http://bit.ly/35jdBJq

Common genetic link between autism and Tourette's impairs brain communication

Lancaster University researchers have discovered, for the first time, how a genetic alteration that increases the risk of developing Autism and Tourette's impacts on the brain.

Their research also suggests that ketamine, or related drugs, may be a useful treatment for both of these disorders.

Autism affects an estimated 2.8 million people in the UK while Tourette's Syndrome - a condition that causes a person to make involuntary sounds and movements called tics -affects an estimated 300,000 people in the UK. The treatments available for both disorders are limited and new treatments are urgently required. Recent research has also shown that these disorders are genetically linked.

People with a genetic deletion known as chromosome 2p16.3 deletion often experience developmental delay and have learning difficulties. They are also around 15 times more likely to develop Autism and 20 times more likely to develop Tourette's Syndrome, but the mechanisms involved are not completely understood.

Using brain imaging studies, neuroscientists have shown that deletion of the gene impacted by 2p16.3 deletion (Neurexin1) impacts on the function of brain regions involved in both conditions. A key finding is that this genetic deletion disrupts a brain area known as the thalamus, compromising its ability to communicate with other brain areas. Lead researcher Dr Neil Dawson of Lancaster University said: "We currently have a very poor understanding of how the 2p16.3 deletion dramatically increases the risk of developing these disorders.

However, we know that the 2p16.3 deletion involves deletion of the Neurexin1 gene, a gene that makes a protein responsible for allowing neurons to communicate effectively."

Deletion of the Neurexin1 gene affects brain areas involved in Autism and Tourette's including the thalamus, a collection of brain regions that play a key role in helping other brain areas communicate with each other. Changes were also found in brain regions involved in processing sensory information and in learning and memory.

Importantly, the researchers also found that the ability of the thalamic brain regions to communicate with other brain areas was impaired by the genetic deletion. They then tested the ability of a low dose of the drug ketamine, a drug used clinically at higher doses as an anesthetic, to normalize the alterations in brain function induced by the genetic deletion.

Dr Dawson said: "Intriguingly our data suggest that ketamine can restore some aspects of the brain dysfunction that results from 2p16.3 deletion and suggests that ketamine, or other related drugs, may be useful in treating some of the symptoms seen in Autism and Tourette's. The brain circuits affected suggest that these drugs may be particularly useful for the cognitive and motor problems experienced by people with these disorders."

Interestingly, ketamine was shown to normalise activity in the thalamic regions found to be hyperactive as a result of the genetic deletion and re-established the ability of these regions to communicate with other brain areas. This suggests that ketamine, or related drugs, may be a useful treatment for people with 2p16.3 deletion or with Autism and Tourette's Syndrome, although more research is needed.

Dr Dawson urges caution to those who may be thinking of using ketamine therapeutically.

"While this data gives us important new information on the brain circuits affected by 2p16.3 deletion and of the potential usefulness of ketamine to help people with Autism and Tourette's much more research needs to be conducted to prove its clinical potential. We

know that ketamine impacts on the activity of several brain regions in addition to the thalamus, and the effects in these other regions are likely to cause unwanted side-effects. In addition, long-term ketamine treatment may have negative consequences that are not yet fully understood. We also think ketamine may not be the best therapeutic option due to its relatively short lifespan in the body.

"However, the findings of this study give us important clues regarding the types of drugs that may be useful in the treatment of these disorders, and we are using this information to actively pursue the validation of these drugs for the potential treatment of these disorders."

http://bit.ly/2rHfroJ

Inflammatory marker linked to dementia

Elevated levels of marker associated with brain atrophy, decline in executive functions

University of Texas Health Science Center at San Antonio

An inflammatory marker called sCD14 is related to brain atrophy, cognitive decline and dementia, according to a study of more than 4,700 participants from two large community-based heart studies. The study was published Monday, Dec. 9, in the journal Neurology.

"We have strong reason to believe that sCD14 can be a useful biomarker to assess a person's risk of cognitive decline and dementia," said study senior author Sudha Seshadri, M.D., professor of neurology at UT Health San Antonio and director of the university's Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases.

"The most exciting part is that we could assess this risk in advance, when there is ample time to intervene and change the course of a person's life," Dr. Seshadri said.

"Higher levels of sCD14 were associated with markers of brain aging and injury, such as total brain atrophy and a decline in executive functioning--the decision-making needed for many activities of daily life," said study lead author Matthew Pase, Ph.D., of the Florey Institute for Neuroscience and Mental Health in Melbourne, Australia.

The researchers studied risk of dementia in 1,588 participants from the Framingham Heart Study and 3,129 participants from the Cardiovascular Health Study. Dr. Pase and Dr. Seshadri are Framingham investigators.

Plasma sCD14 was measured in participants' blood upon study enrollment. In the Framingham group, brain MRI and cognitive testing were performed within one year after the blood draw for sCD14. A second round of tests was performed after seven years. Surveillance for dementia was conducted over an average of nine years.

In the Cardiovascular Health Study, the first brain MRI was obtained three to four years after enrollment and a second round five years later. "Cost-effective, blood based biomarkers are greatly needed to detect and track the progression of preclinical brain injury predisposing to dementia," the researchers state in the paper. "Such biomarkers could also act as endpoints in clinical trials of disease-modifying interventions and expand our understanding of disease biology."

There are not yet any drug trials to see if lowering sCD14 levels would help cognition in humans. However, treatment with several targeted anti-inflammatory medications--such as statins--can lower sCD14. "There is a growing recognition of the role of inflammation in neurodegeneration and vascular injury-related cognitive decline and dementia," Dr. Seshadri said.

Reference: "Association of CD14 with incident dementia and markers of brain aging and injury," Neurology, Matthew P. Pase, et al.

Funding: National Heart Foundation of Australia Future Leader Fellowship; National Heart, Lung, and Blood Institute, U.S.A.; National Institute on Aging, U.S.A.; National Institute of Neurological Disorders and Stroke, U.S.A.

Acknowledgment: The authors thank the Framingham Heart Study and Cardiovascular Health Study participants for their time.

http://bit.ly/2RQxbsf

Stunning Warrior Grave — Complete with Chariot, Horses — Uncovered in England

Archaeologists are calling it one of the most important discoveries in the U.K.

By Owen Jarus

Inside a 2,200-year-old grave, archaeologists have discovered a stunning Iron Age shield, along with a chariot and two ponies buried in a leaping pose, in what archaeologists are calling one of the most important discoveries in the U.K.

About 30 inches (75 centimeters) in diameter, this shield was found in July 2018; but it wasn't until conservation was complete that its decorations and details could be seen. **Image: © Map Archaeological Practice**

A team of archaeologists led by Paula Ware of MAP Archaeological Practice Ltd. discovered the grave near Pocklington, England. The shield, which is about 30 inches (75 centimeters) across, "was discovered in July 2018, but its true glory was only revealed recently once conservation was completed," Ware told Live Science. The restoration revealed that the shield is decorated with a series of complex swirls and what looks like a sphere protruding from its center.

The grave also held the remains of a man who was in his 40s when he died. In addition to the chariot and two "leaping" ponies, the site was filled with several pig joints and a feasting fork attached to a pork rib, Ware said. Two small brooches — one made of bronze and the other of glass — were also found in the tomb. The elaborate nature of the burial indicates that the deceased man must have been "a significant member of his society," Ware said.

Ware agreed with what other media outlets have suggested about the significance of the find: It is one of the most important ancient discoveries ever made in the U.K. "Yes, especially as it has been excavated under modern archaeological conditions," she told Live Science.

Ancient chariots are not altogether uncommon in burials. A 2,000-year-old Thracian chariot was discovered in 2008 alongside the bones of two horses and a dog in what is now Bulgaria, Live Science previously reported. The practice of burying noblemen near chariots in Bulgaria was especially popular during the time of the Roman Empire, which lasted from about 2,100 to 1,500 years ago. Some 2,500 years ago, a Celtic prince in what is today France was buried in a lavish tomb complete with gorgeous pottery, a gold-tipped drinking vessel and … a chariot, Live Science reported. Archaeologists announced in 2014 that they had discovered a 4,000-year-old burial chamber holding two four-wheeled chariots and plenty of treasures in the country of Georgia, in the south Caucasus.

The newfound grave and chariot were discovered when the archaeological team was excavating an area where homes were going to be built. The researchers plan to submit a paper describing the finds to a scientific publication.

http://bit.ly/2qMJ6MI

Less ploughing leads to higher crop yields

Satellite data confirms importance of leaving soil alone.

By Natalie Parletta

Scientists have used modern technology to show that an ancient approach to agriculture may be the best.

Satellite imagery of nine US corn belt states – covering around one million square kilometres – and soybeans in three states shows that reducing crop tillage (ploughing) produces notably greater yields of both crops over the longer term.

The practice, known as "conservation tillage", is a key principle of conservation agriculture that seeks to revitalise soil and, in turn, improve long-term crop productivity.

Emerging after the 1930s Dust Bowl in the US and adopted more broadly in the 1980s and '90s, it is now applied on more than 150 million hectares globally – particularly in South America, Oceania and North America.

However, some farmers remain wary because the benefits are long term, and many previous studies – carried out over the short term and often in research settings that don't reflect real-world practices – have produced inconsistent outcomes.

"Worries that it can hurt crop yields have prevented some farmers from switching practices," says Jillian Deines from Stanford University, US, the lead author of a paper published in the journal *Environmental Research Letters*.

While indigenous cultures used no-tillage or minimal tillage, modern farmers have long ploughed the land to help control weeds, mix nutrients and prevent dirt from compacting.

damages its structure, reduces water retention and interferes with resident bacteria that are pivotal to soil health and crop yields.

This year the US produced more than 300 million metric tonnes of corn and 100 of soybeans, representing a third of global production, for food, oil, feedstock, ethanol and export.

To compare the yield of farmers who engaged in conservation versus conventional tilling, the Stanford team accessed published data from satellite imagery taken between 2005 and 2017.

Conservation tillage covered nearly half the total corn cropland in 2017, an increase of 17% since 2012. Cover cropping – one of three stalwarts of conservation agriculture, along with lower tillage and crop rotation – only covered 3.4% of the area, albeit an increase of 75%.

The researchers analysed long-term crop yields using a forest-based machine learning algorithm, accounting for other variables such as weather and soil conditions.

Overall, they found that corn yields increased on average by 3.3% and soybeans by 0.74% in fields where long-term conservation tillage practices had been adopted, amounting to an extra 11 million metric tonnes of corn and 800,000 million of soy.

The increased corn yield alone matched the whole 2018 output of South Africa, Indonesia, Russia or Nigeria.

The yields were higher in some areas and lower in others, largely due to differences in soil water content and seasonal temperatures, with better outcomes in drier, warmer regions.

Wet conditions were favourable to conservatively ploughed crops except during the early season when conventional tillage helps to dry and aerate water-logged soils.

"Figuring out when and where reduced tillage works best could help maximise the benefits of the technology and guide farmers into the future," says senior author David Lobell.

The best results come from continuous, long-term implementation; according to the team's calculations, corn farmers won't see the full benefits for 11 years and soy farmers double that period.

But this is counterbalanced by lower costs for labour, fuel and farming equipment, and small positive gains start even during the first year, accruing over time as the soil's fertility improves.

Conservation tillage can also reduce water requirements and the need to leave fields fallow for soil regeneration, yielding further spin-off benefits, the authors note, although socioeconomic factors need to be considered in future analysis and adoption of the practice.

https://wb.md/2LSWDcS

Flu Season Gets Bad Weeks Earlier Than Last Year, CDC Says

Influenza season is in full swing several weeks early, with an unexpected virus strain causing a lot of illness, according to a report from the Centers for Disease Control and Prevention (CDC).

Troy Brown, RN

Approximately half of jurisdictions in the United States now report high or moderate influenza activity; at this time last year, only four states had done so. Influenza activity continued to vary in different areas of the United States during the week ending November 30 (week 48), with southern states particularly hard hit, according to the CDC.

Several influenza indicators are at or above levels 3 weeks earlier than they were last influenza season. The percentage of outpatients seeking healthcare for influenzalike symptoms during week 48 was 3.5% and has now been above the baseline of 2.4% for 4 weeks.

Last season at this time, that percentage exceeded the baseline at 2.3% during week 47 but remained below 3% until week 51, when it rose to 3.3%. The baseline last season was 2.2%.

A total of 26,576 specimens were tested in clinical laboratories during week 48; of those, 2713 (10.2%) were positive for influenza. That's an increase from week 47, when 1702 (8.0%) of 21,367 specimens were positive for influenza.

Predominant Strain Different

This season, the predominant viral strain differs from that which began the 2018–2019 season. Nationally, B/Victoria now predominates, followed by A(H1N1)pdm09 and A(H3N2).

Last season at this time, influenza A(H1N1)pdm09, influenza A(H3N2), and influenza B viruses co-circulated; however, influenza A(H1N1)pdm09 viruses have been predominant since late September 2018. Influenza B viruses became predominant later in the season.

Thirteen jurisdictions (Puerto Rico, Alabama, Georgia, Louisiana, Minnesota, Mississippi, Nebraska, Nevada, New Mexico, South Carolina, Tennessee, Texas, and Washington) reported high influenza activity during the week that ended November 30, up from eight the week before.

