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Extinct squid relative entombed in amber for 100 million years

One of the very first marine organisms ever found in amber

By Joshua Sokol

The latest discovery in a cache of ancient Burmese amber has revealed something completely unexpected: an extinct squidlike organism called an ammonite, which swam Earth's seas while dinosaurs dominated the land 100 million years ago. This is the first ammonite and one of the very first marine organisms ever found in amber; because the gemstone is fossilized tree resin, it traps mostly land organisms.

Bo Wang

The specimen (above) came to light when a collector in Shanghai, China, bought it for about $750 from a dealer who claimed it was a land snail. Under the x-rays of a computerized tomography scanner, though, the shell revealed the intricate internal chambers characteristic of ammonites.

The ammonite's precise type confirms the Burmese amber is from the Cretaceous period, as previous dating studies have argued. But the 3-centimeter-long piece of ancient resin is a veritable surf and turf of land and sea creatures, also preserving at least 40 other animals—mites, spiders, millipedes, cockroaches, beetles, flies, wasps, and marine gastropods, the researchers report today in the *Proceedings of the National Academy of Sciences*.

To explain this unique amber piece, researchers have conjured up three scenarios. Perhaps resin dripped down from a forest next to a beach, catching first land critters and then seashells. Or a tsunami flooded low-lying trees, washing sea creatures into resin pools. Or, possibly, storm winds simply blew seashells into the forest. Regardless, scientists say, it's a welcome surprise.

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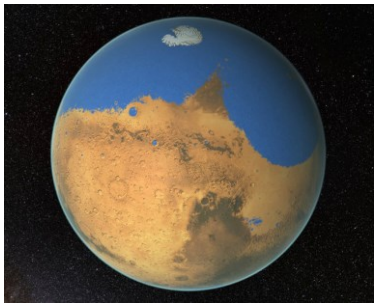
A Giant Hole in the Martian Atmosphere Is Venting All Its Water into Space

There's a hole in the Martian atmosphere that opens once every two years, venting the planet's limited water supply into space — and dumping the rest of the water at the planet's poles.

By Rafi Letzter, Staff Writer

That's the explanation advanced by a team of Russian and German scientists who studied the odd behavior of water on the Red Planet. Earthbound scientists can see that there's water vapor high in the Martian atmosphere, and that water is migrating to the planet's poles. But until now, there was no good explanation for how the Martian water cycle works, or why the once-drenched planet is now a dry husk.



Before this slow process dried out the planet, Mars may have been covered by a vast ocean. This illustration shows how the planet may have looked billions of years ago. Credit: NASA/GSFC

The presence of water vapor high above Mars is puzzling because the Red Planet has a middle layer of its atmosphere that seems like it should be shutting down the water cycle altogether.

"The Martian middle atmosphere is too cold to sustain water vapor," the researchers wrote in the study, which was published April 16 in the journal Geophysical Research Letters.

So how is water crossing that middle-layer barrier?

The answer, according to computer simulations in the current study, has to do with two atmospheric processes unique to the Red Planet.

On Earth, summer in the Northern Hemisphere and summer in the Southern Hemispheres are pretty similar. But that's not the case on

Mars: Because the planet's orbit is much more eccentric than Earth's, it's significantly closer to the sun during its southern hemisphere summer (which happens once every two Earth years). So summers on that part of the planet are much warmer than summers in the Northern Hemisphere.

When that happens, according to the researchers' simulations, a window opens in Mars' middle atmosphere between 37 and 56 miles (60 and 90 kilometers) in altitude, allowing water vapor to pass through and escape into the upper atmosphere. At other times, the lack of sunlight shuts down Martian water cycles almost entirely.

Mars is also different from Earth in that the Red Planet gets frequently overtaken by giant dust storms. Those storms cool the planet's surface by blocking light. But the light that doesn't reach Mars' surface instead gets stuck in the atmosphere, warming it and creating conditions better suited to moving water around, the scientists' simulations showed. Under global dust-storm conditions, like the one that enveloped Mars in 2017, tiny particles of water ice form around the dust particles. Those lightweight ice particles float into the upper atmosphere more easily than other forms of water, so during those periods more water move into the upper atmosphere.

Dust storms can move even more water into the upper atmosphere than the southern summers, the researchers showed.

Once the water passes through the middle boundary, the researchers wrote, two things happen: Some of the water drifts north and south, toward the poles, where it's eventually deposited. But ultraviolet light in the upper atmosphere can also sever the bonds between the oxygen and hydrogen in the molecules, causing the hydrogen to escape into space, leaving the oxygen behind.

This process could be part of the story of how a once-drenched Mars has ended up so dry in its current epoch, the researchers wrote.

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Study shows people fail to recognise male postnatal depression

New research led by Anglia Ruskin University shows significant gender differences

A new study shows that people are almost twice as likely to correctly identify signs of postnatal depression in women than in men.

The research, published in the *Journal of Mental Health* and led by Professor Viren Swami of Anglia Ruskin University, involved 406 British adults aged between 18 and 70.

The participants were presented with case studies of a man and a woman both displaying symptoms of postnatal depression, a mental health issue which affects as many as 13% of new parents.

This new study found that participants of both sexes were less likely to say that there was something wrong with the male (76%) compared to the female (97%).

Of the participants who did identify a problem, they were significantly more likely to diagnose postnatal depression in the female case study than the male case study. The study found that 90% of participants correctly described the female case study as suffering from postnatal depression but only 46% said the male had postnatal depression.

The participants commonly believed that the man was suffering from stress or tiredness. In fact, stress was chosen 21% of the time for the man compared to only 0.5% for the woman, despite identical symptoms.

Overall the study found that attitudes were significantly more negative towards the male case study compared to the female. It found that participants reported lower perceived distress towards the male case study's condition, believed that the male's condition

would be easier to treat, expressed less sympathy for the male and were less likely to suggest that the male seek help.

Lead author Viren Swami, Professor of Social Psychology at Anglia Ruskin University, said: "Our findings suggest that the British public are significantly more likely to believe that something is 'wrong' when seeing a woman displaying the symptoms of postnatal depression, and they are also far more likely to correctly label the condition as postnatal depression.

"There may be a number of reasons for this gender difference. It is possible that general awareness of paternal postnatal depression still remains relatively low and there might be a perception among the British public that postnatal depression is a 'women's issue' due to gender-specific factors such as pregnancy-induced hormonal changes and delivery complications.

"What is clear is that much more can be done to promote better understanding of paternal postnatal depression, so people don't brush it off as simply tiredness or stress. This is particularly important as many men who experience symptoms of depression following the birth of their child may not be confident about asking for help and may be missed by healthcare professionals in the routine assessments of new parents."

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In the deep, dark, ocean fish have evolved superpowered vision

Fish swimming deeper than sunlight can penetrate have developed vision highly attuned to the faint of other creatures

By Elizabeth Pennisi

When the ancestors of cave fish and certain crickets moved into pitchblack caverns, their eyes virtually disappeared over generations. But fish that ply the sea at depths greater than sunlight can penetrate have developed super-vision, highly attuned to the faint glow and twinkle given off by other creatures. They owe this power, evolutionary biologists have learned, to an extraordinary increase in the number of genes for rod opsins, retinal proteins that detect dim light. Those extra genes have diversified to produce proteins capable of capturing every possible photon at multiple wavelengths—which could mean that despite the darkness, the fish roaming the deep ocean actually see in color.

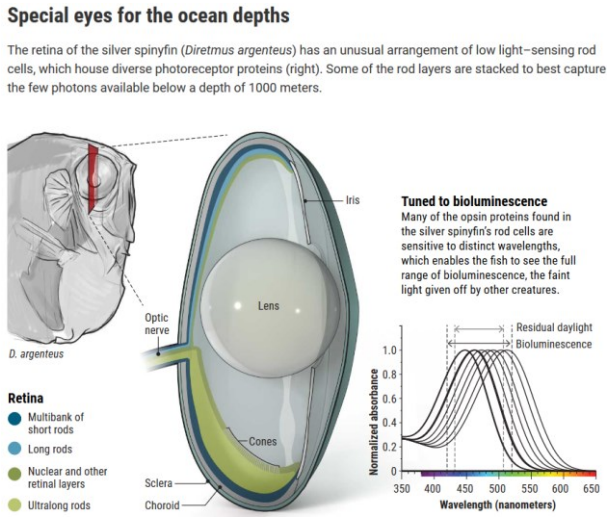
Living in the gloom 2000 meters down, the silver spinyfin may see color.
Pavel Riha/University of South Bohemia

The finding "really shakes up the dogma of deep-sea vision," says Megan Porter, an evolutionary biologist studying vision at the University of Hawaii in Honolulu who was not involved in the work. Researchers had observed that the deeper a fish lives, the simpler its visual system is, a trend they assumed would continue to the bottom. "That [the deepest dwellers] have all these opsins means there's a lot more complexity in the interplay between light and evolution in the deep sea than we realized," Porter says.

At a depth of 1000 meters, the last glimmer of sunlight is gone. But over the past 15 years, researchers have realized that the depths are pervaded by a faint bioluminescence from flashing shrimp, octopus, bacteria, and even fish. Most vertebrate eyes could barely detect this subtle shimmer. To learn how fish can see it, a team led by evolutionary biologist Walter Salzburger from the University of Basel in Switzerland studied deep-sea fishes' opsin proteins. Variation in the opsins' amino acid sequences changes the wavelength of light detected, so multiple opsins make color vision possible. One opsin, RH1, works well in low light. Found in the eye's rod cells, it enables humans to see in the dark—but only in black and white.

Salzburger and his colleagues searched for opsin genes in 101 fish species, including seven Atlantic Ocean deep-sea fish whose genomes they fully sequenced. Most fish have one or two RH1 opsins, like many other vertebrates, but four of the deep-sea species stood apart, the researchers report this week in *Science*. Those fish—the lantern-fish, a tube-eye fish, and two spinyfins—all had at least five RH1 genes, and one, the silver spinyfin (*Diretmus argenteus*), had 38. "This is unheard of in vertebrate vision," says K. Kristian Donner, a sensory biologist at the University of Helsinki.

To make sure the extra genes weren't just nonfunctional duplicates, the team measured gene activity in 36 species, including specimens of 11 deep-sea fish. Multiple RH1 genes were active in the deep-sea species, and the total was 14 in an adult silver spinyfin, which thrives down to 2000 meters. "At first it seems paradoxical—this is where there's the least amount of light," Salzburger says.



(Graphic) V. Altounian/*Science*; (Data) Zuzana Musilova/University Of Basel/Charles University

Researchers can predict the wavelengths that an opsin protein is most sensitive to from its amino acid sequence. The deep-sea fish had a total of 24 mutations that alter the function of their RH1 proteins, fine-tuning each to see a narrow range of blue and green wavelengths—the colors of bioluminescence. "Some of these opsins might be tuned to detect particular bioluminescent signals associated with food, danger, or social interactions," says Gil Rosenthal, a behavioral ecologist at Texas A&M University in College Station.

