar said while researchers who study epilepsy have started to look more closely at how preventing excessive neurogenesis after brain injury could prevent seizures, neuroscientists have traditionally viewed the process as helpful to overall brain recovery.

Studying laboratory rats, Rutgers scientists found, however, that within a month after experimental brain injury, the number of new brain cells declined dramatically, below the numbers of new neurons that would have been detected if an injury had not occurred.

When scientists were able to prevent the excessive neurogenesis which occurs within days of the injury with a drug similar to one under trial for chemotherapy treatments, the rate of birth of new brain cells went back to normal levels and risk for seizures was reduced.

"That's why we believe that limiting this process might be beneficial to stopping seizures after brain injury," she said.

While the regenerative capability of brain cells, in the hippocampus - the part of the brain responsible for learning and memory - slows down as part of the aging process, the Rutgers scientists determined that the process that occurred after a head injury was related to injury and not age.

"It is normal for the birth of new neurons to decline as we age," said Santhakumar. "But what we found in our study was that after a head injury the decline seems to be more rapid."

The Rutgers study was funded by the NJ Commission on Brain Injury Research. An estimated 12,000 to 15,000 New Jersey residents suffer brain injuries annually.

http://bit.ly/2y6pwZY

'Exciting' discovery on path to develop new type of vaccine to treat global viruses

Scientists at the University of Southampton have made a significant discovery in efforts to develop a vaccine against Zika, dengue and Hepatitis C viruses that affect millions of people around the world.

In a study published in Science Immunology, researchers have shown that natural killer cells (NK cells), which are a fundamental part of the body's immune system, can recognise many different viruses including global pathogens such as Zika, dengue and Hepatitis C viruses, through a single receptor called KIR2DS2.

Lead researcher Salim Khakoo, Professor of Hepatology, said the findings are very exciting and could change the way viruses are

targeted by vaccines but warned that the research is still at an early stage, and animal studies/clinical trials will be needed to test the findings.

Vaccines work by stimulating the immune response to the coat of proteins on the virus enabling the body to fight off the virus and recognise it in the future. However, the viruses are able to change their coat proteins, helping the virus to evade the antibodies, meaning some viruses can be very hard to vaccinate against.

The Southampton team have shown that this NK cell receptor is able to target a non-variable part of the virus called the NS3 helicase protein, which is essential in making the virus work properly. Unlike other proteins, the NS3 helicase protein does not change, which allows the immune system to grab hold of it and let the NK cells deal with the threat.

Professor Khakoo said: "The NS3 helicase protein could be the key in unlocking the defence of lethal viruses that affect so many people around the world. It is very exciting to discover that other viruses similar to Hepatitis C, such as Zika virus, dengue virus, yellow fever virus, Japanese encephalitis virus and in fact all flaviviruses, contain a region within their NS3 helicase proteins that is recognised by exactly the same KIR2DS2 receptor. We believe that by targeting this NS3 helicase region, we could make a new type of vaccine based upon natural killer cells, which can be used to help protect people from these infections."

The study, which was funded by the Wellcome Trust and the Medical Research Council, analysed DNA from more than 300 patients exposed to the Hepatitis C virus, which showed that the KIR2DS2 receptor was associated with successfully clearing the virus. The team then identified that the immune system targeted the NS3 helicase protein of this using the receptor and found that it prevented the virus multiplying.

They went on to demonstrate that this same mechanism icould be important for many different viruses for example the Zika and dengue viruses, which also contain a region within their NS3 helicase protein that is recognised by the KIR2DS2 receptor.

The researchers now need to determine whether these KIR2DS2+ NK cells are protective during acute flaviviral infections, and are hoping to develop a vaccine that targets natural killer cells. They believe that a similar process could be used to target cancer.

Professor Khakoo added: "Cancer treatments that use the body's own immune system are becoming more common. Our findings present a completely new strategy for virus therapeutics which could be easily translated into the field of cancer. The next few years are going to be very exciting in this field."