Fifteen jurisdictions (New York City, Arizona, Arkansas, Colorado, Connecticut, Florida, Hawaii, Kentucky, Maryland, Missouri, New Jersey, North Dakota, Oklahoma, Utah, and Virginia) reported moderate activity, an increase from seven the week before.

The District of Columbia and eight states reported low influenza activity, and 16 states reported minimal activity. There were insufficient data to determine an activity level for the US Virgin Islands.

Deaths from pneumonia and influenza are still below threshold this season, at 4.8% (the threshold is 6.4%). One pediatric death was reported; there have been a total of six this season.

Approximately Half of US Currently Affected

Geographically, influenza is widespread in 16 states (Alabama, California, Connecticut, Georgia, Indiana, Louisiana, Massachusetts, Mississippi, Nevada, New Mexico, New York, Pennsylvania, South Carolina, Tennessee, Texas, and Virginia).

The flu is regional in Puerto Rico and 14 states (Alaska, Arizona, Colorado, Florida, Idaho, Kentucky, Minnesota, Montana, Nebraska, Oklahoma, Oregon, Utah, Washington, and Wisconsin).

Last season at this time, influenza was widespread in only Minnesota and was regional in nine states.

Influenza is local in 17 states (Arkansas, Delaware, Hawaii, Illinois, Iowa, Maine, Maryland, Michigan, Missouri, New Hampshire, New Jersey, North Carolina, North Dakota, Ohio, South Dakota,

Vermont, and Wyoming) and sporadic in the District of Columbia, the US Virgin Islands, Kansas, Rhode Island, and West Virginia.

There were 784 laboratory-confirmed influenza hospitalizations reported between October 1, 2019, and November 30, 2019. The overall hospitalization rate was 2.7 per 100,000 population, with the highest rates among adults aged 65 years or older (7.0 per 100,000 population), followed by children aged 0 to 4 years (4.6 per 100,000 population) and adults aged 50 to 64 years (2.7 per 100,000 population).

The CDC stresses that it is not too late to get vaccinated against influenza.

CDC. Weekly US Influenza Surveillance Report, updates for week 48. Full text

http://bit.ly/36urTqA

Work is a fundamental part of being human. Robots won't stop us doing it

Hardly a week goes by without a report announcing the end of work as we know it.

Jean-Philippe Deranty Professor, Macquarie University

In 2013, Oxford University academics Carl Frey and Michael Osborne were the first to capture this anxiety in a paper titled: "The Future of Employment: How susceptible are jobs to computerisation?".

They concluded 47% of US jobs were threatened by automation. Since then, Frey has taken multiple opportunities to repeat his predictions of major labour market disruptions due to automation.

In the face of threats to employment, some progressive thinkers advocate jettisoning our work ethic and building a world without work. If machines can do our work, why not reduce the working week drastically? We should be mature enough to decide what truly matters to us, without tying our identity to a job, or measuring happiness in dollars and professional status. Right?

Not quite.

The reality is that work is tied to our constitution as a species. And this fact is too often overlooked in discussions about the future of work.

Work is a feature of the human species

Recent studies have raised alarms that advances in automation and artificial intelligence (AI) will leave all sectors open to the threat of machines replacing human workers.

The power of AI will supposedly, according to these studies, even make high-skilled specialists redundant - threatening medical practitioners, bank associates, and legal professionals.

Predictions about the rise of the robots either take a pessimistic stance, focusing on disruptions to economic organisations, or view "undoing work" as an opportunity to move to a fairer social model.

However, these views disregard the central role work has played in humanity's development.

Working on environments

Philosophers including Karl Marx, Henri Bergson, and John Dewey argued that working is a defining trait of humans.

Findings over the past two decades have confirmed that features of modern *Homo sapiens* are directly tied to their tendency to work.

Three basic ideas of the old philosophers are reaffirmed by contemporary research in archaeology, anthropology and genetics.

First, humans haven't evolved to fit into their environments as seamlessly as other animals. Humans have had to compensate for a lack of fit. They did this by learning about the ecosystems around them, the plants and animals they could eat, and the natural processes they could use, or should avoid. This knowledge was applied to create instruments, tools and weapons.

Very early on, humans mobilised their knowledge and skills to shape their immediate surroundings and become the dominant animal. Knowledge of nature, technical skills and intervention in the environment are all characteristics of humans' capacity to work.

These allowed us to adapt to highly diverse geographies and climates.

Working on ourselves, and with others

Each new generation has to learn the skills and knowledge that will enable it to sustain its particular mode of survival.

Australian philosopher Kim Sterelny has shown in detail how evolution selected genetic traits that sustain humans' capacity to learn, specifically by enhancing social behaviour and tolerance towards the young. And as humans worked on nature, they also worked in ways that influenced their minds, and their bodies.

It has been demonstrated that cooperation in humans reaches a level unknown in other species. This cooperative capacity has its roots in each individual's dependency on the knowledge, skills and efforts of others. No human is able to sustain themself on their own, and collaboration exceeds what each person can produce alone. Even the most brilliant astrophysicist calls the plumber to fix a broken toilet.

Humans have to work to survive, and this entails working with, and for, others.

The future of work

Acknowledging the anthropological depth of work means admitting current scenarios advocating "the end of work" are not the right answer. They take an unrealistic view of who we are.

We need to recognise work as a human need. As Marx said:

… labour has become not only a means of life, but life's prime want.

The question should not be whether there's room for human work in an automated future. The question should be: how will human work find its place next to machines and robots?

Even if automation becomes widespread, we'll still apply our minds, bodies and hands to productive tasks. We'll still experiment and learn from others.

If machines could truly do all human work, then they'd make humans redundant, as 2001: A Space Odyssey anticipated back in 1968. While this isn't a pleasant scenario, it's not a likely one either.

Automation might bring major social and economic disruptions in the short-term, but it won't get rid of the need for humans to work.

Human needs are also infinitely complex. Nobody can foretell what new activities, techniques, and consequent modes of working will fulfil future needs.

Even if we reject the modern work ethic, we'll still find ways to learn through action and emulate experts.

Human intelligence is geared towards producing useful goods, so we'll continue to look for purposeful activities, too. And we'll seek collaboration with others for mutual benefit.

This is the influence of work on us. We are heir to thousands of years of evolution, and it would be pretentious to assume evolution could stop with us.

Jean-Philippe Deranty receives funding from The Australian Research Council.

http://bit.ly/35kQOwv

First Pig-Monkey Chimeras Were Just Created in China

What's got the body of a piglet and cells from a monkey? This pig-monkey chimera.

By Nicoletta Lanese - Staff Writer 4 days ago

Two piglets recently born in China look like average swine on the outside, but on the inside, they are (a very small) part monkey.

A team of researchers generated the pig-primate creatures by injecting monkey stem cells into fertilized pig embryos and then implanting them into surrogate sows, according to a piece by New Scientist.

Two of the resulting piglets developed into interspecies animals known as chimeras, meaning that they contained DNA from two distinct individuals — in this case, a pig and a monkey.

"This is the first report of full-term pig-monkey chimeras," co-author Tang Hai, a researcher at the State Key Laboratory of Stem Cell and Reproductive Biology in Beijing, told New Scientist. Eventually, Hai and his colleagues aim to grow human organs in animals for use in transplant procedures.

For now, the team plans to stick with monkey cells, as developing human-animal chimeras presents a slew of "ethical issues," the authors noted in a report published Nov. 28 in the journal Protein & Cell.

To create pig-primate chimeras, Hai and his co-authors first grew cells from cynomolgus monkeys (*Macaca fascicularis*) in lab dishes. The team then altered the cells' DNA by inserting instructions to build a fluorescent protein, which caused the cells to glow a bright green.

These luminescent cells gave rise to equally radiant embryonic stem cells, which the researchers then injected into prepared pig embryos. These glowing spots allowed the researchers to track the monkey cells as the embryos grew into piglets.

In total, 4,000 embryos received an injection of monkey cells and were implanted in surrogate sows. The pigs bore 10 piglets as a result of the procedure, but only two of the offspring grew both pig and monkey cells.

By scanning for spots of fluorescent green, the team found monkey cells scattered throughout multiple organs, including the heart, liver, spleen, lungs and skin.

In each organ, between one in 1,000 and one in 10,000 cells turned out to be a monkey cells — in other words, the interspecies chimeras were more than 99% pig.

Although low, the ratio of monkey to pig cells still outnumbered the maximum amount of human cells ever grown in a human-animal chimera.

In 2017, scientists created human-pig chimeras that grew only one human cell for every 100,000 pig cells. The interspecies embryos were only allowed to develop for a month for ethical reasons, including the concern that humans cells might grow in the chimera's brain and grant the animal human-like consciousness, according to New Scientist.

Despite these ethical qualms, the same team of researchers went on to create human-monkey chimeras earlier this year, according to a July report from the Spanish newspaper El País. The results of the controversial experiment have not yet been reported, but the scientists said that no human-primate embryos were allowed to develop for more than a few weeks, the paper reported.

Hai and his co-authors may have avoided the ethical issues involved with human-animal chimeras, but one expert wasn't impressed with their interspecies piglets.

Stem-cell biologist Paul Knoepfler of the University of California, Davis, told New Scientist that the low ratio of monkey to pig cells seems "fairly discouraging." Additionally, the two chimeras and all eight other piglets died shortly after being born, he noted.

The exact reason for the piglets' death remains "unclear," Hai told New Scientist, but he said that he suspects the deaths are linked to the in vitro fertilization (IVF) procedure rather than the injection of monkey DNA.

Other scientists have also found that IVF doesn't consistently work in pigs, according to a 2019 report in the journal Theriogenology.

In the immediate future, Hai and his colleagues aim to increase the proportion of monkey cells to pig cells in future chimeras, and eventually, grow entire monkey organs in their pigs, Hai told New Scientist.

In their paper, the authors noted that their work in pigs could help "pave the way" toward the "ultimate goal of human organ reconstruction in a large animal."

http://bit.ly/2Ph0hQ4

Weird 'Tiger Stripes' on Icy Saturn Moon Enceladus Finally Explained

New research solves some of the mysteries of the "tiger stripes" on Saturn's moon Enceladus.

By Chelsea Gohd - Space.com 3 days ago

The moon has been of particular interest to scientists ever since it was observed in detail by NASA's Cassini spacecraft. With Cassini's data, scientists detected an icy, subsurface ocean on the moon and strange, tiger stripe markings on the moon's south pole that are unlike anything else in the solar system. Icy material from Enceladus' ocean spews into space through these stripes, or fissures, in the moon's surface.

Enceladus has strange, parallel "tiger stipes" at its south pole. **Image: © NASA/JPL-Caltech)**

"First seen by the Cassini mission to Saturn, these stripes are like nothing else known in our solar system," lead author Doug Hemingway said in an emailed statement. "They are parallel and evenly spaced, about 130 kilometers long and 35 kilometers apart. What makes them especially interesting is that they are continually erupting with water ice, even as we speak. No other icy planets or moons have anything quite like them."

In the new study, Hemingway and colleagues Max Rudolph of the University of California, Davis, and Michael Manga of UC Berkeley used models to uncover the physical forces on the moon that cause these fissures to form and keep them in place. The team was also keen to figure out why these cracks are evenly spaced and only on the south pole of Enceladus.

The moon isn't frozen solid, because the gravitational changes caused by its eccentric orbit around Saturn stretches it out slightly. This deformed shape causes the ice sheets at the poles to be thinner and more susceptible to splitting open, they found. This led them to conclude that the fissures that make up these tiger stripes could have formed on the moon's north pole just as well as the south pole, but the south pole just cracked first.

They also found that the stripes are parallel because, after the first stripe (named for the city of Baghdad) split open, it stayed open. So ocean water spewed from it, which caused three other, parallel cracks to form as ice and snow built up along the edges of the first fissure as water jets froze and fell back down. This weight built up pressure and caused the new cracks.

"Our model explains the regular spacing of the cracks," Rudolph said in the statement. He further explained that the weight of the icy material falling back to the edges of the first crack "caused the ice sheet to flex just enough to set off a parallel crack about 35 kilometers (22 miles) away."

They additionally found that the cracks stay open and continue to erupt in part because of the tidal effects of Saturn's gravity which changes with the moon's strange orbit. The fissures continue to widen and narrow, bringing water through them. This prevents them from closing up for good.

"Since it is thanks to these fissures that we have been able to sample and study Enceladus' subsurface ocean, which is beloved by astrobiologists, we thought it was important to understand the forces that formed and sustained them," Hemingway said. "Our modeling of the physical effects experienced by the moon's icy shell points to a potentially unique sequence of events and processes that could allow for these distinctive stripes to exist."

This work was published Dec. 9 in the journal Nature Astronomy.

https://go.nature.com/35jeeCF

Greenland rocks suggest Earth's magnetic field is older than we thought

Analysis finds that the planet's protective shield was in place by at least 3.7 billion years ago, as early life arose.

Alexandra Witze

San Francisco, California - Magnetic minerals in ancient Greenlandic rocks suggest that Earth's magnetic field arose at least 3.7 billion years ago. The finding pushes back the time of the magnetic field's birth to about 200 million years earlier than the commonly accepted estimate — around the time life first appeared on Earth.

Scientists think that having a magnetic field makes Earth more hospitable to life. The field, which is generated by liquid iron sloshing about in the planet's core, shields Earth from energetic particles flowing from the Sun. It helps the planet hold on to its atmosphere and maintain liquid water on its surface.