The four deep-sea species belong to three different branches of the fish family tree, indicating that this supervision evolved repeatedly. "This indicates that animals living in extreme light environments may be subject to extreme natural selective pressures to improve visual performance," says Eric Warrant, a visual ecologist at Lund University in Sweden.

The bountiful opsins also help explain the unusual anatomy of the spinyfin retina. Some of its rod cells are much longer than usual, and many are stacked one on top of another rather than arranged in a single layer. The enlarged cells and the stacking help ensure more incoming photons are detected, but researchers have long assumed these rods all had the same opsin. Now, it appears that, like the layers in old photographic film, rods of different sizes might capture different wavelengths of light. "We now have to accept that our view [of deep-sea vision] has been too limited," Donner says.

Because of the depths these fish inhabit, it's impossible to collect live specimens to test their vision. But the multiple rod opsins may enable them to distinguish color, Salzburger and others agree. For these fish, the faint bioluminescence in the inky depths could be as vivid and varied as the bright surface world.

http://bit.ly/2Vw6OWP

The moon is quaking as it shrinks

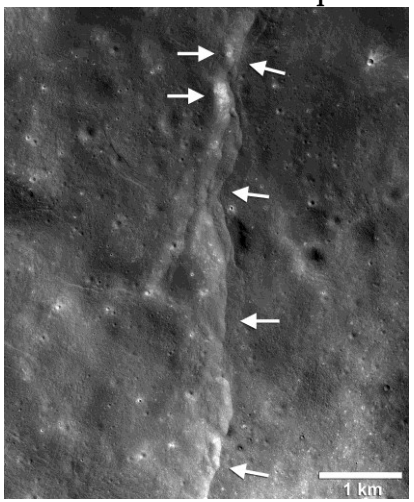
The moon may still be shrinking today and actively producing moonquakes along thrust faults

by University of Maryland

A 2010 analysis of imagery from NASA's Lunar Reconnaissance Orbiter (LRO) found that the moon shriveled like a raisin as its interior cooled, leaving behind thousands of cliffs called thrust faults on the moon's surface.

A new analysis suggests that the moon may still be shrinking today and actively producing moonquakes along these thrust faults. A team of researchers including Nicholas Schmerr, an assistant professor of geology at the University of Maryland, designed a new algorithm to re-analyze seismic data from instruments placed by NASA's Apollo missions in the 1960s and '70s. Their analysis provided more accurate epicenter location data for 28 moonquakes recorded from 1969 to 1977.

The team then superimposed this location data onto the LRO imagery of the thrust faults. Based on the quakes' proximity to the thrust faults, the researchers found that at least eight of the quakes likely resulted from true tectonic activity—the movement of crustal plates—along the thrust faults, rather than from asteroid impacts or rumblings deep within the moon's interior.



This prominent thrust fault is one of thousands discovered on the moon by NASA's Lunar Reconnaissance Orbiter (LRO). These faults resemble small stair-shaped cliffs, or scarps, when seen from the lunar surface. The scarps form when one section of the moon's crust (left-pointing arrows) is pushed up over an adjacent section (right-pointing arrows) as the moon's interior cools and shrinks. New research suggests that these faults may still be active today. **LROC NAC frame M190844037LR; NASA/GSFC/Arizona State University/Smithsonian**

Although the Apollo instruments recorded their last quake shortly before the instruments were retired in 1977, the researchers suggest that the moon is likely still experiencing quakes to this day. A paper describing the work, co-authored by Schmerr, was published in the journal *Nature Geoscience* on May 13, 2019.

"We found that a number of the quakes recorded in the Apollo data happened very close to the faults seen in the LRO imagery," Schmerr said, noting that the LRO imagery also shows physical evidence of geologically recent fault movement, such as landslides and tumbled boulders. "It's quite likely that the faults are still active today. You don't often get to see active tectonics anywhere but Earth, so it's very exciting to think these faults may still be producing moonquakes."

Astronauts placed five seismometers on the moon's surface during the Apollo 11, 12, 14, 15 and 16 missions. The Apollo 11 seismometer operated only for three weeks, but the four remaining instruments recorded 28 shallow moonquakes—the type produced by tectonic faults—from 1969 to 1977. On Earth, the quakes would have ranged in magnitude from about 2 to 5.

Using the revised location estimates from their new algorithm, the researchers found that the epicenters of eight of the 28 shallow quakes were within 19 miles of faults visible in the LRO images. This was close enough for the team to conclude that the faults likely caused the quakes. Schmerr led the effort to produce "shake maps" derived from models that predict where the strongest shaking should occur, given the size of the thrust faults.

The researchers also found that six of the eight quakes happened when the moon was at or near its apogee, the point in the moon's orbit when it is farthest from Earth. This is where additional tidal stress from Earth's gravity causes a peak in the total stress on the moon's crust, making slippage along the thrust faults more likely.

"We think it's very likely that these eight quakes were produced by faults slipping as stress built up when the lunar crust was compressed by global contraction and tidal forces, indicating that the Apollo seismometers recorded the shrinking moon and the moon is still tectonically active," said Thomas Watters, lead author

of the research paper and senior scientist in the Center for Earth and Planetary Studies at the Smithsonian Institution in Washington.

Much as a grape wrinkles as it dries to become a raisin, the moon also wrinkles as its interior cools and shrinks. Unlike the flexible skin on a grape, however, the moon's crust is brittle, causing it to break as the interior shrinks. This breakage results in thrust faults, where one section of crust is pushed up over an adjacent section. These faults resemble small stair-shaped cliffs, or scarps, when seen from the lunar surface; each is roughly tens of yards high and a few miles long.

The LRO has imaged more than 3,500 fault scarps on the moon since it began operation in 2009. Some of these images show landslides or boulders at the bottom of relatively bright patches on the slopes of fault scarps or nearby terrain. Because weathering gradually darkens material on the lunar surface, brighter areas indicate regions that are freshly exposed by an event such as a moonquake.

Other LRO fault images show fresh tracks from boulder falls, suggesting that quakes sent these boulders rolling down their cliff slopes. Such tracks would be erased relatively quickly, in terms of geologic time, by the constant rain of micrometeoroid impacts on the moon. With nearly a decade of LRO imagery already available and more on the way in the coming years, the team would like to compare pictures of specific fault regions from different times to look for fresh evidence of recent moonquakes.

"For me, these findings emphasize that we need to go back to the moon," Schmerr said. "We learned a lot from the Apollo missions, but they really only scratched the surface. With a larger network of modern seismometers, we could make huge strides in our understanding of the moon's geology. This provides some very promising low-hanging fruit for science on a future mission to the moon."

More information: *Shallow seismic activity and young thrust faults on the Moon, Nature Geoscience (2019). DOI: 10.1038/s41561-019-0362-2 , https://www.nature.com/articles/s41561-019-0362-2*

https://wb.md/2w3OcDh

'Quantum Leap' in Severe Head Injury Survival With EMS Protocol

Training paramedics to implement prehospital guidelines for traumatic brain injury (TBI) has dramatically improved survival in patients with severe head trauma, new data show.

Megan Brooks

Results from the Excellence in Prehospital Injury Care (EPIC) study, which included more than 21,000 TBI patients, showed a doubling of the survival rate in severe TBI victims and a tripling of the survival rate in those who were intubated with prehospital guideline implementation by paramedics.

"In medicine, improved outcomes are almost always incremental, and very few things that we do in medicine improve the ultimate outcome, which is surviving versus dying. This is a quantum leap. This is not incremental," Daniel Spaite, MD, professor of emergency medicine at the University of Arizona in Tucson, who led the study, told *Medscape Medical News*. Findings from the study were published online May 8 in *JAMA Surgery*.

"Astounding" Results

In the study, more than 11,000 paramedics from 130 EMS agencies across Arizona took a 2-hour training session on prehospital TBI treatment guidelines, which emphasize avoidance/treatment of hypoxia, prevention/correction of hyperventilation, and avoidance/treatment of hypotension.

The before-and-after analysis included 21,852 patients with moderate, severe, or critical TBI — 15,228 in the preimplementation period and 6624 in the postimplementation period.

Implementing the prehospital TBI guidelines did not affect overall survival, but did significantly improve survival in the severe TBI subgroup (adjusted odds ratio [aOR], 2.03; 95% confidence interval [CI], 1.52 - 2.72; *P* < .001) and the severe intubated TBI subgroup (aOR 3.14; 95% CI, 1.65 - 5.98; *P* < .001).

"The results are astounding and show that the first 20 minutes of care dramatically impacted the final outcome," Spaite said. "The last 40 years of attempts to find ways to improve brain injury outcomes in the prehospital setting is literally a graveyard full of failed drugs and procedures," he added.

An important point, emphasized Spaite, is that "medics already know how to do this and it doesn't require EMS systems to buy expensive equipment. This can basically be applied anywhere in the world."

Major Clinical Implications

In a statement, Patrick Bellgowan, PhD, program director at the National Institute of Neurological Disorders and Stroke, said the results demonstrate "the significance of conducting studies in real-world settings and brings a strong evidence base to the guidelines. It suggests we can systematically increase the chances of saving lives of thousands of people who suffer severe traumatic brain injuries."

Reached for comment, Robert Glatter, MD, an emergency physician at Lenox Hill Hospital in New York City, noted that this is the first "major prehospital study to evaluate the impact of national prehospital TBI treatment guidelines, which were developed after years of research superseding decades of management based on outdated protocols."

Glatter said the findings have important implications for the prehospital management of patients with severe TBI, "which will lead to increased survival and improve neurological outcomes."

"Implementing simple interventions by EMS providers — addressing hypoxia, hypotension, and avoiding hyperventilation — can make a clear difference in outcome in those with severe neurological impairment after TBI," said Glatter, who was not involved with the current study.

"Simply put," he added, "what we do in the early stages after acute injury is an extension of principles of critical care that continue in the hospital. By focusing and adhering to principles that maximize oxygenation, reduce hypotension, and avoid hyperventilation, we can make a difference in who survives."

The study was supported by the National Institute of Neurological Disorders and Stroke (NINDS). The authors and Glatter have disclosed no relevant financial relationships.

JAMA Surg. Published online May 8, 2019. Abstract

https://wb.md/2VsptD3

Potential Biomarker for Suicidal Thoughts Identified in PTSD

Metabotropic glutamatergic receptor 5 (mGluR5) is a potential biomarker for suicidal thoughts in patients with posttraumatic stress disorder (PTSD), new research suggests.

Michael Vlessides

Investigators used positron emission tomography (PET) to quantify mGluR5 density in five brain regions in patients with PTSD or major depressive disorder (MDD) and in healthy controls.

The study showed that compared to healthy controls, mGluR5 availability was significantly higher in all five brain regions in patients with PTSD, as well as in three brain regions in those with MDD.

"Although both depression and PTSD are stress disorders that are prevalent in our society, it appears that some of the markers regulated by these disorders are different. As such, psychotherapy for these disorders could also be different," study investigator Irina Esterlis, MD, associate professor in psychiatry at Yale University

School of Medicine, New Haven, Connecticut, told *Medscape Medical News*. The findings were published online today in the *Proceedings of the National Academy of Sciences*.