1. Paper details: KIR2DS2 recognizes conserved peptides derived from viral helicases in the context of HLA-C. Naiyer et al. Sci. Immunol. 2, eaal5296 (2017)

http://bit.ly/2haVdKO

Deprescribing gets support from Canada's seniors, survey shows

New national survey finds many Canadians worry it's all too much Medication

MONTREAL - Most Canadians over 65 years of age take a lot of prescription drugs -- two-thirds, in fact, take more than five a day, while two out of every five of Canadians over 80 take more than 10 a day. And many worry it's all too much, a new national survey by Université de Montréal researchers has found.

The phone survey of 2,665 men and women ages 65 years or older was done last year between August and October. Preliminary data were presented at scientific meetings in April and May in Toronto and Texas and the results are published today in the Journal of the American Geriatrics Society.

The survey is the first of its kind in the world to find out what ordinary people, rather than clinicians or scientists, know about the growing movement of "deprescribing" -- reducing or stopping medications that are of no apparent benefit to patients and which, in some cases, might actually be doing them harm.

Dr. Justin Turner, a post-doctoral fellow in pharmacy at UdeM and a researcher at the Institut universitaire de geriatrie de Montréal, designed the survey and analysed its results with his supervisor at the Institut, Dr. Cara Tannenbaum, an UdeM professor of medicine and pharmacy.

Among their findings:

60% of Canadians 65 or older think appropriate prescribing should be a national government priority;

65% know that some medications can potentially be harmful to seniors;

48% have gone online or elsewhere to learn more about the harmful effects of medications;

only 7% have heard the word "deprescribing" before;

41% have asked their doctor about stopping certain medications;

francophone Canadians are 72% less likely to be aware of harmful effects of medications than anglophones;

patients who actively seek information about the potential harms of their medications are four times more likely to ask their doctor about deprescribing;

This summer, the Canadian Deprescribing Network launched a bilingual website on medication safety and deprescribing for the general public. Medications are defined as inappropriate when the potential for harm outweighs the potential for benefit, particularly when safer alternatives exist.

"One in four older adults takes at least one potentially inappropriate prescription medication each year, increasing the risk of medication-related hospital admission and unnecessary expenditure to the health care system," Tannenbaum and Turner note in their study.

"70% of older adults are willing to deprescribe a medication, yet the prevalence of inappropriate medications remains unchanged," they add, singling out the 20% of family and internal medicine doctors and 50% of pharmacists who either don't raise the issue or are simply unaware there might be one.

Outside nursing homes, which were not included in the survey, "two-thirds of Canadian older adults are aware that some prescriptions can cause harm, half [of them] research information about medications, and only 6.9% are familiar with the term 'deprescribing,'" the researchers noted.

"Very few older adults are familiar with the term deprescribing," the authors conclude. "Healthcare providers have an important role to play in empowering older adults with information about medication harms in order to trigger safer medication management."

The telephone survey was conducted in English or French in all 10 provinces and three territories. The survey is considered accurate within two percentage points, 19 times out of 20.

"Older adults' awareness of deprescribing: a population-based survey," by Justin Turner and Cara Tannenbaum, was published Sept. 15, 2017, in the Journal of the American Geriatrics Society. Funding provided by a Partnership for Health System Improvement Grant from the Canadian Institutes of Health Research (201410PHE-PHE-337814-96399) and a National Chair Award from the Fonds de recherche du Québec - Santé; (2016/2017-33087).

http://bit.ly/2hachnX

Medical students not trained to prescribe medical marijuana

Many states allow medical pot, but few med schools address it

Although 29 states and the District of Columbia allow marijuana use for medical purposes, few medical students are being trained how to prescribe the drug. Researchers at Washington University School of Medicine in St. Louis surveyed medical school deans, residents and fellows, and examined a curriculum database maintained by the Association of American Medical Colleges (AAMC), learning that medical marijuana is not being addressed in medical education.

Their findings are available online in the journal Drug and Alcohol Dependence.