But very few rocks that are billions of years old, and thus could preserve evidence of when the magnetic field arose, have survived to the present day. The new report is a rare glimpse at what Earth was like billions of years ago.

"I hope you are as excited as I am," Claire Nichols, a palaeomagnetist at the Massachusetts Institute of Technology in Cambridge, told a meeting of the American Geophysical Union in San Francisco, California, on 9 December.

Rare rocks

Nichols led two expeditions to western Greenland in the summers of 2018 and 2019. She was targeting a set of ancient rocks in the Isua region, north of the capital city Nuuk, that researchers have long studied in search of clues to early life. The Isua rocks have inspired fierce debates, including whether they contain fossils of complex organisms from 3.7 billion years ago.

Geological forces have squeezed and heated the rocks so much over the past few billion years that most scientists thought the rocks had lost most of their magnetism. But Nichols and her team travelled to the northernmost part of Isua to study rocks that had been least affected by this squeezing and heating.

Iron minerals in those rocks yielded information on the direction of Earth's magnetic field when the minerals formed. Because the rocks are 3.7 billion years old, the magnetic signal must be, too, Nichols said. Her team ran various tests to try to confirm that the signal was real and not some sort of weak magnetism introduced later as the rocks were heated and squeezed.

Tantalizing clues

"It does sound super-exciting," says Nicholas Swanson-Hysell, a geoscientist at the University of California, Berkeley, who was in the audience at Nichols's talk. He met up with her afterwards to brainstorm ideas about how to confirm her team's finding. One idea might be to look at rocks from parts of northeastern North America that were connected to Greenland in the past, to see whether they can illuminate more of the geological history of the Isua rocks, he says.

John Tarduno, a palaeomagnetist at the University of Rochester in New York, was more sceptical of Nichols's claim. "I'd like it to be true, but I'd like to see more," he says.

In 2015, Tarduno and his colleagues reported finding signs of Earth's magnetic field from more than 4 billion years ago, inside zircon crystals from Australia. Other scientists recently challenged that paper, saying the magnetic minerals inside the zircons could not be accurately dated[1].

Aside from those contested Australian zircons, the oldest-known evidence of Earth's magnetic field — rocks in South Africa — dates to around 3.5 billion years ago.

doi: 10.1038/d41586-019-03807-7

http://bit.ly/38CGp1u

Report discusses potential role of coffee in reducing risk of Alzheimer's and Parkinson's

Research suggests that a lifelong regular intake of coffee may have protective effect related to cognitive decline and neurodegenerative conditions[1-3]

A new report from the *Institute for Scientific Information on Coffee (ISIC)* highlights the potential role of coffee consumption in reducing the risk of neurodegenerative disorders such as Alzheimer's and Parkinson's diseases[1-3].

For the first time in history most people can expect to live into their 60s and beyond, however with increasing age, the risk of disease and disabilities rises[4,5]. The number affected with Alzheimer's disease is estimated to increase globally from today's 47 million to 75 million 2030 and to 132 million in 2050[6].

Parkinson's disease, the second most common age-related neurodegenerative disorder, affects 7 million people globally[7]. Research has suggested that lifestyle may be an important part of the risk for neurodegenerative conditions for which there is currently no curative treatment[8-10].

The new report, authored by Associate Professor Elisabet Rothenberg, Kristianstad University, discusses the role of dietary components, including coffee and caffeine, in reducing the risk of neurodegenerative disorders.

The report considers the mechanisms involved in the positive associations between coffee and Alzheimer's and Parkinson's diseases which are not yet well understood. The role of caffeine and other plant-based compounds present in coffee such as phytochemicals and polyphenols are of particular academic interest[11-13].

Key research findings highlighted in the report include:

- ***Dietary pattern may have an impact on the risk of developing neurodegenerative disorders[5,6]***
- ***Coffee consumption may help reduce the risk of neurodegenerative conditions or relieve symptoms[1-3]***
- ***Considering PD, men might benefit more from coffee consumption than women possibly because oestrogen may compete with caffeine[9,10]***
- ***Further research is required for better understanding of the associations[11-13]***

Readers interested in finding out more about coffee & health can visit:
http://www.coffeeandhealth.org

Notes to editors

- *Moderate coffee consumption can be defined as 3-5 cups per day, based on the European Food Safety Authority's review of caffeine safety[14].*
- *To read a full overview of coffee and cardiovascular disease, click here.*

Author of the report: Associate Professor Elisabet Rothenberg, Kristianstad University

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http://bit.ly/2YN8mit

Scientists eager to explain brain rhythm boost's broad impact in Alzheimer's models

MIT neuroscientists who've pioneered "gamma" rhythm power in the brain can't yet explain why it happens

The sweeping extent to which increasing 40Hz "gamma" rhythm power in the brain can affect the pathology and symptoms of Alzheimer's disease in mouse models has been surprising, even to the MIT neuroscientists who've pioneered the idea. So surprising, in fact, they can't yet explain why it happens.

In three papers, including two this year in Cell and Neuron, they've demonstrated that exposing mice to light flickering or sound buzzing at 40Hz, a method dubbed "GENUS" for Gamma ENtrainment Using Sensory stimuli, strengthens the rhythm across the brain and changes the gene expression and activity of multiple brain cell types. Pathological amyloid and tau protein buildups decline, neurons and their circuit connections are protected from degeneration and learning and memory endure significantly better than in disease model mice who do not receive GENUS.

In a new review article in *Trends in Neurosciences* two researchers leading those efforts lay out the few knowns and many unknowns that must be understood to determine how the widespread effects take place. It's a challenge they relish because the answers could both break new scientific ground and help them improve how GENUS could become a therapeutic or preventative approach for people.

"While we know it affects pathology in mice, we want to understand how because that will help us understand and refine potential treatment," said lead author Chinnakkaruppan Adaikkan, a postdoc in the lab of senior author Li-Huei Tsai, Picower Professor of Neuroscience and director of The Picower Institute for Learning and Memory.

Adaikkan has been interested in understanding how neural activity produces brain rhythms since his doctoral research. At MIT, he is channeling that passion into understanding how sensory stimulation can entrain oscillations.

"That's what drives me to come to the lab every day to study these mechanisms," Adaikkan said. "When we got the data from the first mouse where we recorded from the visual cortex, the hippocampus and the prefrontal cortex we were surprised to see that visual stimulation entrains in these brain regions. That was very exciting but we have a very long way to go to understand how this happens."

The new paper raises that question and many others for the field. What cells underlie the brain's response to GENUS? How do gamma rhythms engage non-neuronal cells such as astrocytes and microglia? How does it propagate beyond the brain regions responsible for perception? How extensively can enhancing gamma affect cognition? Does long-term stimulation affect brain circuit connections and how they change?

Cell roles

Studies of how groups of neurons engage in coherent oscillations of electrical activity have yielded two models to explain gamma rhythms. Both involve an interplay between excitatory and inhibitory neurons but differ on which type leads the interaction, Adaikkan and Tsai wrote. In his work, Adaikkan is attempting to dissect the roles of specific neuron types in GENUS and how closely those patterns mirror other sources of gamma, such as that invoked by cognitive tasks.

GENUS affects more than neurons. Tsai's lab has found that microglia change their gene expression, their physical form, their protein-consuming behavior and their inflammatory response depending on the Alzheimer's model involved. Work from another group showed that blocking vesicle release in astrocytes can hinder gamma power in mice and Tsai's group found that auditory GENUS

recruits an increase reactive astrocytes, which are more inclined to consume pathological proteins.

The new paper offers three hypotheses about how such "glial" cells are involved: They might contribute directly to gamma entrainment by regulating the flow of ions that carry electrical charge; even if they don't contribute to rhythms, their ionic sensitivity may still make them responsive to gamma changes; they might instead be affected by changes in levels of neurotransmitters as a result of gamma. Moreover, different glia may also become involved because of their proximity to electrical couplings between neurons called synapses, or because of how their activity is otherwise governed by neural activity.

The broader brain

That GENUS extends to the hippocampus, which is key for memory, and the prefrontal cortex, which is key for cognition, is likely a factor in how it preserves brain function. But again there are competing models for how increased gamma could facilitate multi-regional communication. In one, the authors write, coherence at the same frequency optimizes communication, while in the other model, one region's gamma activity directly drives activity in regions downstream. New experiments that directly manipulate inter-regional circuits, they argue, could help resolve which model better explains gamma entrainment's effects.

Finally, the effects of GENUS on brain function and behavior also aren't fully explained. The Tsai lab's has shown significant effects on spatial memory and some effects on other forms of memory, depending on the stimulation method. Other studies have shown that stimulating brain rhythms by other means, such as via genetic or optogenetic manipulations in mice, or via transcranial stimulation in humans, can also improve functions such as working memory. Adaikkan is interested in closing a gap between those studies and the Tsai lab's work: Most studies measure cognitive performance during stimulation, while the Tsai lab has done so after the conclusion of repeated stimulation. He said he'd like to also test how mice perform while GENUS is actively underway.

"Our lab is excited to tackle these many hypotheses and to see how the field tackles many more," Tsai said. "GENUS has created many intriguing new questions for neuroscience."

The JPB Foundation, The Robert A. and Renee E. Belfer Foundation, and the Jeffrey and Nancy Halis Family Foundation have supported the work.

http://bit.ly/2rCwfxg

Lice-Filled Dinosaur Feathers Found Trapped in 100-Million-Year-Old Amber

Prehistoric insects that resemble modern lice infested animals as early as the mid-Cretaceous, living and evolving along with dinosaurs and early birds

By Brian Handwerk

Anyone who's had to deal with a lice infestation knows how annoying the persistent little pests can be. But humans are far from the first animals to suffer at the expense of these hair- and feather-inhabiting parasites. As far back as the Cretaceous period, insects that resemble modern lice lived and fed on the bodies of dinosaurs.

Scientists examining amber fossils discovered 100-million-year-old insects preserved with the damaged dinosaur feathers on which they lived. The bugs provide paleontologists' first glimpse of ancient lice-like parasites that once thrived on larger animals' feathers and possibly hair.

Mesophthirus angeli ***crawling on the dinosaur feathers in mid-Cretaceous amber.*** **(Taiping Gao)**

"The preservation in amber is extremely good, so good it's almost like live insects," says Chungkun Shih, a paleoentomologist and co-author of a study detailing the new find in *Nature Communications*.

While dinosaurs may garner an outsized share of attention, the tiny prehistoric pests and parasites that lived on them are a particular specialty of Shih and colleagues at Capital Normal University (CNU) in Beijing. The scientists are fascinated by insects that spent their lives sucking the blood, or gnawing the skin, hair and feathers of their much larger hosts. Though small in scope, parasitic insects have caused enormous suffering by spreading modern diseases like the plague and typhus.

"In human history you can see that the flea caused the black plague, and even today we are affected by blood sucking or chewing parasites," Shih says. Studying the ancestors of living ectoparasites, which live on the outside of their hosts, can help scientists understand how these pests evolved over millions of years into the species that live among and on us today.

Some finds have proven surprising. In 2012, CNU researchers reported a new family of huge, primitive fleas—more than two centimeters (three-fourths of an inch) long—that survived for millions of years in northeastern China. The supersized fleas gorged on the blood of Jurassic-period dinosaurs some 165 million years ago.

While it stands to reason that feathered dinosaurs were plagued by lice-like insects just as their living bird descendants are, the newly discovered insects encased in amber are the first example to emerge in the fossil record. The Cretaceous period's lice-like insects are so small that they have not been found preserved in other fossils.

The earliest bird louse previously known lived in Germany some 44 million years ago, and by that relatively late date the insect had become nearly modern in appearance. Consequently, early forms of lice and their evolutionary history have remained a mystery to scientists.

Shih and colleagues found ten, tiny insect nymphs, each less than 0.2 millimeters long, distributed on a pair of feathers. Each feather was encased in amber some 100 million years ago in what is today the Kachin Province of northern Myanmar. During five years of studying amber samples these two were the only ones found to contain the lice-like insects. "It's almost like a lottery game, where you win once in a while. And we got lucky," Shih says.

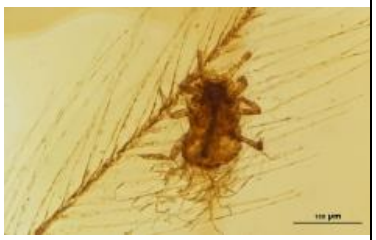
The bugs may not technically be lice, as their taxonomical relationship to the louse order Phthiraptera is unknown. But the insects in question, *Mesophthirus engeli*, appear as a primitive species very much resembling modern lice. The ancient bugs have different antennae and leg claws from a modern louse, but their wingless bodies look similar, and they feature the large chewing mandibles that cause so much irritation to their hosts.

One feather shows signs of significant gnawing damage, suggesting that lice had established feather feeding lifestyles in the mid-Cretaceous. The bugs may have evolved to exploit the expansion of feathered dinosaurs and early birds.

Shih says that the team originally thought that the feathers in question belonged to early birds, but an expert on fossil feathers and co-author on the study, Xing Xu, believes that they were actually from non-avian dinosaurs.

"One of the two feathers with feeding damage is consistent with the feathers that have been found alongside a dinosaur tail fragment in Burmese amber, while the other feather seems more similar to those that have been found alongside primitive toothed birds in the deposit," Ryan McKellar, a curator of invertebrate paleontology at the Royal Saskatchewan Museum who specializes in dinosaur feathers, says in an email. "The authors have made a really strong case for these insects being generalist feeders on feathers from a wide range of Cretaceous animals. It looks as though they have probably found the same group of insects feeding on feathers from both flying and flightless animals."