Target of Interest

PTSD is an important risk factor for suicidal ideation and attempts as well as death by suicide, Esterlis noted. However, little is known about the biology underlying suicide in PTSD. Not surprisingly, limited pharmacologic options exist to treat PTSD patients at high risk for suicide.

In recent years, mGluR5 has emerged as a target of interest for PTSD and suicide research, as previous studies have implicated the receptor in mood and anxiety symptoms.

Furthermore, Esterlis and colleagues recently found that patients with PTSD had significantly higher mGluR5 availability than did matched control groups across many brain regions.

Other research has come to similar conclusions, including a 2014 postmortem study that showed upregulation of mGluR5 gene expression in the locus coeruleus was associated with suicide in tissue from depressed individuals.

Nevertheless, the relationship between mGluR5 and suicidal behavior has yet to be explored *in vivo* among patients with PTSD.

"A lot of the literature lumps depression and PTSD into one 'stress disorder' model, whereas we've been seeing — at least with respect to this marker — that depression and PTSD could be quite different. So we wanted to see if the mGluR5 marker is regulated differently with respect to suicidality in these two disorders," Esterlis said.

The investigators hypothesized that dysregulation in mGluR5 may affect the development of suicidal behavior, both directly and through downstream effects.

The study included 29 people with PTSD (mean age, 35.5 years; 16 females), 29 individuals with MDD (mean age, 36.6 years; 14 females), and 29 individuals acting as the healthy controls group (mean age, 37.4 years; 14 females). The three groups were matched by age, race, sex, and smoking status. Interestingly, 16 of the 29 patients with PTSD also met criteria for MDD.

All 87 participants completed a battery of physical, psychiatric, and neurologic examinations at an initial screening visit, both to establish their diagnosis and to rule out any major medical or neurologic illnesses. The presence of suicidal ideation was established based on participants' scan-day report on the Montgomery-Asberg Depression Rating Scale (MADRS) and self-reported Beck Depression Inventory II.

The participants all underwent T1-weighted MRI scans, which were used to evaluate potential structural abnormalities as well as facilitate co-registration with PET data.

Regions of interest for PET scanning comprised three subdivisions of the prefrontal cortex — the ventromedial PFC, orbitofrontal cortex, and dorsolateral prefrontal cortex — as well as the hippocampus and amygdala.

Greater mGluR5 Availability

The investigators first performed multivariate analysis of variance (ANOVA) tests to evaluate group differences in mGluR5 availability, an exercise that revealed significant differences between the groups. In fact, mGluR5 availability was significantly higher in the PTSD group than in the healthy controls group in each of the five regions of interest.

Similarly, mGluR5 availability was also higher in patients with PTSD than in their counterparts with MDD in the orbitofrontal cortex (15%, $P = .007$), dorsolateral prefrontal cortex (17%, $P = .007$), and hippocampus (15%, $P = .007$). No differences were observed in mGluR5 availability between the MDD and control groups.

With respect to the relationship between mGluR5 availability and suicidal ideation, the study showed that the main effect of suicidal

ideation was significant in the PTSD group (P = .01) but not in the MDD group (P = .96).

Post-hoc tests among individuals with PTSD and suicidal ideation showed significantly higher mGluR5 availability in each of the five regions of interest, with an average 24% difference.

In a series of secondary analyses, the researchers investigated the relationship between mGluR5 availability and a number of suicide-related endophenotypic variables. These analyses revealed a divergent pattern of associations between mGluR5 availability and Profile of Mood States (POMS) scores, which is a measure of mood disturbance.

Total POMS score was positively correlated with mGluR5 availability in the PTSD group (P < .001) and inversely correlated with mGluR5 availability in the MDD group (P = .003).

Further examinations revealed that the association between mGluR5 availability and total POMS score in the PTSD group was driven by the patients with PTSD and suicidal ideation (P = .005), as no such association was observed in those with PTSD but *without* suicidal ideation.

The findings have the potential for significant implications in both research and treatment, and support the idea that downregulating mGluR5 may reduce PTSD symptomology, Esterlis said.

"If you look at the animal literature, there's a lot of support for using this marker as treatment," she said. "But it's not clear when it's best to administer medications that target this marker — whether it's immediately after trauma to prevent consolidation of the memory or at some later point when the person actually exhibits symptoms of PTSD.

"Targeting this receptor can have both positive and negative benefit," Esterlis added. "So in order to not make the symptoms worse, this is something we need to figure out."

A First Biomarker

Commenting on the findings for *Medscape Medical News*, Gregor Hasler, MD, University of Fribourg, Switzerland, said effective treatments for suicide prevention in individuals with PTSD have been lacking.

"So one way to solve this problem is to have really good markers to indicate what kind of people are at high risk of suicide," said Hasler, who was not involved in the study. "And this is one of the first biomarkers that has a link to suicidal thoughts."

However, Hasler noted that immediate clinical benefits from the study may not be soon forthcoming, given the cost associated with PET scans. "But there are various drugs that specifically target mGluR5, so these findings may inspire pharmaceutical companies or academia to target these various drugs in PTSD," he said.

Hasler did see a potential link between the findings and the potential use of lithium. "We can't give lithium to everyone. But the mGluR5 receptor is linked to the effect of lithium. So if we have a marker, that would be really helpful," he said.

"Suicide is still rare in veterans, but if you could help identify these people, you might be able to give them lithium and perhaps prevent these suicides," Hasler added.

The study authors and Hasler have disclosed no relevant financial relationships.

Proc Natl Acad Sci. Published online May 13, 2019. Abstract

http://bit.ly/2JsqLMz

Philadelphia's sweetened drink sales drop 38% after beverage tax

Findings from Penn study support beverage taxes as a promising policy tool to help improve public health

Philadelphia - One year after Philadelphia passed its beverage tax, sales of sugary and artificially sweetened beverages dropped by 38 percent in chain food retailers, according to Penn Medicine researchers who conducted one of the largest studies examining the

impacts of a beverage tax. The results, published this week in JAMA, translate to almost one billion fewer ounces of sugary or artificially sweetened beverages - about 83 million cans of soda - purchased in the Philadelphia area. The findings provide more evidence to suggest beverage taxes can help reduce consumption of sugary drinks, which are linked to the rise in obesity and its related non-communicable diseases, such as type II diabetes.

On January 1, 2017, Philadelphia became the second city in the United States to implement a tax on the distribution of sugary and artificially sweetened beverages. The goal of the 1.5 cent per ounce tax was to generate revenue to support universal pre-K, community schools, and improvements to parks and recreation centers, with the potential side benefit of curbing consumption of unhealthy drinks.

"Taxing sugar-sweetened beverages is one of the most effective policy strategies to reduce the purchase of these unhealthy drinks. It is a public health no-brainer and a policy win-win," said first author Christina A. Roberto, PhD, an assistant professor of Medical Ethics & Health Policy in the Perelman School of Medicine at the University of Pennsylvania. "It's likely to improve the long-term health of Philadelphians, while generating revenue for education programs in the city of Philadelphia."

Countries across the globe, like Mexico and the United Kingdom, have turned beverage taxes into public health tools to help slow the increasing rates of obesity, a global epidemic. In the United States alone, two-thirds of the adult population is obese or overweight. In Philadelphia, more than 68 percent of adults and 41 percent of children are overweight or obese. Additionally, according to Philadelphia's Community Health Assessment, 32 percent of adults and 18 percent of teens in the city consume one or more sugar-sweetened beverages each day. Beverage taxes have now been passed in seven U.S. cities and are being considered at the state level in Connecticut and Colorado. The first city to pass the tax, Berkeley, Calif., reduced overall sales of sugary beverages by 10 percent and consumption by 52 percent among its low-income residents, according to recent studies.

To determine the impact the new law would have on prices and sales in Philadelphia, the researchers analyzed store-wide beverage price and sales data one year before and one year after the tax was implemented at 291 chain retailers. Stores included supermarkets, mass merchandisers, and pharmacies, which together represent the largest sources of sugary beverage sales. The study does not include restaurants or independent stores. The team included stores within the city limits and those just outside to understand how many taxed drinks were being purchased across city lines to avoid the tax. They also compared their results to Baltimore, which has no beverage tax. Data was obtained from Information Resources, Inc., a company that tracks and compiles sales data from U.S. retailers. The researchers also calculated how much prices increased after the tax.

One year after the tax was implemented, the cost of sugary and artificially sweetened drinks increased by 0.65, 0.87, and 1.56 cents per ounce at supermarkets, mass merchandisers, and pharmacies, respectively.

Between January 2016 and December 2017, there was a 59 percent reduction in taxed beverage sales at supermarkets, a 40 percent reduction at mass merchandisers, and a 13 percent reduction at pharmacies. Overall, people purchased nearly 1.3 billion fewer ounces after the tax, which is over a 50 percent decrease in total volume of ounces. However, sales in Pennsylvania border zip codes did increase by 308.2 million ounces. Therefore, after accounting for some consumers crossing the city lines to buy drinks outside the city, the overall sales of taxed beverages dropped 38 percent among chain food retailers in the area, the researchers reported. In a separate study published earlier this year in PLOS ONE, the Penn researchers found that filings of unemployment claims in

Philadelphia industries potentially affected by the beverage tax did not change in the year after the tax was implemented.

"Philadelphia's tax on sweetened drinks led to a huge reduction in sales of these unhealthy drinks one year after it was implemented and generated revenue for thousands of pre-k slots. That's great news for the well-being of the people of Philly," Roberto said.

Co-authors on the study include Hannah G. Lawman, PhD, Michael T. LeVasseur, PhD, MPH, Nandita Mitra, PhD, Ana Peterhans, MPH, Bradley Herring, PhD, and Sara N. Bleich, PhD.

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http://bit.ly/2JoFxEh

You are what you eat: How the pursuit of carbs changed mammals' genes and saliva

A study of 46 mammal species explores the evolutionary history of amylase, a compound that breaks down carbs

BUFFALO, N.Y. -- Starch, a complex carbohydrate, is a vital source of nutrition for many mammals. Humans farm it in the form of rice, wheat, corn, potatoes and oats. Rats comb our garbage piles for scraps of pizza and bread. Wild boars root for tubers.

Now, a new study is providing insight into how the pursuit of starch may have driven evolutionary adaptations in these and other hungry mammals.

The research, conducted on 46 mammal species, focuses on a biological compound called amylase, which is produced by humans and other animals to break down starch.

The study finds that in the course of mammalian evolution, the genetic machinery that teaches the body how to make amylase has been something of a chameleon. It has evolved in different ways in different beasts, and it's capable of changing rapidly, possibly in accordance with what animals eat.

The study finds that mammals with starchy diets tend to have more copies of the amylase gene, which carries instructions for building amylase, than mammals that consume little starch (at least among the species studied).

The research also presents evidence that evolutionary changes related to amylase -- including duplications of the amylase gene and the ability to produce amylase in saliva -- may have arisen independently in some different species. Called convergent evolution, this phenomenon often signals a particularly useful adaptation.

Findings were published on May 14 in eLife. Overall, the study paints a colorful picture of the evolutionary history of amylase across mammals, ranging from humans, dogs and house cats to hedgehogs and ring-tailed lemurs, along with baboons that store food in their cheeks.