"Medical education needs to catch up to marijuana legislation," said senior author Laura Jean Bierut, MD, the Alumni Endowed Professor of Psychiatry at Washington University and a member of the National Advisory Council on Drug Abuse. "Physicians in training need to know the benefits and drawbacks associated with medical marijuana so they know when or if, and to whom, to prescribe the drug."

Doctors are being asked to guide patients through areas in which most have no training, she explained.

The research team, led by first author Anastasia B. Evanoff, sent surveys to medical school curriculum deans at 172 medical schools in North America, including 31 that specialize in osteopathic medicine, and received 101 replies. Two-thirds (66.7 percent) reported that their graduates were not prepared to prescribe medical marijuana. A quarter of deans said their trainees weren't even equipped to answer questions about medical marijuana.

The researchers also surveyed 258 residents and fellows who earned their medical degrees from schools around the country before coming to Washington University School of Medicine and Barnes-Jewish Hospital in St. Louis to complete their training. Nearly 90 percent felt they weren't prepared to prescribe medical marijuana, and 85 percent said they had not received any education about medical marijuana during their time at medical schools or in residency programs throughout the country.

Using data from the AAMC database, the researchers found that only 9 percent of medical schools had reported teaching their students about medical marijuana.

"As a future physician, it worries me," said Evanoff, a third-year medical student. "We need to know how to answer questions about medical marijuana's risks and benefits, but there is a fundamental mismatch between state laws involving marijuana and the education physicians-in-training receive at medical schools throughout the country."

However, several states -- Missouri among them -- have not legalized medical marijuana, and published studies about potential risks and benefits of medical marijuana often are contradictory. So what are schools to teach?

"You address the controversy," said co-investigator Carolyn Dufault, PhD, assistant dean for education at Washington University and an instructor in medicine. "You say, 'This is what we know,' and you guide students to the points of controversy. You also point out where there may be research opportunities."

The authors argue that as more states legalize marijuana for medical and recreational use, doctors need to have at least enough training to answer patients' questions.

"More medical students are now getting better training about opioids, for example," said Evanoff. "We talk about how those drugs can affect every organ system in the body, and we learn how to discuss the risks and benefits with patients. But if a patient were to ask about medical marijuana, most medical students wouldn't know what to say."

Evanoff, AB, Quan T, Dufault C, Awad M, Bierut LJ. Physicians-in-training are not prepared to prescribe medical marijuana. Drug and Alcohol Dependence, vol 180(11), pp. 151-155, Nov. 1, 2017 (published online Sept. 4, 2017).

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Washington University School of Medicine's 2,100 employed and volunteer faculty physicians also are the medical staff of Barnes-Jewish and St. Louis Children's hospitals. The School of Medicine is one of the leading medical research, teaching and patient-care institutions in the nation, currently ranked seventh in the nation by U.S. News & World Report. Through its affiliations with Barnes-Jewish and St. Louis Children's hospitals, the School of Medicine is linked to BJC HealthCare.

http://wb.md/2x9nFEm

Does the Mole Always Come Before the Melanoma?

Do Melanomas Arise From Preexisting Moles?

Arefa Cassoobhoy, MD, MPH

Hello. I'm Dr Arefa Cassoobhoy, a practicing internist, Medscape advisor, and senior medical director for WebMD. Welcome to Morning Report, our 1-minute news story for primary care.

It's a widely held assumption that melanomas are malignant transformations of moles. But it turns out that most are not.

A recent study[1] reported that only 29% of more than 20,000 melanomas were associated with a preexisting nevus, and 71% arose de novo. Patients whose melanomas came from a mole were significantly younger, by about 5 years. And those melanomas tended

to be less thick. The most common locations for melanoma in both groups were extremities and the trunk.

These findings suggest that patients should be taught not only to look for changes in existing moles, but to inspect their skin for any new lesions. In addition to risk factor assessment, clinicians can use the "EFG" rule—elevation, growing, and firm—when deciding which patients should be referred to a dermatologist.