Just how big of a scourge were lice during the days of the dinosaurs? With limited evidence, paleontologists can't say exactly how common the insects were, but Shih believes the rarity of his team's find is due to difficulties of preservation, not a scarcity of the prehistoric pests.



Mesophthirus angeli ***feeding on dinosaur feathers in 100-million-year-old amber.*** **(Taiping Gao)**

"Insects have their ways of populating themselves on a host, and at that time there was no insecticide to kill them," he says. "Basically, they could grow and diversify and populate themselves, so I think that the numbers were probably fairly high."

Perhaps future amber fossil finds will help illuminate how often dinosaurs suffered from lice. "With any luck, future studies will be able to find these insects as adults, or on feathers that are still attached to an identifiable skeleton in amber, and narrow down the ecological relationships a little," McKellar says. "In the meantime, it is a neat addition to the growing record of parasites like ticks and mites that have been associated with Cretaceous feathers."

The find also illustrates just how resilient such parasites are, since the same type of insects have lived at the expense of larger animals for at least 100 million years, even as their hosts died out and were replaced by new animals for the bugs to feed on.

http://bit.ly/2LVTq4W

Breathing new life into the rise of oxygen debate

Research strongly suggests the distinct 'oxygenation events' that created Earth's breathable atmosphere happened spontaneously

New research strongly suggests that the distinct 'oxygenation events' that created Earth's breathable atmosphere happened spontaneously, rather than being a consequence of biological or tectonic revolutions.

The University of Leeds study, published in the journal *Science*, not only shines a light on the history of oxygen on our planet, it gives new insight into the prevalence of oxygenated worlds other than our own.

The early Earth had no oxygen in its atmosphere or oceans until roughly 2.4 billion years ago when the first of three major oxygenation events occurred. The reasons for these 'stepwise' increases of oxygen on Earth have been the subject of ongoing scientific debate.

In a new study, Leeds researchers modified a well-established conceptual model of marine biogeochemistry so that it could be run over the whole of Earth history, and found that it produced the three oxygenation events all by itself.

Their findings suggest that beyond early photosynthetic microbes and the initiation of plate tectonics—both of which were established by around three billion years ago—it was simply a matter of time before oxygen would reach the necessary level to support complex life. This new theory drastically increases the possibility of high-oxygen worlds existing elsewhere.

Study lead author Lewis Alcott, a postgraduate researcher in the School of Earth and Environment at Leeds, said: "This research really tests our understanding of how the Earth became oxygen rich, and thus became able to support intelligent life.

"Based on this work, it seems that oxygenated planets may be much more common than previously thought, because they do not require multiple—and very unlikely—biological advances, or chance happenings of tectonics."

The first "Great Oxidation Event" occurred during the Paleoproterozoic era—roughly 2.4 billion years ago. The subsequent wholesale oxygenation events occurred in the Neoproterozoic era around 800 million years ago and finally in the Paleozoic Era roughly 450 million years ago, when atmospheric

oxygen rose to present day levels. Large animals with high energy demands require high levels of oxygen, and evolved soon after the last of these steps, ultimately evolving into dinosaurs and mammals.

Currently, the two prevailing theories suggest the drivers of these oxygenation events were either major steps in biological revolutions—where the evolution of progressively more complex lifeforms essentially "bioengineered" oxygenation to higher levels—or tectonic revolutions—where oxygen rose due to shifts in the style of volcanism or make-up of the crust.

The new study instead highlights a set of feedbacks that exist between the global phosphorus, carbon and oxygen cycles, which are capable of driving rapid shifts in ocean and atmospheric oxygen levels without requiring any 'stepwise' change in either tectonics or biology.

Study co-author Professor Simon Poulton, also from the School of Earth and Environment at Leeds said: "Our model suggests that oxygenation of the Earth to a level that can sustain complex life was inevitable, once the microbes that produce oxygen had evolved."

Their 'Earth system' model of the feedbacks reproduces the observed three-step oxygenation pattern when driven solely by a gradual shift from reducing to oxidizing surface conditions over time. The transitions are driven by the way the marine phosphorus cycle responds to changing oxygen levels, and how this impacts photosynthesis, which requires phosphorus.

Senior author Dr. Benjamin Mills, who leads the biogeochemical modelling group at Leeds, said: "The model demonstrates that a gradual oxygenation of Earth's surface over time should result in distinct oxygenation events in the atmosphere and oceans, comparable to those seen in the geological record.

"Our work shows that the relationship between the global phosphorus, carbon and oxygen cycles is fundamental to understanding the oxygenation history of the Earth. This could help us to better understand how a planet other than our own may become habitable."

The paper "Stepwise Earth oxygenation is an inherent property of global biogeochemical cycling" is published online in *Science* on 10 December 2019.

More information: *"Stepwise Earth oxygenation is an inherent property of global biogeochemical cycling" Science (2019). DOI: 10.1126/science.aax6459*

https://bbc.in/2suKp3f

'Four hours to walk off pizza calories' warning works, experts say

Food packs should display how much exercise a person would need to take to burn off the calories contained in the product, UK researchers say.

By Michelle Roberts Health editor, BBC News online

Appreciating it would take four hours to walk off the calories in a pizza or 22 minutes to run off a chocolate bar creates an awareness of the energy cost of food, they say. The labels would help people indulge less, exploratory studies suggest.

The aim is to encourage healthier eating habits to fight obesity.

According to the researchers from Loughborough University, who looked at 14 studies, this type of labelling could cut about 200 calories from a person's daily average intake.

About calories

- ***The amount of energy in an item of food or drink is measured in calories (kcal)***
- ***Men need about 2,500 kcal a day and women about 2,000 kcal to provide enough energy for your body to function - for everything from breathing to running***
- ***Eating more calories than you burn off causes obesity because the excess calories are stored as fat***
- ***Even eating a little bit too much every day adds up***

This may not sound like much but, they say in the Journal of Epidemiology and Community Health, it would have an impact on obesity levels across the country.

More than two-thirds of adults in the UK are overweight or obese.

Lead researcher Prof Amanda Daley said: "We are interested in different ways of getting the public to make good decisions about what they eat and also trying to get the public more physically active."

And labelling food with "exercise calories" made it easier for people to understand what they were eating and nudge them into making better choices.

Prof Daley said many people would be shocked to realise how much physical exercise would be required to burn off calories from certain snacks and treats. "We know that the public routinely underestimate the number of calories that are in foods," she said. "So if you buy a chocolate muffin and it contains 500 calories, for example, then that's about 50 minutes of running.

"This definitely isn't about dieting. "It's about educating the public that when you consume foods, there is an energy cost, so that they can think, 'Do I really want to spend two hours burning off that chocolate cake? Is the chocolate cake really worth it?'"

'Triggering' risk

The Royal Society for Public Health would like to see the labelling introduced as soon as possible and says it is a move many consumers would also welcome.

It says: "This type of labelling really does put an individual's calorie consumption in the context of energy expenditure and knowing how out of kilter we can be partly explains the record levels of obesity we face.

"Small changes can make a big overall difference to calorie consumption, and ultimately weight gain."

Prof Daley hopes a large food chain or company will be willing to try the new labels on their products so the system can be given a "real life" trial.

But concerns have been raised about labelling food in this way.

Tom Quinn, from the eating disorder charity Beat, said: "Although we recognise the importance of reducing obesity, labelling food in this way risks being incredibly triggering for those suffering from or vulnerable to eating disorders.

"We know that many people with eating disorders struggle with excessive exercising, so being told exactly how much exercise it would take to burn off particular foods risks exacerbating their symptoms."

https://wb.md/2qPRhI7

Board Games a Major Win for the Brain

Playing board games may protect against cognitive decline and even boost cognitive function in seniors, new research suggests.

Batya Swift Yasgur, MA, LSW

Results of a large, longitudinal study showed that higher frequency of playing board games, which are also known as analog games, seemed to guard against cognitive decline.

Even among individuals in their 70s, those who played more board games experienced less decline in memory and other cognitive measures compared to their counterparts who either did not play board games or who played fewer board games.

"Playing games might have a modest effect on the healthy decline of cognitive abilities, but this study was not an intervention, so we do not have surefire causal evidence," lead author Drew M. Altschul, PhD, a research fellow in cognitive epidemiology, University of Edinburgh, United Kingdom, told *Medscape Medical News*.

"Playing games can be seen as one facet in a healthy lifestyle that consists of other behavioral modifications a person can make, such as getting more exercise, not smoking, not drinking to excess, and eating healthier foods [all of which] might be beneficial for healthy cognitive aging," he said.

The study was published online November 18 in the *Journals of Gerontology: Psychological Sciences*.

Exceptional Dataset

"Computerized brain training is a controversial subject at the moment, as are the effects of analog games on cognitive functions — although analog games are much less studied," Altschul said.

Previous studies of analog games have been limited because they have not examined cognitive changes over time or they have not controlled for confounding effects.

The researchers used data from the Lothian Birth Cohort of 1936 (LBC1936) — a community-dwelling sample of 1091 initially healthy individuals born in 1936.

At age 11 years, participants received a group-administered intelligence test (the Moray House Test–12), which included word classification, proverbs, spatial items, and arithmetic.

Participants received cognitive and health testing in four waves:

- ***Age 70 (n = 1091)***
- ***Age 73 (n = 866)***
- ***Age 76 (n = 697)***
- ***Age 79 (n = 550)***

The LBC1936 "is exceptional because we have early-life measures of many variables, as well as many cognitive tests from the eighth decade, and a variable in which the participants told us how often they played games," said Altschul.

Participants were required to be free of dementia and cognitive impairment; 11 participants were excluded from the analysis at age 70, and another 37 were excluded because they had developed dementia or cognitive impairment between ages 70 and 79.

At age 70, participants were asked how often they engaged in playing games (eg, cards, chess, bingo, or crosswords). At wave 3 (age 76), the researchers also assessed whether individuals reported any increase in the frequency of game playing between ages 70 and 76 and, if relevant, the degree of change.

Potential confounders included sociodemographic variables (sex, years of education, and social class); other activities in which participants might have engaged; and medical risk factors for cognitive decline (history of hypertension, stroke, diabetes, or cardiovascular disease).

"Key Results"

At age 70, 33% of participants reported playing games daily or nearly every day, and 20% played games less than once a year or never. The remaining participants fell in between.

The largest number of participants reported playing daily; the second-largest number of participants reported playing less than once a year or never — a distribution the researchers described as U-shaped.

Some participants changed their game-playing habits between the ages of 70 and 76, with 160 playing more games than they had prior to age 70.

A regression analysis showed that playing games was positively associated with cognitive function at age 70 (std $\beta = 0.094$; $t = 4.07$; $P < .001$). Higher cognitive function at age 11, female sex, higher social class, and higher educational level were also associated with higher cognitive function at age 70.

In addition, those who played more games during that period experienced positive change in cognitive function, with "visible" changes between individuals who were more vs less frequent game

players (std β = 0.095; *t* = 4.07; *P* < .001) — a finding the researchers called a "key result."

Lower cognitive function at age 11, female sex, higher social class, and higher educational level were associated with positive cognitive change that was calculated to be equivalent to a gain of approximately 1.42 IQ-like points per standard deviation (SD) increase in playing games.

Using a model of expected life course relationship among the variables, the researchers found that cognitive function at age 11 "has a positive downstream association with education, social class, and age 70 cognitive function, as well as playing games."

Even after controlling for the direct and indirect associations of age 11 function, education, and social class, playing more games was still associated with higher cognitive function at age 70 (std β = 0.083; *z* = 3.24; *P* = .001).

"In this model, there was a 1.25 IQ-like point gain from age 11 to age 70 per standard deviation increase in playing games," the authors comment.

Although there was a mean cognitive decline across the eighth decade in all participants, the decline was "more severe" in less-frequent game players.

However, another key result obtained using latent growth curve models showed that playing more games was associated with less decline in general cognitive function from age 70 to age 79 (β = .068; *z* = 2.523; *P* = .012).

In particular, reduced decline was significant for the memory and processing speed subdomains (β = .204; *z* = 3.114; *P* = .002; and β = .110; *z* = 2.689; *P* = .007, respectively) but did not reach significance for the other domains.

In IQ-terms, 1 SD of increased game playing was associated with a 1.02-point less reduction in general cognitive ability and a 3.06-point less reduction in memory ability during the years between ages 70 and 79.

"For members of the general public, playing games might help with cognitive aging, and it certainly wouldn't hurt," Altschul said.

Fun, Inexpensive, Beneficial

Commenting on the study for *Medscape Medical News*, Ria Vaportzis, PhD, lecturer in psychology, School of Social Sciences, University of Bradford, West Yorkshire, United Kingdom, noted that the study sample is unique.

"There aren't many data available that allow us to look at people's cognitive function over such a long period of time — it basically looks at people's lifetime, [which is] not something we can easily replicate."

It is, however, "difficult to make any practical suggestions based on the findings, given that some of the data were collected retrospectively," Vaportzis, who was not involved in the study, added.

Nevertheless, "analog games are widely available, they can be a cheap and fun activity that can keep people engaged both mentally and socially, so the bottom line is that they do no harm, and there's some evidence that they can be potentially good."

Altschul agreed.