"Amylase is a case where diet may have the potential to change our genes. This is fascinating," says Omer Gokcumen, PhD, assistant professor of biological sciences in the University at Buffalo College of Arts and Sciences. "The duplications we see in the amylase gene give a very flexible and rapid way in which gene functions can evolve, and this mechanism of evolution is underappreciated."

"Past studies have explored the evolution of amylase in select species, such as humans and dogs, but our research takes a broader perspective," says Stefan Ruhl, PhD, DDS, professor of oral biology in the UB School of Dental Medicine. "We examine dozens of mammalian species from different branches of the evolutionary tree, and we see that when it comes to amylase in saliva, genetics and biology may respond to what we eat."

The study was led by Gokcumen, Ruhl and first author Petar Pajic, a UB oral biology and biological sciences researcher.

The research - supported by the National Institute of Dental and Craniofacial Research, National Cancer Institute and National Science Foundation - included researchers from UB, the Foundation for Research and Technology in Greece, SUNY

Plattsburgh, Cornell University and the Friedrich-Loeffler-Institut in Germany.

Details on the findings:

Mammals with starchy diets appear to have adapted, genetically, to stomach more carbs: Of the species studied, those with starch in their diets generally have more copies of the amylase gene, which carries instructions for making amylase, than animals like carnivores and herbivores whose strict diets tend to exclude starch. Carb-munching humans, house mice, brown rats, dogs, pigs and boars have lots of copies, while mammals like mountain lions, which subsist on meat, and hedgehogs, which dine on foods such as insects and snails, have few.

This is important because the gene is akin to a mold in a factory: the more units you have, the more amylase you can theoretically produce. As for how the extra copies of the amylase gene evolved, "It's like the chicken and the egg - we cannot really tell what came first," Ruhl says. "Starch in the diet may have led to more amylase, and the ability to digest starch may have led to increased starch intake, and so forth."

In some cases, close contact with humans -- and access to human food -- may have spurred an adaptation to starch. The study confirmed past findings from other teams showing that mice and domestic dogs, which live alongside people, have more copies of the amylase gene than their wild cousins (wolves and wild rodents, respectively). The brown rat (Rattus norvegicus) -- a species commonly known as the street or sewer rat -- also has many copies of the amylase gene.

The genetic expansion of amylase likely occurred independently in multiple species: Based on genetic evidence, the study concluded that mice, rats, dogs, pigs and humans likely acquired some of their extra copies of the amylase gene independently, at separate times in their evolution, rather than inheriting all the copies from a common ancestor. This phenomenon, called convergent evolution, can signal a particularly useful adaptation.

Amylase in saliva is more widespread than previously known (some pet dogs produce it, for example): Most amylase is produced in the pancreas, but some animals also secrete it in saliva. The new research finds that this capability is more common than previously known, and proposes salivary amylase as another adaptation that may have arisen through convergent evolution in some species.

When scientists tested for amylase in the drool of 22 mammalian species, they found it in 15 species, including six species that were not previously known to have amylase in saliva. Perhaps unsurprisingly, baboons and rhesus macaques that store food in cheek pouches for long periods of time were among the most prolific producers of salivary amylase among the mammals tested.

Pet dogs were among the species that were newly identified as salivary amylase producers. While not all dogs have amylase, the research found it in several breeds, such as English cream golden retrievers, Labradors and pitbulls.

"This study provides the most comprehensive picture, to date, on how amylase has evolved in the mammalian lineage at both the genetic level and at the level of protein expression in saliva," says Pajic, the study's first author. "From a broader theoretical stance, it also reveals how quickly evolution can happen and how something simple, like the food you eat, may drive otherwise unrelated species to evolve similarly."

For animals who don't store food in their cheeks, the evolutionary advantage of having amylase in saliva is unclear. But Ruhl, a leading salivary researcher, says one theory is that it helps animals and humans identify starchy foods as desirable to eat.

"Humans have a lot of salivary amylase, but why?" he says. "Unlike the baboons who predigest food in their cheek pouches, we humans do not keep food in our mouths long enough for any

substantial digestion to happen. One idea is that salivary amylase evolved to help our ancestors detect starch: They would not be able to taste it otherwise. Amylase liberates sugar in starch, and this may help animals develop a taste preference for starch-rich foods like potatoes or corn."

Other hypothesized purposes for salivary amylase include cleaning sticky starch residues from teeth: "Amylase in saliva might act as a kind of biochemical toothbrush nature has provided us with," Ruhl says with a smile. "It could help to regulate the make-up of the oral microbiome."

http://bit.ly/2LPlLUA

New doctors' DNA ages six times faster than normal in first year

Long work hours of intern year associated with accelerated shortening of telomere regions of chromosomes

In just a few short weeks, tens of thousands of newly minted doctors will start the most intense year of their training: the first year of residency, also called the intern year.

A new study suggests that between now and next summer, that experience will make their DNA age six times faster than normal. And the effect will be largest among those whose training programs demand the longest hours.

The findings about the effect of residency focus on the stretch of DNA called telomeres - which keep the ends of chromosomes intact like the plastic end of shoelaces. The discovery that telomeres shrink in an accelerated way among interns suggest the importance of ongoing efforts to reduce the strain of medical training.

But the researchers say their study also holds implications for other professions and situations that expose people to prolonged stress and months of long hours.

Published online in the journal *Biological Psychiatry*, the new study is the first to measure telomere length before and after individuals faced a common prolonged intense experience. It involved 250 interns from around the country who volunteered for the Intern Health Study, based at the University of Michigan, and a comparison group of college students from U-M.

"Research has implicated telomeres as an indicator of aging and disease risk, but these longitudinal findings advance the possibility that telomere length can serve as a biomarker that tracks effects of stress, and helps us understand how stress gets 'under the skin' and increases our risk for disease," says Srijan Sen, M.D., Ph.D., the U-M neuroscientist and psychiatrist who is the study's senior author and heads the Intern Health Study.

He adds, "It will be important to study how telomere changes play out in larger groups of medical trainees, and in other groups of people subjected to specific prolonged stresses such as military training, graduate studies in the sciences and law, working for startup companies, or pregnancy and the first months of parenting."

Sen's team worked with Kathryn Ridout, M.D., Ph.D., the new study's first author, during the research portion of her residency at Brown University. She is now a psychiatrist at Kaiser Permanente in California as well as having an appointment at Brown.

"The current model of intern year training during residency increases trainee stress, which impacts their mental health and wellbeing. These results extend this work and are the first to show that this stress reaches down to the biological level, impacting the well accepted marker of aging and disease risk, telomere length," says Ridout. "I was particularly surprised to see the relation of number of hours worked to telomere shortening."

Sen notes that after the discovery that telomeres protect the DNA in chromosomes from damage - a discovery that earned the 2009 Nobel Prize - research on them in humans has focused on taking snapshots of telomere length, mainly in older adults. This has

yielded important discoveries about the links between shrunken telomeres and disease.

Ridout analyzed data from dozens of telomere studies for a meta analysis published in 2016 that showed clear links between telomere length and the risk and severity of depression.

In the new study, Sen and his colleagues asked recently graduated medical students to contribute a sample of their DNA before they began their intern year, and then followed up to get another sample at the end of that year. The interns also took a lengthy questionnaire before their training began, and again at several points during and at the end of the intense year.

The results show that some new doctors went into residency with telomeres that were already shorter than their peers. This included those who said their family environment early in life was especially stressful - which echoes previous findings about the impacts of such an upbringing on telomere length.

Those who scored high on personality traits that together are classed as "neuroticism" -- being quick to react and slow to relax, and a tendency to respond with negativity - also had shorter telomeres at the start of intern year.

But when the team looked at the results of the DNA tests taken after intern year ended, only one factor that they studied emerged with a clear link to telomere shrinkage: the number of hours the interns worked each week.

On average, all the interns in the study said they worked an average of 64.5 hours a week. But the more the interns worked, and therefore the more days they put in that were at or above the national limit of 16 hours in effect at the time, the faster their telomeres shrank.

"The responses given by some of the interns in these surveys indicated that some were averaging more than 80 hours of work a week, and we found that those who routinely worked that many hours had most telomere attrition," says Sen. "Those whose hours were at the lower end of the range had less telomere attrition."

By contrast, the comparison group of 84 first-year U-M undergraduate students experienced no telomere shrinkage, despite also being in a stressful year-long situation of coping with life at an elite institution of higher education. These students were taking part in a study led by Sen's colleague at the U-M Molecular and Behavioral Neuroscience Institute, Huda Akil, Ph.D.

Sen's Intern Health Study has begun collecting DNA samples from many more interns, and is now monitoring their mood, sleep and activity using smartphone apps and commercial activity trackers. He hopes to study the telomeres of future groups of interns to gather more data about how they change over the intern year and how those changes match up with their experiences during the year.

For instance, the frequent changes in shift time - from day to night and back again - during residency has already emerged in Sen's work as an important factor in mood and circadian disruption. Future studies will explore if this sort of shiftwork increases telomere attrition.

He also hopes that researchers can evaluate whether any practices can protect telomeres from shrinkage or even spur repair and lengthening of these protective stretches of DNA. For now, he says, "Residency directors should do as much as they can to keep their interns' work hours and work load towards the lower end of the current range."

And as new doctors prepare to graduate and head into their intern years, he advises them to focus on their mood, sleep and stress-relieving activities as much as they can.

Ridout says she hopes the results will be heeded by the Accreditation Council for Graduate Medical Education and others. "Having completed residency myself and understanding the stress that can come with this training and extended work hours, I am

hopeful these data can help inform the decisions of governing bodies that have been debating the importance of regulating resident work hours," she says. "Our results suggest that reforms in intern training and work hours with a renewed focus on wellbeing is necessary to protect the health and viability of our physician workforce."

The Intern Health Study is now enrolling graduating medical students who will begin residency this summer. For more information visit https://www.internhealthstudy.org/

In addition to Ridout, Sen and Akil, the new study's authors are Samuel Ridout, M.D., Ph.D., also of Kaiser Permanente, Constance Guille, M.D., of the Medical University of South Carolina, and Douglas Mata, M.D., M.P.H., of Harvard University. The study was funded by the National Institutes of Health (MH101459), the American Foundation for Suicide Prevention and the Office of Naval Research (ONR N00014-12) and the Pritzker Foundation.

http://bit.ly/2VMzX5h

Being wise is good for your health -- review looks at emerging science of wisdom

Can science measure what it means to be wise?

A growing body of evidence suggests that wisdom is a complex concept that contributes to mental health and happiness, according to a review in the May/June issue of *Harvard Review of Psychiatry*.

Different aspects of wisdom may be traced to specific areas of the brain, and might possibly be enhanced by behavioral interventions, suggests the article by Dilip V. Jeste, MD, and Ellen E. Lee, MD, of the Sam and Rose Stein Institute for Research on Aging, University of California San Diego. They write, "Wisdom has important implications at both individual and societal levels, and warrants further research as a major contributor to human thriving."