References

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http://bbc.in/2jyWu2H

Why is it so hard to swat a fly?

Try to swat a fly and it will soon become clear that they're faster than you. Much faster. But how on Earth do these tiny creatures - with their minuscule brains - outwit us so easily?

By Rory Galloway Science writer

You've probably pondered it after chasing a fly around your house and flailing your shoe with repeated, unsuccessful swats. How does it move so fast? Can it read my mind?

It was the question put to the BBC World Service CrowdScience team for our most recent episode addressing the apparent super powers of tiny animals. The answer is that, compared with you and me, flies essentially see the world in slow motion.

To illustrate this, have a look at a clock with a ticking hand. As a human, you see the clock ticking at a particular speed. But for a turtle it would appear to be ticking at twice that speed. For most fly species, each tick would drag by about four times more slowly. In effect, the speed of time differs depending on your species.

This happens because animals see the world around them like a continuous video. But in reality, they piece together images sent from the eyes to the brain in distinct flashes a set number of times per second. Humans average 60 flashes per second, turtles 15, and flies 250.

Time is relative

The speed at which those images are processed by the brain is called the "flicker fusion rate". In general, the smaller the species, the faster its critical flicker fusion rate - and flies, in particular, put us to shame.

Professor Roger Hardie, from the University of Cambridge, investigates how flies' eyes work, and he has an experiment to determine their flicker fusion rate.

"The flicker fusion rate is simply how fast a light has to be turning on and off before it's perceived or seen as just a continuous light" says Prof Hardie.

Roger inserts tiny glass electrodes into the living light sensitive cells of their eyes - photoreceptors - before flashing LED lights at faster and faster speeds. Each flash of the LED produces a tiny electrical current in the photoreceptors that a computer can graph onto a screen. Tests reveal the fastest fly records distinct responses to flickering up to 400 times per second, more than six times faster than our own rate.

The fastest vision of all is found in a species literally called a "killer fly". It's a tiny predatory species found in Europe that catches other flies out of the air with super-fast reactions. In her "fly lab" at Cambridge University, Dr Paloma Gonzales-Bellido demonstrates the killer flies' hunting behaviour by releasing fruit fly prey into a special filming box with a female killer fly.

Paloma records the behaviour at 1,000 frames per second using slow motion video cameras with a recording buffer. The attached computer constantly saves the video, over-writing itself every twelve seconds. When the fly moves, Paloma clicks a button to permanently save the last 12 seconds. "Our reaction time is so slow that if we were to stop it when we think something is happening it would have happened already," says Dr Gonzales-Bellido. Essentially, we can't even click a button before the behaviour has happened, it's that fast.

Fly vs fly

With the killer flies and their prey in the filming box, initially the killer fly just sat around motionless, but as one of the fruit flies flew

about 7cm above it, there was a flash of movement and suddenly the killer fly was at the bottom of the box chomping into the quivering fruit fly.

Only looking at the slowed-down footage on the computer did it become clear what happened; the killer fly took off, circled the fruit fly three times as it tried to grab it repeatedly, before succeeding in capturing the elusive fruit fly with its front legs.

The whole behaviour from take-off to landing took just one second. It appears as a flash to our eyes, so conversely, the swatting hand of a human must appear at a snail's pace.

To enable this incredible speed of the killer fly, which is faster even than other fly species, the light-detecting cells in the killer fly eyes contain many more mitochondria (the "batteries" of biological cells) than are present in the same cells of other flies.

These are the batteries of the cell, so the speedy vision must take more energy than slow vision, explaining why all eyes aren't just set to the highest flicker fusion rate.

The carnivorous diet of the killer fly provides the large amounts of energy it needs to power these high-energy cells. But even if we had the same number of mitochondria in the cells or our own eyes, we wouldn't have the same vision speed because flies' light-sensitive cells have a totally different design to those of vertebrates.