"Games are an inexpensive way to have fun, spend time with people you care about, and maybe do something positive for your brain health," he said.

The study was supported by the University of Edinburgh Center for Cognitive Ageing and Cognitive Epidemiology, which is funded by the Biotechnology and Biological Sciences Research Council and the Medical Research Council. Altschul is funded by an MRC Mental Health Data Pathfinder award. The LBC1936 data were collected using a Research Into Ageing Program grant; this research continues as part of the Age UK-funded Disconnected Mind project. Altschul, his study coauthor, and Vaportzis report no relevant financial relationships.

J Gerontol B Psychol Sci Soc Sci. Published online November 18, 2019. Full text

https://wb.md/2LV2hvd

Aspirin in Older Adults Linked to Fewer Deaths

New analysis finds older adults who regularly took aspirin had significant reduction in mortality from all causes and from cancer compared to those who didn't take aspirin

Liam Davenport

UPDATED WITH COMMENTS December 12 — A new analysis has found that older adults (> 65 years) who regularly took aspirin had a significant reduction in mortality from all causes and from cancer compared with individuals who didn't take aspirin.

"This observation was consistent across all causes of mortality...however, the greatest reduction in risk was noted for colorectal cancer (CRC) mortality among individuals who used aspirin three or more times per week," say the researchers.

The risk of dying from any cause was reduced by 19%, from any cancer by 15%, from GI cancer by 25%, and from CRC by 29%.

The findings come from a new analysis of data from the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, which involved more than 145,000 individuals. The study was funded by grants from the National Cancer Institute and the Stuart and Suzanne Steele MGH Research Scholarship.

The new results are reported by Holli A. Loomans-Kropp, PhD, MPH, Division of Cancer Prevention, National Cancer Institute, Rockville, Maryland, and colleagues, who note that the impact of aspirin on mortality risk appears to be modulated by body mass index (BMI).

"The efficacy of aspirin as a cancer preventive agent may be associated with BMI," they write. Participants who were underweight (i.e., BMI < 20 kg/m^2) had no observable benefit associated with aspirin use but aspirin use in those with a BMI ≥ 20 kg/m^2 was associated with reduced mortality risk. The greatest reductions in mortality risk were seen in individuals with a higher BMI (25–29.9 kg/m^2). The study was published in the December issue of *JAMA Network Open*.

The authors acknowledge that their findings require "further confirmation" and note that the significant reduction in mortality associated with aspirin use contrasts with results from other studies. Nevertheless, they say that their finding of an impact of BMI on the effect of aspirin suggests the "increasing rates of overweight and obesity globally may substantially alter the population-based efficacy of cancer prevention prophylactics."

Recent Study Showed Higher Mortality

The new findings of a significant reduction in mortality are in stark contrast to recent data from the United States and Australia, which showed higher mortality in individuals taking aspirin.

Those data come from the Aspirin in Reducing Events in the Elderly (ASPREE) study, which examined the efficacy of 100-mg aspirin in individuals aged ≥ 70 years in the United States and Australia (≥ 65 years for US black or Hispanic participants). As reported by *Medscape Medical News*, the study showed higher all-cause and cancer-related mortality with aspirin therapy.

Loomans-Kropp says the new findings add "to what's already known about the use of aspirin as a cancer preventative mechanism."

She continued: "It's something for people to keep in mind when they're considering whether or not to begin taking aspirin according to either doctor’s recommendations or whatever recommendations they choose to look at."

Approached for comment, Michael N. Passarelli, PhD, Department of Epidemiology, Geisel School of Medicine at Dartmouth, Hanover, New Hampshire, told *Medscape Medical News* that the results from ASPREE were "very unexpected," and the current study "supports what was our knowledge before ASPREE."

He noted that, based on ASPREE and two other recent studies, "there has been some major rethinking of clinical recommendations for daily aspirin use, specifically among older people." However, he underlined that "we're still in an uncertain place," and that the design of ASPREE and the current analysis were quite different.

"[The current analysis] is a very large study. It has strength because of its long duration of follow-up and its size; it's much larger than ASPREE," he said. Passarelli continued: "It just doesn't have that strength of having randomized aspirin versus placebo. It's looking at the natural occurrence of aspirin as reported by the participants, so there's a lot of other factors related to the choice of using aspirin that could explain these results."

Aspirin Taken for Various Reasons

In an interview with *Medscape Medical News*, Loomans-Kropp explained that for the current study, her team created an aggregate measure of aspirin use that could be used as a surrogate longitudinal measure. "We collapsed the aspirin use frequency variables into no aspirin use or less than once per month, one to three times per month, one to two times per week, and three or more times per week," the team explains in the article.

Consequently, the use of aspirin by the trial participants could reflect various reasons for taking the drug. "At least for the US population, aspirin is readily available, so they could be taking it for relatively minor pain relief throughout the week," Loomans-Kropp said. "It could be that individuals are using aspirin as a cancer preventative agent, as it's part of the US Preventive Services Task Force [USPSTF] recommendations," she said. But it could also be that individuals are taking aspirin to reduce cardiovascular risk.

The USPSTF recommends low-dose aspirin for cardiovascular disease and CRC prevention in certain individuals aged 50–59 years. However, the Task Force also recommends an individualized approach for those aged 60–69 years, and note the evidence in individuals at least aged 70 years is considered insufficient.

Details of the New Analysis

The PLCO Cancer Screening Trial ran from 1993-2001 at 10 centers in the United States, and individuals aged 55-74 years were randomized to either a screening or control group.

The current analysis looked at participants aged ≥ 65 years at baseline or who had survived until 65 years, and who had a valid baseline questionnaire and reported their aspirin use.

The study involved 146,152 individuals with a mean age at baseline of 66.3 years. Just over half (51.1%) were women and 88.6% were non-Hispanic white.

Over a median follow-up of 12.5 years, 40,419 individuals died, including 12,421 who died of any cancer and 1425 who died of gastrointestinal cancer (814 from CRC, 353 from esophageal cancer, and 258 from gastric cancer).

The team found that any use of aspirin was associated with reduced all-cause and cancer-specific mortality.

Specifically, aspirin use from one to three times per month was associated with a reduced risk of all-cause mortality compared with no use, at a hazard ratio of 0.84 ($P < .001$), as well as cancer mortality, at a hazard ratio of 0.87 ($P < .001$).

Aspirin use three or more times a week was also associated with a decreased risk of all-cause mortality versus no use, at a hazard ratio of 0.81 ($P < .001$), and cancer mortality, at a hazard ratio of 0.85 ($P < .001$).

In addition, aspirin use at least three times a week was linked to significantly reduced gastrointestinal cancer mortality versus no aspirin use, at a hazard ratio of 0.75 ($P < .001$), and CRC, at a hazard ratio of 0.71 ($P < .001$). When researchers stratified participants by BMI, they found the impact of aspirin use appeared to be greater in more overweight individuals.

Among people with a BMI of 20–24.9 kg/m^2, aspirin use at least three times a week was associated with a reduced risk of all-cause mortality versus no use, at a hazard ratio of 0.82 (P < .001), and cancer mortality, at a hazard ratio of 0.86 (P < .001).

For individuals with a BMI of 25–29.9 kg/m^2, aspirin use three times a week or more was associated with reduced all-cause mortality and cancer mortality compared with no use, at hazard ratios of 0.82 and 0.86, respectively (P < .001 for both).

In addition, there was a reduced risk of gastrointestinal cancer mortality, at a hazard ratio of 0.72 (P < .001), and CRC mortality, at a hazard ratio of 0.66 (P = .001), in this group with thrice weekly or more aspirin use.

Passarelli commented that the BMI results are "not one of the most important takeaways from this study."

"It's difficult to say whether this is really biological or a consequence of the fact that very few older people have a BMI that low, which affects precision in a study like this," he explained.

"The vast majority (over 95% in this study) have a BMI over 20 kg/m^2, and the aspirin association actually seemed pretty consistent across BMI categories over 20 kg/m^2," he added.

Passarelli believes that, based on the current evidence, "it's not clear whether aspirin recommendations should be altered to account for a patient's weight or body mass index."

He said that recent research has suggested higher doses of aspirin "may be necessary among those who weigh more."

"I think any future study would probably probe that a lot further by considering a sort of tailored, personalized aspirin dosing approach — a specific dose according to age, weight, and other comorbidities — to see if we can ideally strike a balance between any of these long-term benefits and the more immediate harms related to gastrointestinal bleeding," Passarelli said.

JAMA Netw Open. 2019;2:e1916729. Full text

http://bit.ly/2PK75EN

Iminosugars | Podcast | Chemistry World

This week – dogs, drugs and deoxynorijimycin. Mike Freemantle explores the buzz around iminohoney…

By Michael Freemantle

Holly, a black Labrador, had been healthy for almost 13 years. Then, in October 2016, an ominous lump appeared on her lower lip. Other growths soon appeared on her nose. The vet thought they might quickly spread to her lungs. Hazel, the owner, did not want Holly to undergo surgery or chemotherapy. Instead, she put iminohoney on the dog's food every three days. After six weeks, the lumps disappeared. She continued the treatment for two more weeks. The cancer never returned and Holly led an active life for another 18 months.

The story is one of several case studies published in *Our Dogs* newspaper on 22nd February 2019. In each case, iminohoney was found to cure dogs diagnosed with terminal cancer or prolong their active lives.

Iminohoney is distinct from other honeys in that it contains a type of alkaloid known as an iminosugar or iminosaccharide. Alkaloids are naturally-occurring organic compounds with complicated molecular structures that contain at least one nitrogen atom, usually as part of a ring. Iminosugars have similar molecular structures to sugar molecules. Each iminosugar molecule has a nitrogen atom in its ring instead of the usual oxygen atom.

The compounds occur widely in plants, bacteria and fungi throughout the world. For example, in 2007, scientists reported the isolation of ten iminosugars from the leaves of the African sandalwood tree. The iminohoney added to the dog food in the case studies contained an iminosugar found in the common myrtle, a species of flowering plant native to Mediterranean countries, India, and western Asia.

The first naturally-occurring iminosugar detected was a glucose analogue. In 1965, scientists in Japan discovered the compound in *Streptomyces nojiriensis*, a species of bacterium isolated from the soil at Lake Nojiri in Japan. The iminosugar was shown to be 5-amino-5-deoxy-glucopyranose. It exhibited antibiotic properties and was given the name nojirimycin.

Biwa Island on Lake Nojiri, Japan **Source: Qurren [CC BY-SA 3.0]**

The discovery led to the synthesis in 1968 of 1-deoxynorijimycin, that is nojirimycin with one of its hydroxyl groups removed. The compound was later found to occur naturally in the fruit and leaves of mulberry trees and in some British lichen species.

1-Deoxynorijimycin became a model for research into the therapeutic benefits of iminosugars. It is more stable than nojirimycin and, most importantly, inhibits alpha-glucosidases. These are enzymes that catalyse the hydrolysis of starch and other complex carbohydrates to form simpler sugars such as glucose.

Inhibition of the enzymes lowers the rate of digestion of carbohydrates in the small intestine and reduces blood sugar levels. Drugs that act in this way are known as alpha-glucosidase inhibitors, and are used to treat type 2 diabetes. One such drug is a derivative of 1-deoxynorijimycin known as miglitol. Its trade name is Glyset.

Another derivative, miglustat, is used to treat Gaucher disease, an inherited genetic disorder in which a glucocerebroside, a fatty compound partly composed of glucose, accumulates in the liver, spleen, lymph nodes and nervous system. Glyset and miglustat, under the trade name Zavesca, were the first two iminosugar prescription drugs to be launched onto the market.

1-Deoxynorijimycin has also been shown to inhibit infection by viruses such as HIV. In May 2019, a team of Chinese researchers found that the compound could also ameliorate symptoms associated with angina pectoris, such as chest pain, in patients with coronary heart disease.

Some 200 naturally-occurring iminosugars have now been reported. Most fruits and vegetables that are considered healthy contain iminosugars of one sort or another, often in addition to antioxidants, according to PhytoQuest, an R&D company based at Aberystwyth University in Wales. The company develops novel pharmaceutical medicines from natural iminosugar-containing plant extracts. It suggests that iminosugars may be the major contributors to health, rather than the antioxidants.

The director of the company is Robert Nash. It was his company, Sugars for Health, that supplied the iminohoney used to treat the dogs in the case studies. He notes that iminosugars have the remarkable ability to correct many of the age-related weaknesses in the immune system that can lead to infections and diseases such as cancer.

Nash and other researchers in the field agree that iminosugars promise to open up even more avenues for the discovery of new medicines and health products, both for pets and human beings.

It is amazing that such a small change – replacing an oxygen atom in a sugar molecule with a nitrogen atom – can have wide ranging therapeutic and nutritional benefits.

http://bit.ly/2Ppy61n

The Startling Secret of an Invincible Virus

Joseph Bondy-Denomy knew he could find viruses that would be hard to kill. But he wasn't expecting to discover one that was quite so invincible.

The viruses that Bondy-Denomy studies at the University of California at San Francisco don't bother humans. Known as phages, they infect and kill bacteria instead. Bacteria can defend themselves against these assaults. They can recognize the genes of the phages

that threaten them, and deploy scissorlike enzymes to slice up those genes and disable the viruses. This defense system is known as CRISPR. Billions of years before humans discovered it and used it as a tool for editing DNA, bacteria were using CRISPR to fight off phages.