Research Helps Define Wisdom and Its Impact on Our Lives

What is wisdom? While it has been discussed in religion and philosophy for centuries, scientific research on wisdom has accelerated in the past few decades. While it may seem impossible to define and measure wisdom, Drs. Jeste and Lee note that research has demonstrated the validity of other psychological constructs such as consciousness, stress, and resilience.

Based on an in-depth review from ancient writings to modern times, Drs. Jeste and Lee propose that wisdom can be defined as "a complex human trait with several specific components: social decision making, emotion regulation, prosocial behaviors, self-reflection, acceptance of uncertainty, decisiveness, and spirituality."

Over the years, several approaches to measuring wisdom have been proposed, although each has its limitations.

The basic concept of wisdom has always been the same, suggesting that it "probably has an underlying neurobiological basis." Drs. Jeste and Lee propose a model of the neurobiology of wisdom, localized mainly to two areas of the brain: the prefrontal cortex and limbic striatum. "Emerging research suggests that wisdom is linked to better overall health, well-being, happiness, life satisfaction, and resilience," the researchers add.

Wisdom seems to increase with age despite decreased physical health, and has been linked to better quality of life. Enhancing wisdom in older age may even confer an evolutionary advantage: "Despite the loss of their own fertility and physical health, older adults help increase their children's well-being, health, longevity, and fertility - the 'Grandma Hypothesis' of wisdom." The authors propose a model of the development of wisdom, involving genetics, environment, and epigenetics.

Wisdom's positive effects on health and well-being raise an intriguing question: Can wisdom be increased? While research is limited so far, psychosocial and possibly biological interventions to enhance the function of brain areas involved might lead to enhanced wisdom. The researchers call for "a greater emphasis on promoting wisdom through our educational systems from elementary to professional schools."

Such efforts might have important benefits, with increases in wisdom leading to improved health and well-being on the societal as well as individual level. Drs. Jeste and Lee conclude, "There is a need to expand empirical research on wisdom, given its immense but largely untapped potential for enhancing mental health of individuals and promoting well-being of the society at large."

Click here to read "The Emerging Empirical Science of Wisdom"

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http://bit.ly/2VKAqov

'Zombie Cells' Buildup in Body May Play Role in Aging

The field of zombie cells is still young. But at least a dozen companies have launched efforts to pursue treatments.

NEW YORK (AP) — Call them zombie cells — they refuse to die.

As they build up in your body, studies suggest, they promote aging and the conditions that come with it like osteoporosis and Alzheimer's disease. Researchers are studying drugs that can kill zombie cells and possibly treat the problems they bring.

Basically the goal is to fight aging itself, which hopefully will in turn delay the appearance of age-related disease and disabilities as a group, says geriatrics specialist Dr. James Kirkland of the Mayo Clinic in Rochester, Minnesota. That's in contrast to playing a "whack-a-mole game" of treating one disease only to see another spring up, he said.

The research has been done chiefly in mice. Earlier this year, the first test in people was published and provided some tantalizing results.

Zombie cells are actually called senescent cells. They start out normal but then encounter a stress, like damage to their DNA or viral infection. At that point, a cell can choose to die or become a zombie, basically entering a state of suspended animation.

The problem is that zombie cells release chemicals that can harm nearby normal cells. That's where the trouble starts.

What kind of trouble? In mouse studies, drugs that eliminate zombie cells — so-called senolytics — have been shown to improve an impressive list of conditions, such as cataracts, diabetes, osteoporosis, Alzheimer's disease, enlargement of the heart, kidney problems, clogged arteries and age-related loss of muscle.

Mouse studies have also shown a more direct tie between zombie cells and aging. When drugs targeting those cells were given to aged mice, the animals showed better walking speed, grip strength and endurance on a treadmill. Even when the treatment was applied to very old mice, the equivalent of people ages 75 to 90, it extended lifespan by an average of 36 percent.

Researchers have also shown that transplanting zombie cells into young mice basically made them act older: their maximum walking speed slowed down, and their muscle strength and endurance decreased. Tests showed the implanted cells converted other cells to zombie status.

Kirkland and colleagues this year published the first study of a zombie-cell treatment in people. It involved 14 patients with idiopathic pulmonary fibrosis, a generally fatal disease that scars the lining of the lungs. Risk rises with age, and the lungs of patients show evidence of zombie cells.

In the preliminary experiment, after three weeks of treatment, patients improved on some measures of physical fitness, like walking speed. Other measures did not show improvement.

Overall, the results are encouraging and "it really raises enthusiasm to proceed with the more rigorous studies," said Dr. Gregory Cosgrove, chief medical officer of the Pulmonary Fibrosis Foundation, who played no role in the study.

The field of zombie cells is still young. But Kirkland estimates at least a dozen companies have formed or have launched efforts to pursue treatments. He holds shares in one.

Apart from age-related diseases, anti-zombie drugs might be useful for treating premature aging among cancer survivors that brings on the early appearance of some diseases, said Laura Niedernhofer of the University of Minnesota.

Some of these drugs have been approved for other uses or are even sold as supplements. But Niedernhofer and Kirkland stress that people should not try them on their own, nor should doctors prescribe them, for the uses now under study because more research has to be done first.

Niedernhofer said the best drugs may be yet to come. The goal is not to prevent stressed cells from turning into zombies, she said, because they may become cancerous instead. The aim is to trigger death of cells that have already transformed, or to limit the harm they do.

And what about giving them to healthy people who want to ward off aging? That's possible but a long way off, after studies have established that the drugs are safe enough, she said.

"We may not get there," Kirkland said.

In any case, experts are impressed by the research so far. "I think this is very exciting," said Dr. George Kuchel of the University of Connecticut Center on Aging in Farmington. The results from animal studies are "very spectacular. It's very compelling data."

Nir Barzilai, a researcher of aging at the Albert Einstein College of Medicine in New York, said he believes targeting zombie cells will play a role in the overall effort to delay, stop and maybe reverse aging. So much research suggests they promote aging that "we know that it should be true," he said.

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http://bit.ly/2JLIQVn

Thwarting a Protein Reverses Brain Decline in Aged Mice

Blocking an immune-related molecule lodged in blood vessels stops memory loss

By Simon Makin

Something in elderly blood is bad for brains. Plasma from old mice or humans worsens cognition and biological indicators of brain health, when infused into young mice. Conversely, plasma from young mice (or humans) rejuvenates old brains.

Much of this research has come from neurobiologist Tony Wyss-Coray's group at Stanford University, which is pursuing what constituents of blood might be responsible. One previous study identified a protein, which declines with age, that has powerful beneficial effects. That protein can cross from the blood into the brain, but Wyss-Coray wondered how certain molecules contained in blood typically "talk" to the brain. Must they interact with brain cells directly, or can they communicate indirectly, through the gateway to the brain, the blood-brain barrier?

To investigate, Wyss-Coray's team tried a new approach in their latest study, published May 13 in *Nature Medicine*. "We reasoned that the most obvious way plasma would interact with the brain is through blood vessels," Wyss-Coray says. "So, we looked at proteins that change with age and had something to do with the vasculature." One protein that becomes more abundant with age, VCAM1, stood out, and the team showed that it appears to play a pivotal role in the effects of aged blood on the brain. Biological and cognitive measures alike indicated that blocking VCAM1 not only prevents old plasma from damaging young mouse brains but can even reverse deficits in old mice. The work has important implications for age-related cognitive decline and brain diseases. "Cognitive dysfunction in aging is one of our biggest biomedical

challenges, and we have no effective medical therapies. None," says neuroscientist Dena Dubal, of the University of California, San Francisco, who was not involved in the study. "It's such an important line of investigation; it has tremendous implications."

VCAM1 (Vascular Cell Adhesion Molecule–1) is a protein that protrudes from the endothelial cells lining the walls of blood vessels and latches on to circulating immune cells (white blood cells, or "leukocytes"). It responds to injury or infection by increasing in number and triggering immune responses. An enzyme shears VCAM1 off endothelial cells at roughly the same rate it is produced, so the total amount in cells stays fairly stable and the amount in circulation is a good proxy for this.

The researchers first checked whether the increase in circulating VCAM1 with age was also accompanied by more of the protein bound to the cells, which they found to be the case for about 5 percent of brain endothelial cells.

They then used cutting-edge "single cell" genetic sequencing technology to inspect these rare cells, finding that they contain many receptors for pro-inflammatory proteins, known as cytokines. "It's like these cells that express VCAM1 are a type of sensor of the blood environment," Wyss-Coray says.

The researchers wanted to know whether this increase in VCAM1 attached to cells merely accompanies signs of brain aging, or whether it actually helps cause the damage. One sign that a brain is getting older is widespread activation of its immune cells, called microglia. These cellular housekeepers, which normally perform routine housekeeping functions, enter an inflammatory state, releasing cytokines and free radicals. "So, they're not cleaning the house, they're messing it up," Wyss-Coray says. "They really trash the place."

Another indicator is a decline in activity related to the formation of new brain cells in the hippocampus, a brain region involved in memory and one of few regions thought to produce new cells in adulthood. The team used two techniques to block VCAM1: One of them genetically deleted the protein from the mice's brains. Another injected an antibody that binds to it to stop anything else attaching. Both methods prevented signs of brain aging in young mice infused with old plasma and reversed existing markers in elderly mice brains. The researchers then gave the mice learning and memory tests. In one, which involves remembering which of several holes is safe to drop through, treated elderly mice performed as well as youngsters once fully trained. "The aged mice looked like they were young again in terms of their ability to learn and remember," Dubal says. "It's remarkable."

The researchers' working theory for what happens, is that cytokines in aged blood first trigger brain endothelial cells to produce more VCAM1. When leukocytes then attach to the protein, the cells signal the brain to activate microglia. This creates an inflamed environment that puts dampers on the stem cells involved in new neuron formation. "What they're showing here, is the blood-brain barrier's not static, and can sense changes in the blood, then relay those signals to the brain, telling it to become more inflamed, explains Richard Daneman a neuropharmacologist specializing in the blood-brain barrier at the University of California, San Diego.

Stopping leukocytes from interacting with VCAM1 prevents this signaling and thus protects against or even reverses the effects of old blood. "One really has the feeling reading through this, that a major leap has been made [not only] in basic science discovery but also [in pointing to] a new therapeutic pathway for one of our most devastating problems," Dubal contends. The precise molecular details of this pathway remain to be determined, Wyss-Coray says. "Is VCAM1 signalling into the cell, or are immune cells releasing toxic factors?" he asks. "We need to understand, at the molecular level, how this works."

Treatments based on these findings would not necessarily have to cross the blood-brain barrier. “One of our biggest challenges is how do we get treatments into the brain given this fortress wall?” Dubal says. But VCAM1 is on the blood side of that wall. A downside is that blocking a component of the immune system could have side effects. A drug, called Tysabri that binds to leukocytes, stopping them attaching to VCAM1, is already used for treating multiple sclerosis. Problems arose shortly after its approval as some patients harbored a virus before treatment that then ran rampant. Patients are now screened for this virus. “It’s not without risk or caution that we use immunosuppressive therapies,” Dubal says “But they’ve proven very effective in certain conditions.”