Behind the structural differences in the eyes of flies is their evolutionary origin. Arthropods and vertebrates, the groups holding flies and humans, evolved their eyes entirely separately around 700-750 million years ago.

String theory

Flies' eyes evolved to pick up light with a series of tiny string-like structures that lie horizontal to the path that light travels through the eye. These structures react to light mechanically whereas vertebrates have long tube-like cells facing the light, with chemicals that react to light at the base.

This structure in the fly eye is something Roger studies in his lab. "It's more sensitive in terms of being able to give a large signal to the tiniest amount of light and it can also respond faster than the rods and cones in the vertebrate eye," he explains.

There are a few reasons for this higher sensitivity, but what Prof Hardie discovered is that they respond mechanically to light, as opposed to chemically as in cones and rods.

Mechanical responses enable faster neural signals. On top of that, there's a limit to the speed at which neural impulses can travel and the smaller nerve distances from fly eye to fly brain speeds up processing compared to larger vertebrates.

Some vertebrates experience much faster vision than our own. Whether the species is able to fly seems to correlate with faster vision, as does being small. This may be because small flying animals have to react so quickly during flight to avoid approaching obstacles.

It's all relative

The fastest vision of all is found in species that catch flies in the air.

Back with vertebrates, when investigating the vision of the pied flycatcher, a small perching bird that catches flies in flight, scientists at Uppsala University in Sweden discovered that it was able to identify a light flashing on and off 146 times per second from a continuous light source.

The birds were trained to associate a flashing light source with a tasty treat, and would accurately identify the flashing light up to this rate, placing their flicker fusion rate at 146. That's about twice the rate humans can see but still not as fast as the average fly.

This means the birds, like flies, experience each tick of the clock more slowly than humans.

There is an evolutionary pressure on the flycatchers to experience the ticking hand of the clock as slowly as possible in order to outwit their speedy prey. Over evolutionary time, birds that experienced 'slower ticking' could react faster to their prey, allowing them to eat more, raise more chicks and pass this speedy vision to future generations.

The flies that have been chased by the fast-sighted birds will be evolving faster reactions to get away. Creating an evolutionary arms race that has gone on longer even than the existence of birds. Prey flies have been evolving faster vision and reactions to escape predatory flies like the killer fly since they evolved flight.

Next time you try inanely to swat a fly, try not to be so disheartened. Your lumbering, slow motion swats are being thwarted by hundreds of millions of years of natural selection letting the flies watch your attempts in slow motion.

Between you and the fly, time, it seems, is relative.

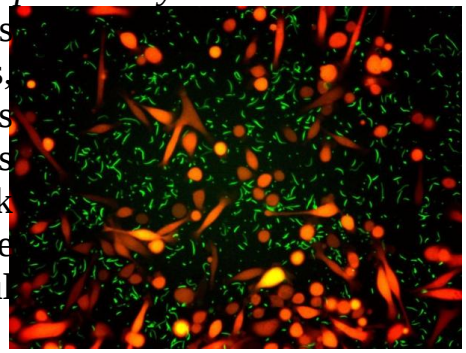
http://bit.ly/2fu5rWp

See jerkface bacteria hiding in tumors and gobbling chemotherapy drugs

They make cancers drug-resistant, but a dose of antibiotics may help, study suggests.

Beth Mole - 9/17/2017, 11:30 PM

Of all the kinds of bacteria, some are charming and beneficial, others are malicious and dangerous—and then there are the ones that are just plain turds. That's the case for *Mycoplasma hyorhinis* and its ilk. Researchers caught the little jerks hiding out among cancer cells, gobbling up chemotherapy drugs intended to demolish their tumorous digs. The findings, reported this week in *Science*, explain how some otherwise treatable cancers can thwart powerful therapies.