But phages have their own countermeasures. In 2012, Bondy-Denomy discovered that some of these viruses are resistant to CRISPR, because they have proteins that stick to those scissorlike enzymes and blunt them. A bacterium can mount its CRISPR defense, but ultimately the virus can still force itself in and triumph. This suggested that bacteria and phages are likely locked in an arms race. The former evolve new kinds of scissor enzymes, and the latter evolve new ways of disabling them. Intrigued, Bondy-Denomy started searching for more CRISPR-resistant phages.

He soon found one that was resistant, and then some. It's called phi-kappa-zeta (or phiKZ)—a name that it coincidentally shares with a sorority. Unusually large for a virus, phiKZ typically infects a bacterium called *Pseudomonas aeruginosa*. Unsurprisingly, it could resist the version of CRISPR used by its host. Unexpectedly, it also resisted every other version of CRISPR that the team tried, including those from bacteria that it would never have naturally encountered. Its armor seemed to work against every possible weapon. No anti-CRISPR protein should work in such a universal way. "It didn't make any sense," Bondy-Denomy says.

He slowly realized what was happening after chatting with David Agard, who works in the same building. In 2017, Agard, along with Joe Pogliano and other colleagues, discovered that another phage does something that viruses are not meant to do. It encapsulates its DNA inside a shell of protein, which it suspends inside itself with thin filaments. That's exceptionally odd. The cells of animals and plants also house their DNA within a special compartment—the nucleus. But such compartments aren't meant to exist in simpler cells, like those of bacteria. And they're certainly not meant to exist in viruses, which some scientists don't even regard as alive. And yet, here was a phage, packaging its DNA in something akin to a nucleus. Why?

Agard told Bondy-Denomy about the phage that surrounds its DNA in a shell. Bondy-Denomy told Agard about the phage that's resistant to all forms of CRISPR. It slowly dawned on the duo that the viruses they were studying were closely related, and that the weird phenomena they had found were linked. CRISPR can't destroy what it can't reach, and the shell stops it from getting at the phage's DNA. The phiKZ phage and its relatives don't need to evolve countermeasures against each and every form of CRISPR when they have ways of excluding them all. "Proving it was the hard part," Bondy-Denomy says. "That took a couple of years."

His student Eliza Nieweglowska confirmed, using a microscope, that the CRISPR scissors really are blocked by the shell. Meanwhile, another student, Senén Mendoza, showed that once the phage's DNA was removed from the shell, the CRISPR scissors were perfectly capable of cutting it up. Mendoza also managed to smuggle the scissors into the shell by fusing them with proteins that are normally allowed to pass. When that happened, the phages were destroyed. "This work definitively shows that the structure protects against CRISPR," says Benjamin Chan, who studies phages at Yale University. The similarity to a nucleus "is fascinating," he adds.

Finding new forms of CRISPR, or new defenses against it, could lead to ways of controlling gene-editing technologies more carefully or efficiently. But on a more basic level, Bondy-Denomy's discovery might hint at a bit of evolutionary history, of our own cells.If viruses can protect their DNA from bacterial enemies using a nucleus-like structure, perhaps the nucleus itself evolved as a way for cells to protect their DNA from viruses? To explore that idea, Bondy-Denomy and his team are trying to

understand more about how the mysterious shell functions. It's incredibly selective, blocking everything except the proteins that the virus uses to copy its DNA and switch on its genes. "It's not clear how it works," Bondy-Denomy says. "But we're really in love with it now."

"It's yet another example of the ingenuity of phages," says Karen Maxwell of the University of Toronto. But why, she wonders, haven't all phages evolved a nucleus-like structure, if it provides such wide-ranging benefits? Is there some downside to that defense that isn't yet clear? Such questions matter, especially because scientists are turning to phages as ways of treating drug-resistant infections. A phage with a protective nucleus "provides a new prototype that could prove useful for these purposes," Maxwell adds.

Phages are often discussed in aggregate, as if they were all roughly the same. But as Bondy-Denomy's work shows, "there's a staggering amount of diversity," he says. "I tell everyone who joins my lab that they can find something cool and new, because every phage does something different."

http://bit.ly/38A4DcJ

Humanity's Oldest Cave Art Shows Shape-Shifting Supernatural Hunters

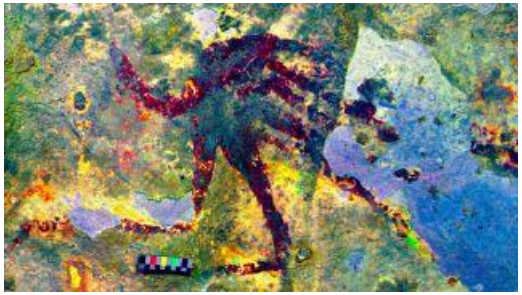
The hunters are decked out with animal snouts and tails.

By Charles Q. Choi - Live Science Contributor

Researchers discovered cave paintings depicting what may be part-animal, part-human figures — decked out with animal snouts — hunting wild pigs and dwarf buffaloes in Indonesia. These may be the oldest known examples of rock art, a new study finds.

The 44,000-year-old artwork may also be the oldest evidence for the human ability to imagine the existence of supernatural beings, scientists added.

The ancient painting was discovered in the limestone cave of Leang Bulu' Sipong 4 in the Indonesian island of Sulawesi in 2017. During a survey for rock art, study co-author Pak Hamrullah noticed "what appeared to be the entrance to a cave located high up in a limestone cliff face, and he climbed several meters up a fig tree vine to investigate it," study co-author Adam Brumm, an archaeologist at Griffith University in Brisbane, Australia, told Live Science.



This therianthrope, showing a human figure with a tail, is part of the hunting scene found in cave art in Leang Bulu' Sipong in Indonesia. **(Image: © Ratno Sardi)**

The people who created the 14.75-foot-long (4.5 meters) cave painting used dark red pigment to depict what appear to be at least eight small, human-like figures using spears or ropes to hunt six animals: two Sulawesi warty pigs and four dwarf buffaloes known as anoas.

"Anoas are small in size, but they are reportedly very fierce, especially when cornered," Brumm said. "From what I have heard from local people, these elusive dwarf bovids have been known to seriously gore and even kill unwary hunters on the island. Indeed, the reputation of anoas is such that the Indonesian army even named their armored personnel carrier, the Anoa, after these creatures."

By analyzing levels of uranium and other radioactive isotopes in mineral growths known as "cave popcorn" that had formed on the rock art since it was created, the researchers estimated that the cave paintings were at least 43,900 years old.

"Our dating work shows that this is the world's oldest dated figurative artwork, an image that resembles the subject matter it is intended to represent," Brumm said. Until now, the oldest known dated example of figurative art was a red disk from the rock art site of El Castillo in Spain, which is about 40,800 years old.

The simplified, highly stylized pictures of the hunters portrayed them with the muzzles, beaks and snouts of birds, reptiles and other animals native to Sulawesi, as well as tails and other bestial traits. These images were therianthropes — part-human, part-animal figures — which occur in the stories of nearly every modern society and are thought of as gods, spirits or ancestral

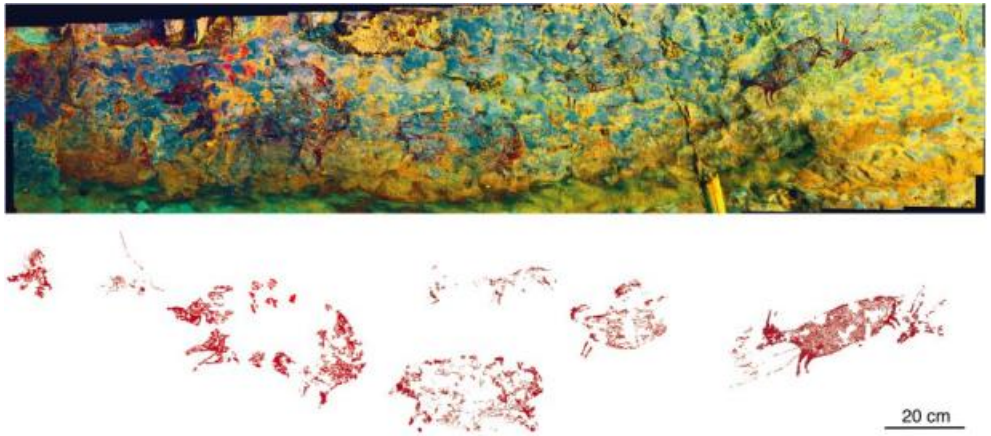
"In Europe, scholars have long been interested in the oldest known images of therianthropes in prehistoric art, because they are generally accepted to represent the earliest evidence for our ability to conceive of abstract entities that do not exist in the natural world," Brumm said. "Depictions of therianthropes are also seen as an indication of early spirituality or religious-like thinking."

These images of therianthropes may be "the oldest evidence for our ability to imagine the existence of supernatural beings, a cornerstone of religious experience." Until now, the oldest known depiction of a therianthrope was a carved figurine of a human with a feline head, from Germany, that dated back about 40,000 years.

All in all, the newfound cave painting depicts a hunting scene. This means the artwork is also the earliest known visual example of human storytelling; until now, the earliest known examples of such scenes in the vast record of prehistoric cave art worldwide dated to about 14,000 to 21,000 years ago, the researchers said.

The origins of rock art

Previous research suggested that humanity's first rock art appeared in Europe and consisted of abstract symbols. By 35,000 years ago, prior work had suggested that early artists graduated to more sophisticated figurative portrayals of horses and other animals. Scenes that depicted multiple interacting subjects were not thought to have developed until about 20,000 years ago.



The prehistoric hunting scene shows possible therianthropes hunting wild pigs and dwarf buffaloes in Indonesia.The prehistoric hunting scene shows possible therianthropes hunting wild pigs and dwarf buffaloes in Indonesia.
(Image credit: Adam Brumm, Ratno Sardi and Adhi Agus Oktaviana)

"The cave painting from Leang Bulu' Sipong 4 suggests that there was no gradual evolution of Paleolithic art from simple to complex around 35,000 years ago — at least, not in Southeast Asia," study co-author Maxime Aubert, at Griffith University in Brisbane, Australia, said in a statement. "All of the major components of a highly advanced artistic culture were present in Sulawesi by 44,000 years ago, including figurative art, scenes and therianthropes."

The scientists noted that they had uncovered hundreds of cave sites with paintings in the Maros-Pangkep limestone karst region of Sulawesi whose ages they had yet to date. For example, in 2014, they found that a limestone cave in this area harbored one of the world's oldest rock-art motifs, a sprayed, red outline of a human hand created at least 40,000 years ago. Similarly, in 2018, researchers discovered a figurative painting of a wild bovine dating to at least 40,000 years ago on the Indonesian island of Borneo. This find suggested that Indonesia may be a key place for

researching the beginnings of cave art and the evolution of human thought, the scientists noted. Unfortunately, at nearly every location they investigated, the researchers have also found that these paintings are flaking away. That includes the site in the new study.

"We need funding to work with our Indonesian colleagues to figure out why this deeply ancient and globally significant art is exfoliating so quickly at almost every site and what to do about it," Brumm said. The scientists detailed their findings in the Dec. 12 issue of the journal Nature.

http://bit.ly/2RRTVbp

Speech could be older than we thought

Speech could have emerged before the 200,000 years ago that linguists currently assert

For 50 years, the theory of the "descended larynx" has stated that before speech can emerge, the larynx must be in a low position to produce differentiated vowels. Monkeys, which have a vocal tract anatomy that resembles that of humans in the essential articulators (tongue, jaw, lips) but with a higher larynx, could not produce differentiated vocalizations. Researchers at the CNRS and the Université Grenoble Alpes, in collaboration with French, Canadian and US teams, show in a 11 December 2019 review article in Science Advances that monkeys produce well differentiated proto-vowels. The production of differentiated vocalizations is not therefore a question of anatomical variants but of control of articulators. This work leads us to think that speech could have emerged before the 200,000 years ago that linguists currently assert. Since speech can be considered as being the cornerstone of the human species, it is not surprising that two pairs of researchers, in the 1930s-1950s, had tested the possibility of teaching a home-raised chimpanzee to speak, at the same time and under the same conditions as their baby. All their experiments ended in failure. To explain this result, in 1969 in a long series of articles a US researcher, Philip Lieberman, proposed the theory of the descended larynx (TDL). By comparing the human vocal tract to monkeys, this researcher has shown that these have a small pharynx, related to the high position of their larynx, whereas in humans, the larynx is lower. This anatomic block reportedly prevents differentiated vowel production, which is present in all the world's languages and necessary for spoken language. Despite some criticisms and many acoustic observations that contradict the TDL, it would come to be accepted by most primatologists.

More recently, articles on monkeys' articulatory capacities have shown that they may have used a system of proto-vowels[1]. Considering the acoustic cavities formed by the tongue, jaw and lips (identical in primates and humans), they showed that production of differentiated vocalizations is not a question of anatomy but relates to control of articulators. The data used to establish the TDL came in fact from cadavers, so they could not reveal control of this nature.