One possibility would be to reduce VCAM1 activity to healthy, youthful levels, rather than block it completely. “We’re not directly blocking immune cells, we’re regulating the target of immune cells, so maybe that allows us to be subtle and not completely block immune activation in cases of injury,” Wyss-Coray says. “That needs to be shown.” Once more is known, there may also be other ways to intervene, such as stopping the signals that tell the brain to become inflamed or prevent VCAM1 from increasing in the first place, Daneman says. “Understanding the whole pathway will potentially enable us to limit those side effects.”

The main caveat, of course, is that whether the findings in mice lead to effective human therapies remains to be seen, but there are reasons for optimism. Human plasma was also used in the mice. “That improves the relevance to humans,” Dubal says, ”And soluble VCAM, in humans, like in mice, increases with aging. We won’t know until we test it, but it’s really promising.” The team is planning to test a VCAM1 antibody in people whose cognition declines after stroke, perhaps because of an immune response. “I’m hoping we can recover or prevent some of these cognitive deficits and recover function after stroke,” Wyss-Coray says.

Numerous antibodies already exist. “VCAM1 antibodies have been developed by many pharma companies,” Wyss-Coray says. “They didn’t pursue them once [Tysabri] got approved, but they could be resurrected and tested. We could translate this relatively quickly, because it’s a target that’s easily accessible and there’s precedent for targeting this pathway.”

https://bbc.in/2HzB522

Glucosamine supplements 'may cut heart risk'

Glucosamine supplements, better known as a remedy for joint pain, may lower a person's risk of cardiovascular disease (CVD), research suggests.

The findings in the British Medical Journal (BMJ) come from nearly half a million people in the UK. Almost one in five of the 466,039 participants said they took glucosamine. Users were less likely to develop heart and artery diseases or stroke, or die from these conditions. The results suggest a possible benefit, but more and longer studies are needed. It could be that users are generally more healthy, rather than glucosamine having a direct effect, experts caution.

What is glucosamine?

Glucosamine is a naturally occurring compound found in joint cartilage. The body can make its own glucosamine, but supplements are sometimes used by people looking to relieve pain and symptoms of osteoarthritis and other joint disorders.

Most glucosamine supplements are sold in pharmacies and health food shops in the UK as a "food supplement" and not a medicine. They are checked for food safety to ensure they won't do you any harm, but they are not checked for quality or quantity of the "active" ingredient. The active ingredient can be made synthetically or derived from the shells of shellfish.

Does it work?

The evidence supporting the effectiveness of glucosamine for joint pain is mixed and very limited. Guidelines for the NHS do not recommend it for osteoarthritis. The new suggested link to a lower risk of cardiovascular disease needs more research. The BMJ study was observational - it can't establish cause. And it did not include detailed information on glucosamine dose or duration of use.

Glucosamine was associated with a 9%-22% lower risk of CVD death, coronary heart disease and stroke, compared to non-use over the 10 years of the study. The researchers believe the supplement may have an anti-inflammatory effect, which could explain the suggested benefit, but more investigations are needed.

Is it safe?

Studies on the safety of glucosamine are limited. People with an allergy to shellfish should not take it, nor should women who are pregnant or breastfeeding. Glucosamine should be avoided by people taking warfarin, as it may affect blood clotting. It may also decrease the effectiveness of some anti-cancer drugs, say experts. Like any supplement or medication, it can cause side-effects in some individuals.

What do experts think of the findings?

Prof Naveed Sattar, from the University of Glasgow, said: "Only a trial can determine whether there is any truth to the lower observed risk. Observational studies can only ever generate new ideas to test.

"Many other supplements have not proven benefits in trials even when observational data suggested there may be health benefits. Some supplements have even been shown to cause harm in trials. So, for now, I would not rush to buy glucosamine to lessen my heart risks when there are many other cost-effective proven ways to do so."

Dr Sonya Babu-Narayan, from the British Heart Foundation, said: "One in four people in the UK still die from heart and circulatory disease. We urgently need to fund research that could result in improved prevention, diagnosis and treatment.

"If a well-known and widely available supplement like glucosamine could help prevent heart and circulatory diseases, including heart attack and stroke, it is an avenue of research worth exploring.

"Meanwhile, an important way to reduce your risk is to maintain a healthy lifestyle and - when relevant - take medications as recommended to you by your doctor."

http://bit.ly/2w9eYdI

Japanese space startup aims to compete with US rivals

Low-cost rocket business in Japan is well-positioned to accommodate scientific and commercial needs in Asia

by Mari Yamaguchi

A Japanese startup that launched a rocket into space earlier this month plans to provide low-cost rocket services and compete with American rivals such as SpaceX, its founder said Wednesday.

Interstellar Technology Inc. founder Takafumi Horie said a low-cost rocket business in Japan is well-positioned to accommodate scientific and commercial needs in Asia. While Japan's government-led space programs have demonstrated top-level technology, he said the country has fallen behind commercially due to high costs.

Japanese entrepreneurs and Founder of Interstellar Technologies Inc. Takafumi Horie speaks during a press conference in Tokyo, Wednesday, May 15, 2019. Horie said a low-cost rocket business in Japan is well-positioned to accommodate scientific and commercial needs in Asia. While Japan's government-led space programs have demonstrated top-level technology, he said the country has fallen behind commercially due to high costs. **(AP Photo/Koji Sasahara)**

"In Japan, space programs have been largely government-funded and they solely focused on developing rockets using the best and newest technologies, which means they are expensive," Horie told reporters in Tokyo. "As a private company, we can focus on the minimum level of technology needed to go to space, which is our advantage. We can transport more goods and people to space by slashing costs."

Horie said his company's low-cost MOMO-3 rocket is the way to create a competitive space business in Japan.

During its May 4 flight, the unmanned MOMO-3 rocket reached 113.4 kilometers (70 miles) in altitude before falling into the Pacific Ocean. The cost to launch the MOMO-3 was about one-tenth of the launch cost of Japan Aerospace Exploration Agency, the country's space agency, according to Interstellar CEO Takahiro Inagawa.

Horie said his company plans to launch its first orbital rocket—the ZERO—within the next few years and then it would technologically be on par with competitors such as Elon Musk's SpaceX, Amazon founder Jeff Bezos' Blue Origin and New Zealand engineer Peter Beck's Rocket Lab.

The two-stage ZERO would be twice as long and much heavier than the compact MOMO-3, which is about 10 meters (32 feet) long and 50 centimeters (1.5 feet) in diameter and weighs about 1 ton. It would be able to send satellites into orbit or carry payloads for scientific purposes.

Development of a low-cost commercial rocket is part of a growing international trend in the space business led by the U.S. and aggressively followed by China and others.

At home, Horie could face competition from space subsidiaries of major companies such as Canon and IHI, which have expertise from working with the government's space agency.

http://bit.ly/2w5GTv3

Ragweed compounds could protect nerve cells from Alzheimer's

Scientists might have discovered a promising new use for some substances produced by ragweed

As spring arrives in the northern hemisphere, many people are cursing ragweed, a primary culprit in seasonal allergies. But scientists might have discovered a promising new use for some substances produced by the pesky weed. In ACS' *Journal of Natural Products*, researchers have identified and characterized ragweed compounds that could help nerve cells survive in the presence of Alzheimer's disease (AD) peptides.

Those with AD, a neurodegenerative disorder, often have impaired judgment, cognition, memory and behavior. Scientists have linked AD to the accumulation of amyloid-β (Aβ) peptides in the brain, which form plaques that kill nerve cells. Unfortunately, the five drugs currently approved for AD treatment only delay disease progression for a short time. When Won Keun Oh and colleagues screened 300 natural plant extracts for activity against AD in a preliminary study, they found a surprising candidate: *Ambrosia artemisiifolia* (common ragweed, ブタクサ). This invasive weed, native to North America, has now spread to South America, Asia and much of Europe. Oh and colleagues decided to isolate and characterize the structures of ragweed compounds responsible for this neuroprotective activity.

The researchers isolated 14 compounds from whole ragweed plants that appeared to protect neurons from Aβ-induced toxicity. They determined the structures of the compounds with nuclear magnetic resonance, mass spectrometry and other analytical techniques. Seven of the chemicals, including terpenoids and spermidine conjugates, had been described previously, but the remainder were

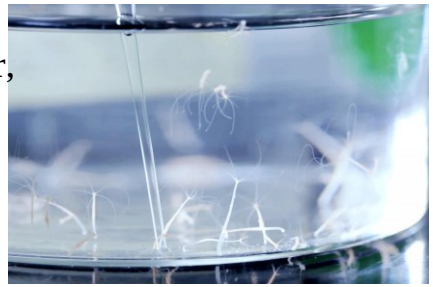
newly identified terpenoids. When the researchers added the two most active new compounds to a lab dish that contained neurons producing Aβ, about 20 percent more cells survived than without treatment.

The authors acknowledge funding from the National Research Foundation of Korea.
The abstract that accompanies this study is available here.

http://bit.ly/2EhBQfq

Over-fed bacteria make people sick

Unnatural and particularly comprehensive nutrient supply may decouple bacteria from their host organism and thus destroy the delicate balance of the microbiome



***The fresh water polyp Hydra as a model system shows possible links between overfed microbes and the development of disease.* Credit: © Kiel Life Science**

Since the end of the Second World War, along with the growing prosperity and the associated changes in lifestyle, numerous new and civilisation-related disease patterns have developed in today's industrialised nations.

Examples of the so-called "environmental diseases" are different bowel inflammations like Crohn's disease or ulcerative colitis. Common causes include disruptions to the human microbiome, i.e. the natural microbial colonisation of the body, and in particular of the intestine.

To date, scientists have explained this disrupted cooperation between host body and microbes with different hypotheses: for example, they postulated that excessive hygiene, the intensive use of antibiotics, or certain genetic factors permanently disrupt the microbiome, thus making people vulnerable to illnesses. However, these explanation attempts have so far been incomplete.

A team from the Collaborative Research Centre (CRC) 1182 "Origin and Function of Metaorganisms" at Kiel University (CAU) has now formulated a new and more comprehensive ecological-evolutionary theory on the development of environmental diseases.

The Kiel researchers suggest that an unnatural and particularly comprehensive nutrient supply decouples bacteria from their host organisms, and thus destroys the delicate balance of the microbiome. The, to some extent, over-fed bacteria in the gut thus promote disease development. The Kiel scientists published this fundamental new approach towards a more complete explanation of environmental diseases yesterday in the journal mBio.

The origin lies in the oceans

The starting point for the Kiel research team was the ecology of marine habitats: research on coral and algae dying off, and the associated effects on important ecosystems in the oceans, suggests that in addition to other factors such as climate change or overfishing, the nutrient conditions in the seawater may be the cause of the problem.

As soon as there is an oversupply of food due to human influences, bacteria living in a community with corals begin to decouple from their hosts. They then no longer feed off the metabolic products of the host, but prefer the richer nutrient supply of the surrounding waters.

The balance of the coral microbiome is disrupted because of the exodus of its symbiotic partner, and diseases occur as a result. "In this connection between nutrient availability and the balance of bacteria-host relationships, we see a universal principle which goes way beyond the very specific example of corals," explained Dr Tim Lachnit, research associate at the CRC 1182 and first author of the study.