Enlarge / An example of an experiment where bacteria (green) and cancer cells (red) are co-cultured. Leore Geller

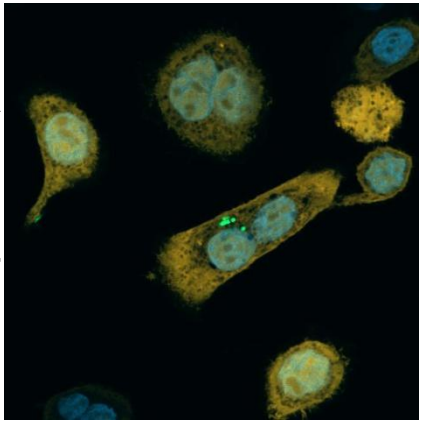
Drug resistance among cancers is a "foremost challenge," according to the study's authors, led by Ravid Straussman at the Weizmann Institute of Science. Yet the new data suggest that certain types of drug-resistant cancers could be defeated with a simple dollop of antibiotics alongside a chemotherapy regimen.

That said, the findings are still mostly from lab and animal experiments. It will be a while before the results are repeated and confirmed in human cancer cases, then possibly translated into new clinical practices for treating certain types and cases of cancers.

Dr. Straussman and his colleagues got a hunch to look for the bacteria after noticing that, when they grew certain types of human cancer cells together in lab, the cells all became more resistant to a chemotherapy drug called gemcitabine. This is a drug used to treat pancreatic, lung, breast, and bladder cancers and is often sold under the brand name Gemzar.

The researchers suspected that some of the cells may secrete a drug-busting molecule. So they tried filtering the cell cultures to see if they could catch it. Instead, they found that the cells lost their resistance after being passed through a pretty large filter—0.45 micrometers. This would catch large particles—like bacteria—but not small molecules, as the researchers were expecting.

Looking closer, the researchers noticed that some of their cancer cells were contaminated with *M. hyorhinis*. And these bacteria could metabolize gemcitabine, rendering the drug useless. When the researchers transplanted treatable cancer cells into the flanks of mice—some with and some without *M. hyorhinis*—the bacteria-toting tumors were resistant to gemcitabine treatment.



***Bacteria (in green) inside a pancreatic cancer cell of the AsPC1 pancreatic cancer cell line. The nucleus of the cancer cell is in blue.* Leore Geller**

And it's not just *M. hyorhinis* that can turn tumors resistant. When the researchers pinpointed the gene that encodes the molecular machinery for disarming gemcitabine in *M. hyorhinis*—a gene called CDD_L—

they found that it's quite common in other bacteria. In initial testing of 27 bacterial species, 13 could knock out gemcitabine. When the researchers searched through the genetics of nearly 2,700 bacteria, they found that hundreds also had the gene for defeating gemcitabine. Most of those bacteria were in the Gammaproteobacteria class, a giant group of bacteria that includes *E. coli* and *Salmonella*.

To see if this may be a real problem in humans, the researchers gathered 113 cell samples from human pancreatic cancers (a cancer type called pancreatic ductal adenocarcinoma). These were all collected during cancer surgeries. The researchers also assembled 20 samples from organ donors that had non-cancerous pancreases (or "pancreata," if we're being persnickety). Of the 113 cancer samples, 86 had signs of bacteria present—mostly Gammaproteobacteria—while only three of the 20 non-cancerous samples had bacteria.

The researchers speculate that bacteria may invade pancreatic tumors by migrating from the duodenum, the top section of the small intestine.

To put all their findings together, the researchers engineered an *E. coli* strain to carry CDD_L—a gene it didn't carry before—then injected the strain into tumor-riddled mice. The researchers used fluorescent markers to track both the bacteria and the tumors. When they treated the mice with either gemcitabine and an antibiotic or just gemcitabine alone, they saw bacteria disappear and tumors shrink in the mice that got the antibiotic-chemotherapy combo. But in the mice with just chemotherapy, the researches saw rapid tumor progression.

The role of bacteria in drug-resistant cancers and the potential for using antibiotics with chemotherapies "merit additional exploration," the authors conclude. Science, *2017. DOI: 10.1126/science.aah5043 (About DOIs).*