This analysis, conducted by pluridisciplinary specialists in the GIPSA-Lab (CNRS/Université Grenoble Alpes/Grenoble INP), in collaboration with the Laboratoire de Psychologie Cognitive (CNRS/Aix-Marseille Université), the University of Alabama (USA), the Laboratoire d'Anatomie de l'Université de Montpellier, the Laboratoire de Phonétique de l'Université du Québec (Canada), CRBLM in Montréal (Canada) and the Laboratoire Histoire Naturelle de l'Homme Préhistorique (CNRS/Muséum National d'Histoire Naturelle /UPVD), opens new perspectives: if the emergence of articulated speech is no longer dependent on the descent of the larynx, which took place about 200,000 years ago, scientists can now envisage much earlier speech emergence, as far back as at least 20 million years, a time when our common ancestor with monkeys lived, who already presumably had the capacity to produce contrasted vocalizations.

https://wb.md/2RVhsZg

Multiple Psych Disorders Genetically Linked -- New Findings

The study begins as a huge genome-wide association study—but man, it has layers

F. Perry Wilson, MD, MSCE

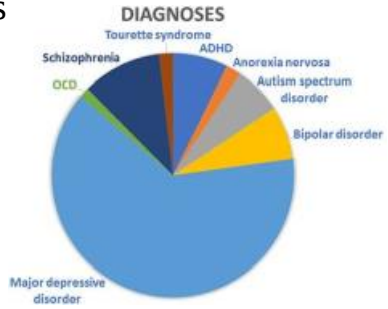
Welcome to Impact Factor, your weekly dose of commentary on a new medical study. I'm Dr F. Perry Wilson.

This week, I've been reading this paper appearing in *Cell*, which described a truly herculean effort to determine some of the genetic underpinnings of psychiatric disorders.

The study begins as a huge genome-wide association study—but man, it has layers. Like an ogre.

Let's start at the top and dig our way in.

Researchers obtained genome data from 232,964 individuals with psychiatric disorders. To put that in context, that's roughly two New Havens' worth of people. The vast majority had major depression, but multiple other psychiatric disorders were also present, as you can see here.



They also had four New Havens' worth of controls—nearly 500,000 individuals with genome data. It's crazy big. However, this population wasn't as diverse as real New Haven; all individuals were of self-identified European descent.

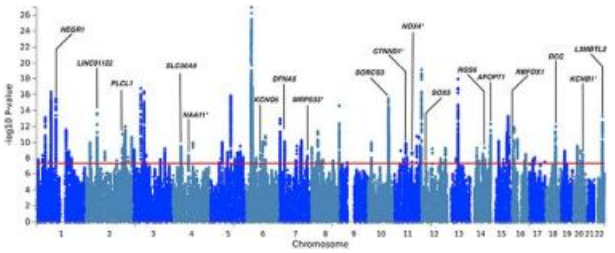
Medscape

But those numbers allowed the researchers to search across the entire genome for small variations in genetic code that were seen much more frequently in those with psychiatric disorders.

All told, they found 136 such hotspots in the genome. That's all the dots above the red line in this Manhattan plot here.

That included 35 never-before-reported hotspots, which is pretty incredible. And they could have stopped there, but this is really just the surface of the paper.

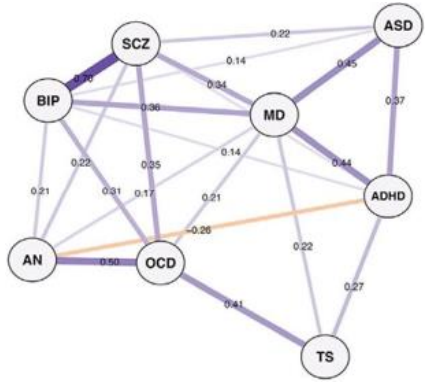
The researchers were on the hunt for so-called "pleotropic loci"—hotspots that didn't appear to confer risk for just one psychiatric disorder but for multiple.



Medscape

The idea is that these hotspots would help us begin to understand whether there are common processes central to all psychiatric disease and, of course, to develop more universal treatments.

One hundred and nine hotspots were pleotropic (linked to more than one disorder). Those genomic connections allowed researchers to create this network map, which reveals how these diagnoses are genetically linked.



Medscape

What I find so cool here is how closely this genetically derived map matches what we observe clinically. Bipolar disorder and schizophrenia are strongly linked, as are anorexia nervosa and obsessive-compulsive disorder. The link between autism spectrum disorder and attention-deficit/hyperactivity disorder is no surprise, but some novel findings bear more research, like the genetic link between autism and major depression.

In fact, several different bioinformatic techniques revealed the pattern you see here: three broad groups of disorders, likely

representing the sequelae of related genetic processes. Someday, this may redefine how we classify psychiatric disease.

I mentioned the hunt for pleiotropy. Well, one hotspot stood out in this manner above all the rest: a small mutation in a gene called *DCC* (of colon cancer fame). It was associated with all eight psychiatric diagnoses in the dataset.

This gene is much more than "deleted in colon cancer," though; it guides axonal growth in neurodevelopment.

Germline loss-of-function mutations in *DCC* cause severe neurodevelopmental syndromes and are often embryonic lethal. We're not talking about a nonfunctioning gene here—just one that is functioning slightly differently, enough to potentially create a brain that is more susceptible to the environmental triggers of psychiatric disorders.

Are drugs targeting *DCC* going to rid the world of psychiatric disease? Of course not, but the understanding we gain from genetic studies may well redefine how we think of psychiatric disease. And though that may panic the editors of DSM-6, it may benefit our patients in the end.

F. Perry Wilson, MD, MSCE, is an associate professor of medicine and director of Yale's Program of Applied Translational Research. His science communication work can be found in the Huffington Post, on NPR, and here on Medscape. He tweets @methodsmanmd and hosts a repository of his communication work at www.methodsman.com.

http://bit.ly/2PR7OUE

Does tapping your can of beer really keep it from fizzing all over you?

Testing the popular notion that tapping a can of beer after it has been shaken will prevent it from spraying

A team of researchers at the University of Denmark has tested the popular notion that tapping a can of beer after it has been shaken will prevent it from spraying when it is opened. Their paper describes a trial they carried out along with their conclusions, and is available on the *arXiv* preprint server.

Anyone who drinks beer on a regular basis knows about tapping the beer container a few times to get it to settle down before opening it. Some drinkers tap the lid or the top, and some tap the side of the bottle or can.

Whichever approach is used, the goal is always the same—to prevent beer from spewing out when the can or bottle is opened. Beer and soda drinkers also know that shaking bottles or cans before opening is a big non-no—doing so will result in beer spewing out like champagne.

In many circles, it is believed that some tapping can reduce or prevent such spewing—but as the researchers with this new effort note, the idea has never been tested scientifically.

To find out if tapping works, the researchers enlisted the assistance of a beer company and were rewarded with over 1000 donated cans of beer. Next, they enlisted student volunteers as testers.

First, all of the cans were weighed to measure the contents. Then half of the cans of beer were put on a mechanical shaker for two minutes; the other half were left as they were delivered.

Then half of the volunteers in both groups were asked to tap a can on its side three times before opening it. All of the cans were weighed again to see how much beer was lost after the can was opened.

The researchers report that they saw no benefit to tapping the can before opening—tapped cans, whether shaken beforehand or not, lost just as much beer after opening as un-tapped cans. The researchers also report that the beer was not wasted—it was given away to anyone on campus who cared to drink it.

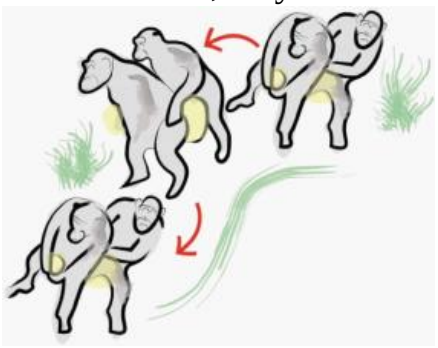
More information: *To beer or not to beer: does tapping beer cans prevent beer loss? A randomised controlled trial, arXiv:1912.01999 [physics.pop-ph] arxiv.org/abs/1912.01999*

http://bit.ly/36E3eQn

How humans learnt to dance; from the Chimpanzee Conga

The evolution of human dance has been studied by psychologists in chimpanzees

Psychologist observing two chimpanzees in a zoo have discovered that they performed a behaviour hitherto never seen, they coordinated together in a rhythmic social ritual.



An illustration of the chimp's conga **University of Warwick**

Two chimpanzees housed in a zoo in the US have sparked the question about how human dance evolved after being observed performing a duo dance-like behaviour, similar to a human conga-line.

In the paper 'Coupled whole-body rhythmic entrainment between two chimpanzees' published today, the 12th of December in the Journal Scientific Reports, researchers led by the University of Warwick found the levels of motoric co-ordination, synchrony and rhythm between the two female chimpanzees matched the levels shown by orchestra players performing the same musical piece.

Other species have been shown to be able to entertain by moving to the pace of a rhythmic tempo by an external stimulus and solo individuals, however this is the first time it hasn't been triggered by nonhuman partners or signals.

Although the newly described behaviour probably represents a new form a stereotypy in captivity in this great ape species, the behaviour forces scientists interested in the evolution of human dance to consider new conditions that may have catalysed the emergence of one of human's most exuberant and richest forms of expression.

Dr Adriano Lameira, from the Department of Psychology at the University of Warwick comments:

"Dance is an icon of human expression. Despite astounding diversity around the world's cultures and dazzling abundance of reminiscent animal systems, the evolution of dance in the human clade remains obscure.

"Dance requires individuals to interactively synchronize their whole-body tempo to their partner's, with near-perfect precision, this explains why no dance forms were present amongst nonhuman primates. Critically, this is evidence for conjoined full-body rhythmic entrainment in great apes that could help reconstruct possible proto-stages of human dance is still lacking."

The researchers report an endogenously-effected case of ritualized dance-like behaviour between two captive chimpanzees - synchronized bipedalism. By studying videos they revealed that synchronisation between individuals was non-random, predictable, phase concordant, maintained with instantaneous centi-second precision and jointly regulated, with individuals also taking turns as "pace-makers".

Paper available to view once embargo lifted at: http://www.nature.com/articles/s41598-019-55360-y DOI: 10.1038/s41598-019-55360-y

http://bit.ly/2sz8FBi

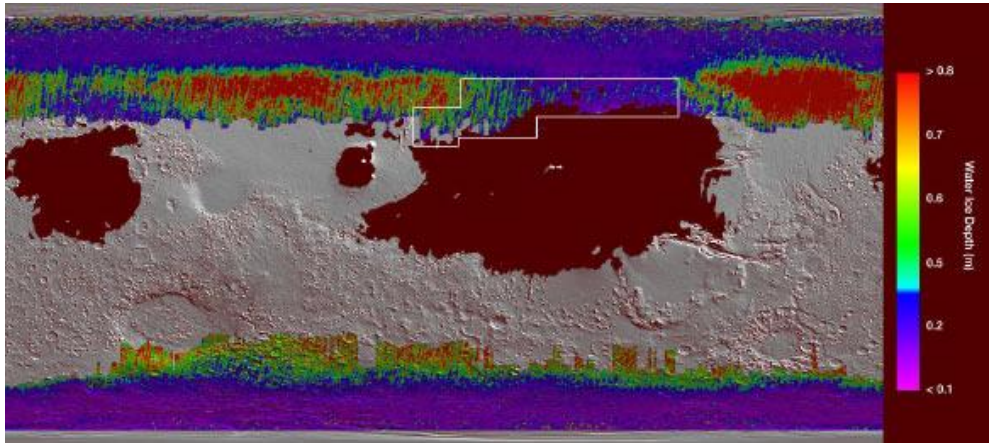
New Map Shows Near-Surface Water Ice on Mars

New map shows water ice is present sometimes just a few inches below the surface, where future landing is realistic

Using data from NASA's Mars Reconnaissance Orbiter and Mars Odyssey orbiter, a team of planetary researchers have crated a map of the water ice depth on the Red Planet. Published in the journal ***Geophysical Research Letters***, the **new map** shows that water ice is present sometimes just a few inches below the surface, at locations where future landing is realistic; this ice could be

exploited on-site for drinking water, breathable oxygen, etc., at a much lower cost than if brought from Earth.

Liquid water can't last in the thin air of Mars. With so little air pressure, it evaporates from a solid to a gas when exposed to the atmosphere. Martian water ice is locked away underground throughout the planet's mid-latitudes.



This map shows near-surface water ice on Mars; cool colors represent less than one foot (30 cm) below the surface; warm colors are over two feet (60 cm) deep; sprawling brown zones on the map represent areas where a landing spacecraft would sink into fine dust; the outlined box represents the ideal region to send astronauts for them to be able to dig up water ice. **Image credit: NASA / JPL-Caltech / ASU.**

"You wouldn't need a backhoe to dig up this ice. You could use a shovel," said Dr. Sylvain Piqueux, a researcher at NASA's Jet Propulsion Laboratory. "We're continuing to collect data on buried ice on Mars, zeroing in on the best places for astronauts to land."

To find this ice, Dr. Piqueux and colleagues relied on two heat-sensitive instruments: the Mars Climate Sounder onboard NASA's Mars Reconnaissance Orbiter (MRO) and the Thermal Emission Imaging System camera on Mars Odyssey.

"We cross-referenced temperatures suggestive of ice with other data, such as reservoirs of ice detected by radar or seen after meteor impacts," the scientists explained.

"The data from Odyssey's Gamma Ray Spectrometer, which is tailor-made for mapping water ice deposits, were also useful."

"As expected, all these data suggest a trove of water ice throughout the Martian poles and mid-latitudes. But the map reveals particularly shallow deposits that future mission planners may want to study further."