"In studies of our model organism, the freshwater polyp Hydra, we were able to experimentally confirm this connection," continued Lachnit. These small cnidarians also showed clear signs of disease

as soon as their normal nutrient uptake was disturbed and an over-supply of food was available instead.

What do corals and cnidarians have to do with people?

With a high degree of probability, the knowledge gained in the experiment can also be transferred to human health. Similar to in seawater, or in the simple body cavity of a freshwater polyp, which during the course of evolution has decoupled from its external environment and a direct food supply, the nutrient supply in the human gut is also changing along with the civilisation-induced changes in eating habits - towards an unbalanced, energy-rich and low-fibre diet.

In addition to direct negative health consequences, a permanently high, easy to process supply of nutrients not only affects the human metabolism it feeds, but also the bacterial colonisation of the intestine, which is also "fed". The microbes switch from the metabolites of the host as their staple food to the abundantly available nutrients from the human food and thus decouple from their interactions with the host organism.

"This over-feeding of the bacteria promotes their growth as a whole, and certain species of bacteria proliferate to the detriment of other members of the microbiome in an increased and uncontrolled manner," emphasised Professor Thomas Bosch, spokesperson of the CRC 1182. "Thus, along with the change in the composition of the bacterial colonisation, the interactions between bacteria and host organism also change, and a serious maladaptation - known as dysbiosis - occurs," explained Dr Peter Deines, research associate at the Kiel metaorganism CRC.

Other civilisation-related factors increase this imbalance of the microbiome. The elimination of periodic fasting resulting from food sources not always being available, the only very rare occurrence of diarrhoea leading to episodic reductions of the intestinal bacterial colonisers and the diet-related impoverishment of the microbial diversity in the gut are just a few examples.

The first two of these represent very fundamental mechanisms, which since the early development of mankind right up to the pre-industrial era enabled the microbiome to return to a normal state at regular intervals, and thus regain a healthy and natural composition.

Does the microbiome heal itself?

The "over-feeding hypothesis" proposed by researchers from the Kiel CRC 1182, in close cooperation with the CAU Cluster of Excellence "Precision Medicine in Chronic Inflammation", offers valuable approaches for further research, right through to potential transfer to future treatments: to date, scientists were particularly looking for ways to correct a disturbed microbiome through external interventions such as probiotics, i.e. the addition of certain types of helpful bacteria, or even faecal transplants to restore the balance.

Now, the ecological-evolutionary perspective has added another dimension. More than ever before, it incorporates the natural ability of the microbiome to readjust itself, and to restore a healthy composition. Therefore, future research approaches lie in the specific mechanisms that balance the microbiome, and the question of whether the "overfeeding" of the bacteria can be reduced by changed eating habits.

"An interesting question will be whether the original evolutionary processes which ensure the balance of the microbiome also have therapeutic potential," said Lachnit. "In the future we will, for example, not only consider the known health benefits of fasting, but also its effects on the composition and function of the microbiome, and thus on the development of inflammatory diseases," continued Lachnit.

https://nyti.ms/2WTf9Fu

Alone, They Stink. Together They Create Dark Chocolate's Alluring Aroma.

With the help of a trained panel of sniffers, chemists uncovered the molecules that give a rich treat its scents.

By Veronique Greenwood

If there was ever a science experiment you'd want to participate in, it might be this one: sitting in a booth and inhaling the tangy, intense aromas of dark chocolates. But not just anyone gets to join this research. The people doing the sniffing were trained to detect subtle differences in scent, helping chemists uncover just which odor molecules are behind the distinctive smell of these rich treats.

In a paper published last week in the Journal of Agricultural and Food Chemistry, the researchers behind this endeavor reveal that dark chocolate's aroma comes down to 25 molecules, in just the right concentrations — some of which you might find rather disgusting if you sniffed them on their own.

The sensory panel was part of a study on chocolates with cacao contents from 90 to 99 percent, which are growing more popular, said Michael Granvogl, a chemist at the University of Hohenheim in Germany who wrote the paper with Carolin Seyfried of the Technical University of Munich. While chocolate flavors — which, like all flavors, are a combination of taste and smell working together — have been studied for decades, this was one of the first times chocolate of such high cacao concentrations has come under the microscope. Or rather, perhaps, the sniff-o-scope.

Fed through a battery of analytical machines, the chocolates yielded 77 compounds that could contribute to the chocolates' aroma. Some were at levels too low to be detected by the human nose. But around 30 others made the sensory cut.

If you looked at a list of what each molecule smells like individually, you might notice something surprising. For instance, acetic acid, the odor molecule present in the highest levels in the chocolates, smells like vinegar by itself. And 3-methylbutanoic acid has a rancid, sweaty stench on its own. Then there's dimethyl trisulfide, which smells like cabbage.

But these and other compounds, at very particular concentrations, work together to play the elaborate pipe organ that is our olfactory system. Together they attach to receptors in the nose and the back of the mouth to play a specific set of keys, creating a neural chord that says not "cabbage" or "sweat" or "vinegar," nor even a mixture of these, but "chocolate." Specifically, in this case, "very dark chocolate."

Working backward to assemble the chord, the scientists were able to re-create the scent to the satisfaction of the trained sniffers using just 25 of those molecules. The goal is not necessarily to create artificial versions of familiar food aromas. Understanding what is behind a smell can help make it clear what has gone wrong when a food product has an off-taste or scent.

The study also suggests that the wonderfully diverse world of flavor and aroma may, thanks to our pipe-organ sense of smell, be generated by a relatively small number of molecules working in concert. In other work, Dr. Granvogl's colleagues have found that with around 226 molecules, they can make mixtures that capture the flavors of about 227 different types of food, from meats, fish and cheeses to chocolate.

"Butter is very easy — you only need four components to mimic butter flavor," he said. It is the concentrations of the molecules, not just their identities, that count, he and his colleagues have found. The exact same molecules make up the flavor of peanuts and hazelnuts, for instance.

"If you mix it in different concentrations, you end up on the one side with a hazelnut flavor and on the other side, a peanut flavor," Dr. Granvogl said.

http://bit.ly/2HAsqVF

Regular crosswords and number puzzles linked to sharper brain in later life

Older adults who regularly take part in word and number puzzles have sharper brains, according to the largest online study to date.

The more regularly adults aged 50 and over played puzzles such as crosswords and Sudoku, the better their brain function, according to research in more than 19,000 participants, led by the University of Exeter and King's College London.

The findings emerge from two linked papers published today (May 16th) in the *International Journal of Geriatric Psychiatry*. The researchers have previously presented their findings on word puzzles at the Alzheimer's Association International Conference in 2018. The new research builds on these findings and also reports the same effect in people who regularly complete number puzzles.

Researchers asked participants in the PROTECT study, the largest online cohort in older adults, to report how frequently they engage In word and number puzzles and undertake a series of cognitive tests sensitive to measuring changes in brain function. They found that the more regularly participants engaged with the puzzles, the better they performed on tasks assessing attention, reasoning and memory.

From their results, researchers calculate that people who engage in word puzzles have brain function equivalent to ten years younger than their age, on tests assessing grammatical reasoning and eight years younger than their age on tests measuring short term memory.

Dr Anne Corbett, of the University of Exeter Medical School, who led the research, said: "We've found that the more regularly people engage with puzzles such as crosswords and Sudoku, the sharper their performance is across a range of tasks assessing memory, attention and reasoning. The improvements are particularly clear in the speed and accuracy of their performance. In some areas the improvement was quite dramatic - on measures of problem-solving, people who regularly do these puzzles performed equivalent to an average of eight years younger compared to those who don't. We can't say that playing these puzzles necessarily reduces the risk of dementia in later life but this research supports previous findings that indicate regular use of word and number puzzles helps keep our brains working better for longer."

The study used participants in the PROTECT online platform, run by the University of Exeter and Kings College London. Currently, more than 22,000 healthy people aged between 50 and 96 are registered in the study, and the study is expanding into other countries including Hong Kong and the US. The online platform enables researchers to conduct and manage large-scale studies without the need for laboratory visits. PROTECT is a 25 year study with participants being followed up annually to explore how the brain ages and what might influence the risk of dementia later in life. PROTECT is funded by the National Institute for Health Research (NIHR) Bioresource, including through its NIHR Clinical Research Network (CRN). In addition to taking part in vital research, participants in the PROTECT study have access to a brain training programme that has already been shown to benefit brain function, as well as having the opportunity to take part in exciting new research studies into brain health and dementia prevention.

Clive Ballard, Professor of Age-Related Diseases at the University of Exeter Medical School, said: "PROTECT is proving to be one of the most exciting research initiatives of this decade, allowing us to understand more about how the brain ages and to conduct cutting-edge new studies into how we can reduce the risk of dementia in people across the UK. If you're aged 50 or over, you could sign up to take part in research that will help us all maintain healthy brains as we age."

The papers are entitled: - *The relationship between the frequency of number?puzzle use and baseline cognitive function in a large online sample of adults aged 50 and over*
- An online investigation of the relationship between the frequency of word puzzle use and cognitive function in a large sample of older adults

http://bit.ly/2JRX4nE

Earliest evidence of the cooking and eating of starch

Early human beings who lived around 120,000 years ago in South Africa were 'ecological geniuses' who were able to exploit their environment intelligently for suitable food and medicines

New discoveries made at the Klasies River Cave in South Africa's southern Cape, where charred food remains from hearths were found, provide the first archaeological evidence that anatomically modern humans were roasting and eating plant starches, such as those from tubers and rhizomes, as early as 120,000 years ago.

The new research by an international team of archaeologists, published in the Journal of Human Evolution, provides archaeological evidence that has previously been lacking to support the hypothesis that the duplication of the starch digestion genes is an adaptive response to an increased starch diet.

"This is very exciting. The genetic and biological evidence previously suggested that early humans would have been eating starches, but this research had not been done before," says Lead author Cynthia Larbey of the Department of Archaeology at the University of Cambridge. The work is part of a systemic multidisciplinary investigation into the role that plants and fire played in the lives of Middle Stone Age communities.

The interdisciplinary team searched for and analysed undisturbed hearths at the Klasies River archaeological site.

"Our results showed that these small ashy hearths were used for cooking food and starchy roots and tubers were clearly part of their diet, from the earliest levels at around 120,000 years ago through to 65,000 years ago," says Larbey. "Despite changes in hunting strategies and stone tool technologies, they were still cooking roots and tubers."

Professor Sarah Wurz from the School of Geography, Archaeology and Environmental Studies at the University of the Witwatersrand in Johannesburg, South Africa (Wits University) and principal investigator of the site says the research shows that "early human beings followed a balanced diet and that they were ecological geniuses, able to exploit their environments intelligently for suitable foods and perhaps medicines".

By combining cooked roots and tubers as a staple with protein and fats from shellfish, fish, small and large fauna, these communities were able to optimally adapt to their environment, indicating great ecological intelligence as early as 120 000 years ago.

"Starch diet isn't something that happens when we started farming, but rather, is as old as humans themselves," says Larbey. Farming in Africa only started in the last 10 000 years of human existence.

Humans living in South Africa 120 000 years ago formed and lived in small bands.

"Evidence from Klasies River, where several human skull fragments and two maxillary fragments dating 120 000 years ago occur, show that humans living in that time period looked like modern humans of today. However, they were somewhat more robust," says Wurz.

Klasies River is a very famous early human occupation site on the Cape coast of South Africa excavated by Wurz, who, along with Susan Mentzer of the Senckenberg Institute and Eberhard Karls Universit?t Tübingen, investigated the small (c. 30cm in diameter) hearths.

The research to look for the plant materials in the hearths was inspired by Prof Hilary Deacon, who passed on the Directorship of the Klasies River site on to Wurz. Deacon has done groundbreaking work at the site and in the 1990's pointed out that there would be plant material in and around the hearths. However, at the time, the micro methods were not available to test this hypothesis.

http://bit.ly/30teblC

Early dengue virus infection could 'defuse' Zika virus

Study shows that a previous dengue infection can protect against Zika-associated damage

"We now know for sure that Zika virus infection during pregnancy can affect the unborn foetus in such a way that the child develops microcephaly and other severe symptoms," explains Prof Felix Drexler, a virologist at the Charité who has been developing diagnostic tests for Zika and other viruses at the DZIF. Just a few years ago, pictures of affected new-borns were cause for worldwide dismay and perplexity. "However, what we did not understand then was that high incidence of microcephaly seemed to occur particularly in northeastern Brazil," says Drexler. Why are expecting mothers in these regions at a higher risk of developing a severe Zika-associated disease than in other regions? The scientists consequently began to search for cofactors that have an influence on whether a Zika infection during pregnancy will develop fatal consequences or not.

A suspected cofactor

Dengue viruses, which are widespread in Latin America and cause dengue fever, were suspected cofactors. Initially, the scientists suspected that the antibodies humans produce against the dengue virus contribute to the foetal damage caused in later Zika infection. It has been known for a long time that these antibodies can enhance subsequent dengue infections under certain conditions.

However, in the case of Zika, the opposite seems to be the case. "Surprisingly, our study has shown that a previous dengue infection can protect against Zika-associated damage," emphasizes Drexler.

The study

As a first step to investigating the interactions between dengue and Zika viruses, the genomes of all known dengue viruses in Brazil were compared to each other. This was to enable the researchers to find out whether perhaps dengue viruses in northeastern Brazil had caused different immunity compared to the immunity observed in other regions in Brazil over the last decades. In addition, the scientists conducted extensive serological tests in Salvador, Brazil: Samples from a case-control study were tested for antibodies against four different dengue serotypes. Samples from 29 mothers who had undergone Zika infection during pregnancy and gave birth to children with microcephaly were investigated. Samples from 108 mothers who also had undergone Zika infection during pregnancy but gave birth to healthy children were used as controls. In this project, scientists from the Charité - Universitätsmedizin Berlin collaborated closely with the Federal University of Bahia and the Institute of Virology of the Bonn University Medical Centre.

Cofactor becomes a protective factor

The study showed that an existing immunity against dengue virus significantly reduces the risk of Zika-associated microcephaly in newly borns. "We can now say that people who have had early infections with dengue do not need to worry much about contracting more severe forms of Zika infection due to this," summarises Drexler.

This is an important message for pregnant women.

Consequently, it could not be confirmed that the dengue virus acts as a cofactor for congenital Zika infection. The scientists are now looking for further cofactors and other possibilities of identifying the risk of microcephaly early on.

Background

Felix Drexler and his research group have already developed several novel Zika virus tests. The Zika diagnostics project in Brazil was brought underway by the DZIF in order to act against the threat of emerging infections. It is also being funded by the EU programme Horizon 2020.

Zika and dengue viruses

Zika viruses are usually transmitted by mosquitoes, particularly by the *Aedes* species, but they can also be transmitted sexually. Symptoms of Zika include rashes, headaches, joint pain and muscle pain, conjunctivitis and sometimes fever.

However, these symptoms are considered mild compared to other tropical diseases that are transmitted by mosquitoes. During pregnancy, the virus can cause microcephaly and other malformations in the unborn child.

The dengue virus is also transmitted by mosquitoes of the *Aedes* species and has similar symptoms to Zika infection. Dengue usually causes high temperatures, headaches, muscle and joint pain. People usually recover within a few days, but complications may also occur. Dengue fever is one of the most common diseases transmitted by mosquitoes worldwide.

http://bit.ly/2w8sUEP

Research reveals insulin-producing beta cells may change function in diabetes

A revolutionary new study using only materials derived from humans has revealed that insulin-producing beta cells can change their function in diabetes - and that this change may be reversible.

Research led by the University of Exeter is the first to look at the cells using an entirely animal-free model, instead using a completely human cell system in laboratories for the first time. The team found that the RNA messaging system which tells proteins how to behave in cells is different in diabetes. The changes lead to some of the beta cells no longer producing insulin which regulates blood sugar, and instead producing somatostatin, which can block the the secretion of other important hormones including insulin itself.

The research is published in Human Molecular Genetics and funded by Animal Free Research UK. The study may give new insights into how high blood sugar can alter the behaviour of important hormone-producing cells, and pave the way to new treatments.

Professor Lorna Harries, of the University of Exeter Medical School, who led the research, said: "These insights are really exciting. Only recently, Exeter researchers discovered that people with type 1 diabetes still retain some insulin-producing cells, but the environment produced by diabetes can be toxic for these cells that remain. Our work could lead to new changes to protect these cells, which could help people maintain some ability to make their own insulin. The method we used of creating an all-human cell system for the first time is significant - I don't think we'd have seen these changes in mouse cells."

Carla Owen, Chief Executive of Animal Free Research UK which funded the research, said: "This is pioneering research at its best - we supported the Exeter team to create a novel method to investigate how diabetes affects humans, rather than animals. Their breakthrough findings would never have been discovered in animals, highlighting the importance of using a human-relevant approach to understanding human diseases. We're proud to be supporting the next phase to take this discovery forward and closer to treatments for people living with diabetes."

The team examined what happens to human beta cells when exposed to an environment that replicated type 2 diabetes.

Beta cell loss occurs in both type 1 and type 2 diabetes. Scientists have previously assumed this was because the microenvironment around the cells causes them to die.

However, the team found for the first time that a proportion of the cells are no longer beta cells that are making insulin. They had actually started to make a different hormone called somatostatin - characteristic of a delta cell.

The team than analysed post mortem pancreas tissue from people with either type 1 or type 2 diabetes. This revealed that they have

more delta cells than they should have, suggesting that diabetes might be causing some of the beta cells to turn into delta cells in people as well as in cells in the laboratory.

Similar findings have been reported in animal models, but the changes are different. In mice, most of the changes are beta to alpha cells, not delta cells. Alpha cells make a different hormone called glucagon. This means that the consequences of changes in cell type might be different between mice and humans.

In the next step, the team investigated why the cells might change from beta cells to delta cells, by looking at gene regulation. They looked at differences in the genes that make the decision as to which type of RNA message is made which helps cells to deal with their environment. In samples from the pancreas of people with type 2 diabetes, they found that about a quarter of genes show disruption to the expected pattern of messages made compared with samples from people with no diabetes. This indicates that the differences in the regulators translate to differences in messages made. The type of RNA message made controls every aspect of cell life or behaviour, and the authors speculate this could be why the treated cells behave differently.

Professor Harries said: "The really exciting finding is that in the laboratory at least, we have been able to reverse the changes - turn the delta cells back to beta cells - if we restore the environment to normal, or if we treat the cells with chemicals that restore the regulator genes and the patterns of RNA messages made to normal. That's very promising when we consider the potential for new therapeutics."

http://bit.ly/2HDrvLD

Big data reveals hidden subtypes of sepsis

Sepsis isn't simply one condition but rather many conditions that could benefit from different treatments

PITTSBURGH - Much like cancer, sepsis isn't simply one condition but rather many conditions that could benefit from different treatments, according to the results of a University of Pittsburgh School of Medicine study involving more than 60,000 patients.

These findings, announced today in JAMA and presented at the American Thoracic Society's Annual Meeting, could explain why several recent clinical trials of treatments for sepsis, the No. 1 killer of hospitalized patients, have failed. Sepsis is a life-threatening condition that arises when the body's response to an infection injures its own tissues and organs.

"For over a decade, there have been no major breakthroughs in the treatment of sepsis; the largest improvements we've seen involve the enforcing of 'one-size fits all' protocols for prompt treatment," said lead author Christopher Seymour, M.D., M.Sc., associate professor in Pitt's Department of Critical Care Medicine and member of Pitt's Clinical Research Investigation and Systems Modeling of Acute Illness Center. "But these protocols ignore that sepsis patients are not all the same. For a condition that kills more than 6 million people annually, that's unacceptable. Hopefully, by seeing sepsis as several distinct conditions with varying clinical characteristics, we can discover and test therapies precisely tailored to the type of sepsis each patient has."

In the "Sepsis ENdotyping in Emergency Care" (SENECA) project, funded by the National Institutes of Health (NIH), Seymour and his team used computer algorithms to analyze 29 clinical variables found in the electronic health records of more than 20,000 UPMC patients recognized to have sepsis within six hours of hospital arrival from 2010 to 2012.

The algorithm clustered the patients into four distinct sepsis types, described as:

- **Alpha: most common type (33%), patients with the fewest abnormal laboratory test results, least organ dysfunction and lowest in-hospital death rate at 2%;**
- **Beta: older patients, comprising 27%, with the most chronic illnesses and kidney dysfunction;**
- **Gamma: similar frequency as beta, but with elevated measures of inflammation and primarily pulmonary dysfunction;**
- **Delta: least common (13%), but most deadly type, often with liver dysfunction and shock, and the highest in-hospital death rate at 32%.**

The team then studied the electronic health records of another 43,000 UPMC sepsis patients from 2013 to 2014. The findings held. And they held again when the team studied rich clinical data and immune response biomarkers from nearly 500 pneumonia patients enrolled at 28 hospitals in the U.S.

In the next part of the study, Seymour and his team applied their findings to several recently completed international clinical trials that tested different promising therapies for sepsis--all of which had ended with unremarkable results.

When trial participants were classified by the four sepsis types, some trials might not have been failures. For example, early goal-directed therapy (EGDT), an aggressive resuscitation protocol that includes placing a catheter to monitor blood pressure and oxygen levels, delivery of drugs, fluids and blood transfusions was found in 2014 to have no benefit following a five-year, $8.4 million study. But when Seymour's team re-examined the results, they found that EGDT was beneficial for the Alpha type of sepsis patients. Conversely, it resulted in worse outcomes for the Delta subtype.

"Intuitively, this makes sense--you wouldn't give all breast cancer patients the same treatment. Some breast cancers are more invasive and must be treated aggressively. Some are positive or negative for different biomarkers and respond to different medications," said senior author Derek Angus, M.D., M.P.H., professor and chair of Pitt's Department of Critical Care Medicine. "The next step is to do the same for sepsis that we have for cancer--find therapies that apply to the specific types of sepsis and then design new clinical trials to test them."

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