The team is planning a comprehensive campaign to continue studying the Martian ice across different seasons, watching how the abundance of this resource changes over time.

"The more we look for near-surface ice, the more we find," said MRO deputy project scientist Dr. Leslie Tamppari, also from NASA's Jet Propulsion Laboratory.

"Observing Mars with multiple spacecraft over the course of years continues to provide us with new ways of discovering this ice."

Sylvain Piqueux et al. *Widespread Shallow Water Ice on Mars at High and Mid Latitudes.* Geophysical Research Letters, *published online December 10, 2019; doi: 10.1029/2019GL083947*

https://bbc.in/38C6KwF

Drug that prevents half of breast cancers carries on working

A drug that halves a woman's risk of breast cancer continues to work long after they stop taking it, say researchers.

By James Gallagher Health and science correspondent

Anastrozole blocks the production of the hormone oestrogen, which fuels the growth of many breast cancers.

It is already available on the NHS, but researchers at Queen Mary University of London said only a tenth of eligible women were receiving it.

Cancer Research UK said the findings were reassuring.

Who can take it?

Anastrozole can be given only after the menopause because it cannot suppress oestrogen in younger women. It is already used as a treatment once breast cancer has been discovered, but now trials are focusing on preventing cancers emerging in the first place.

Previous research, has shown anastrozole halves the risk of breast cancer during the five years women took the drug.

But now, trials on 3,864 women show those taking it had 49% fewer breast cancers, even seven years after stopping treatment.

In other words - the benefit lasts.

The findings have been published in the Lancet and presented at the San Antonio Breast Cancer Symposium in Texas.

"Breast cancer is the commonest cancer in women and continuing to rise very rapidly," Prof Jack Cuzick, the director of the Wolfson Institute of Preventive Medicine at Queen Mary University of London, told the BBC. He added: "We now have an agent that looks really effective, with minimal side-effects."

Isn't this already available?

Post-menopausal women at high risk of developing breast cancer, due to family history and other risk factors, have been recommended to take the drug since 2017. "Uptake has really been quite low," said Prof Cuzick. "Currently its about 10% of these women and we think it should be substantially higher."

One issue is thought to be doctors being concerned about whether there was a long-term benefit. Another was around side-effects such as stiff joints, hot flushes and vaginal dryness.

However, the study showed 75% of women given anastrozole were able to stick with the medication, compared with 77% who were asked to take a daily sugar pill. The academics say this suggests the side-effects are not severe enough to stop women taking the drug.

How does the drug stop cancer?

Cancers are a corrupted version of healthy tissue.

However, a healthy cell does not become cancerous overnight. Instead it goes through multiple mutations that gradually morph it from healthy to cancerous.

Anastrozole seems to be able to kill some cells that have begun the journey to becoming a cancer. "You're setting the clock back 20 years and you have to start from scratch to develop the cancer, which might take quite a long time," Prof Cuzick told the BBC.

Will this eliminate the need for mastectomies?

No.

Drugs to prevent breast cancer mean having breasts removed is no longer the only preventive treatment.

But, some women are at such high risk of developing breast cancer that the danger would be too higher even with medication.

They may decide a mastectomy is still the best option.

In the future it is hoped research will be able to predict who is the most likely to benefit from the drugs or have the least side effects, which should make such decisions easier.

Are there other drugs?

Another drug that interferes with the hormone oestrogen - tamoxifen - can also be used to lower the risk of breast cancer. There was a 49% reduction in breast cancer with anastrozole after 12 years (five on treatment and seven years off). The equivalent figure for tamoxifen is 28%.

Dr Ivana Sestak, from Queen Mary, said: "The findings mean that for every 29 women taking anastrozole for five years, one case of breast cancer will be prevented during a 12-year period. "Around 49 women would need to take tamoxifen for five years to prevent one breast cancer case during the same period."

However, tamoxifen is effective in women before the menopause.

Anastrozole costs about 4p per pill. The list price of tamoxifen is about 9p per tablet.

What do experts say?

Baroness Delyth Morgan, chief executive at Breast Cancer Now, said: "These major findings could be really important in helping post-menopausal women at high risk of breast cancer to decide whether anastrozole is the right option for them.

"It is worrying to hear that it may not be being offered to all that could benefit and we need to understand the extent of this potential issue. "It's essential that we raise awareness of this option among doctors and patients."

Prof Charles Swanton, Cancer Research UK's chief clinician, said: "Up until now we only knew that tamoxifen has long-lasting benefits, so it's reassuring that this study looking specifically at anastrozole, which has fewer long-term side-effects, gives better protection to women years after they stopped taking the drug.

"Doctors may still decide that tamoxifen is more appropriate for some women, but it's great that there are options."

http://bit.ly/2rPoeFa

Herpes's Achilles heel

In a first, scientists use gene-editing to disrupt both latent and active herpes virus in human cells

The herpes simplex virus, commonly known as the cold sore virus, is a devious microbe.

It enters the body through regions lined with mucous membranes--mouth, nose and genitals--but quickly establishes lifelong viral hideouts inside nerve cells. After initial infection, the virus lurks dormant only to be reawakened periodically to cause outbreaks marked by the eruption of cold sores or blisters. In a handful of people, the consequences of viral reawaking can be devastating, including blindness and brain inflammation.

Antiviral medications can prevent recurrent outbreaks, but they are not always effective, so for decades, researchers have sought a solution that would quiet the virus for good.

Now, using human fibroblast cells infected with herpes simplex virus (HSV), researchers at Harvard Medical School have successfully used CRISPR-Cas9 gene editing to disrupt not only actively replicating virus but also the far-harder to reach dormant pools of the virus, demonstrating a possible strategy for achieving permanent viral control.

The team's findings are described Dec. 2 in eLife.

"This is an exciting first step--one that suggests it is possible to permanently silence lifelong infections--but much more work remains to be done," said study lead investigator David Knipe, the Higgins Professor of Microbiology and Molecular Genetics in the Blavatnik Institute at Harvard Medical School.

Notably, the research represents the first successful instance of disrupting latent viral reservoirs through gene editing. Latent reservoirs are notoriously impervious to antiviral medications and have also proven hard to gene-edit.

The experiments also identify the mechanisms by which actively replicating virus becomes uniquely vulnerable to gene editing. These very mechanisms may also explain why latent forms of the virus are less amenable to this technique.

Specifically, the experiments reveal that the DNA of an actively replicating virus is more exposed to the Cas9 enzyme--the molecular scissors in the CRISPR-Cas9 gene-editing system. This is because actively replicating viruses have fewer protective histones that wrap around their DNA to shield it.

"The absence of protective histones makes the DNA more accessible and easier to cut, so it's essentially identified HSV's Achilles heel," Knipe said.

The new findings offer a model system for using gene editing in a localized way to disrupt active replication in specific sites. However, Knipe cautions, the arch-challenge of delivering gene-

editing therapy to neurons--where the virus hides and enters a state of dormancy--remains to be solved, Knipe added.

More than two-thirds of the world population harbors the virus according to the World Health Organization. While most infections are asymptomatic, in a handful of people HSV can cause serious damage. It can infect the eyes, a condition known as herpes keratitis, and lead to blindness. In people with compromised immune systems, HSV can cause brain inflammation. In newborns, the virus can cause disseminated, systemic disease and brain inflammation and can be fatal in a quarter of infected babies.

Thus, one early therapeutic use of this technique could involve local and limited gene-editing of the epithelial cells in the mouth, eyes or genitals of people with established HSV infections as a way to prevent the virus from causing active outbreaks at vulnerable sites, Knipe said.

"If you want to prevent corneal infections, for example, you might be able to use CRISPR-Cas9 editing in the corneal cells to prevent new infections or prevent the virus from reactivating or reduce the reactivation," Knipe said. "People who have recurrent herpes keratitis infection of the cornea start to go blind after a while because of the reactivation and the resulting inflammation that causes clouding of the cornea."

The advantage of limited, localized gene-editing is avoiding the widespread, possible off-target effects that might inadvertently alter the DNA of cells other than those intended.

"We still have a long way to go in ensuring hyperprecision and safety of new gene-editing tools so local editing could offer a safer, more limited first step," Knipe said.

Werner Neuhausser, HMS instructor of obstetrics, gynecology and reproductive biology at Beth Israel Deaconess Medical Center, is co-senior author on the study. Other Harvard investigators included Hyung Suk Oh, Pierce Eggan, Magdalena Angelova, Rory Kirchner and Kevin Eggan.

The work was supported by National Institutes of Health grants AI135423 and AI098681 and a Q-FASTR award from Harvard Medical School.

https://wb.md/34qYWdQ

'Major Finding' in Triple-Negative Breast Cancer

Effective Drug for Difficult Tumor Is Already on Pharmacy Shelf

Nick Mulcahy

SAN ANTONIO — Triple-negative breast cancer (TNBC) is so called because its tumors lack three common receptors known to fuel tumor growth — estrogen, progesterone, and HER2/neu. These biological targets allow many breast tumors to be "druggable" with potentially curative therapies such as tamoxifen and trastuzumab. TNBC is lamented — and feared — because of its paucity of effective treatment options.

Now German investigators indicate that the chemotherapy drug capecitabine impacts this difficult-to-treat breast cancer in early stage disease.

Capecitabine improves both disease-free and overall survival (DFS and OS) when used as an add-on to other standard chemotherapy, either before or after surgery, reported Marion van Mackelenbergh, MD, of the University of Kiel, Germany, and colleagues here at the San Antonio Breast Cancer Symposium 2019.

Capecitabine's efficacy had been hinted at in single studies but only fully surfaced via the German team's new meta-analysis of 12 clinical trials involving more than 15,000 patients, said Priyanka Sharma, MD, University of Kansas Medical Center, Westwood, Kansas, who acted as meeting discussant of the study.

The meta-analysis showed that adding capecitabine to standard chemotherapy in TNBC improves DFS by 18% (hazard ratio [HR], 0.82; $P = 0.004$) and OS by 22% (HR, 0.78; $P = 0.004$).

It's a "MAJOR FINDING," tweeted meeting attendee Harold Burstein, MD, Dana-Farber Cancer Institute, Boston

(@DrHBurstein). "We have undervalued this approach because all-comers trials rarely showed a benefit."

The new study is "big news for #TNBC #SABCS19," posted Burstein, who is known for measured comments about breast cancer research and treatment.

Capecitabine is an oral fluoropyrimidine, which are inactive prodrugs of cytotoxic 5-FU that are absorbed through the gastrointestinal mucosa and converted to 5-FU by enzymes. Capecitabine is approved for use as monotherapy or in combination with docetaxel in metastatic breast cancer.

The new results address usage in early breast cancer.

The results provide evidence to support some current guidelines, observed Sharma. The National Comprehensive Cancer Network and St Gallen guidelines both say that clinicians should "consider adjuvant capecitabine in the setting of residual disease following neoadjuvant taxane/alkylator and anthracycline chemotherapy," she said.

Such choices mean that only early breast cancer patients at highest risk (ie, still have lingering disease after initial chemo) will be exposed to the additional toxicity of capecitabine, Sharma added, in advising about practical application of the new findings.

The new meta-analysis fills a void, said the researchers.

"Despite the large number of patients with early breast cancer that have been treated with capecitabine in randomized trials no individual patient data meta-analysis has yet been conducted," the team wrote in their meeting abstract.

To do so, the German investigators searched for completed randomized trials involving use of capecitabine in early breast cancer as adjuvant or neoadjuvant therapy and having at least 100 patients.

Individual data from 15,457 patients was collected, including 7980 who received capecitabine during the course of their treatment and 7477 patients who were treated in control arms. Median age at diagnosis was 54 years in both groups. Most patients had stage 2 tumors (55.9%) at diagnosis and the majority presented with nodal involvement (74.0%). Estrogen and progesterone receptor positivity was observed in 66.0% and 56.9%, respectively, and 15.1% of patients were diagnosed as HER2-positive. In sum, 2816 patients (18.2%) received neoadjuvant treatment and 12,641 (81.8%) an adjuvant chemotherapy regimen.

Notably, there was also no effect on DFS if studies (n = 5) were selected in which capecitabine was given *instead of* another drug. Thus, seven studies, in which capecitabine was given *in addition to* standard chemo, remained and those showed the above-referenced results.

Sharma has multiple financial ties to pharmaceutical companies. Burstein has disclosed no relevant financial relationships.

San Antonio Breast Cancer Symposium 2019: Abstract GS1-07. Presented December 11, 2019.

http://bit.ly/2LZwxoV

A new study shows an animal's lifespan is written in the DNA. For humans, it's 38 years

Humans have a "natural" lifespan of around 38 years, according to a new method we have developed for estimating the lifespans of different species by analysing their DNA.

Benjamin Mayne Molecular biologist and bioinformatician, CSIRO

Extrapolating from genetic studies of species with known lifespans, we found that the extinct woolly mammoth probably lived around 60 years and bowhead whales can expect to enjoy more than two and a half centuries of life.

Our research, published today in Scientific Reports, looked at how DNA changes as an animal ages – and found that it varies from species to species and is related to how long the animal is likely to live.

The mystery of ageing

The ageing process is very important in biomedical and ecological research. As animals grow older, they experience a decline of biological functions, which limits their lifespan. Until now it has been difficult to determine how many years an animal can live.

DNA is the blueprint of living organisms and it is an obvious place to seek insights into ageing and lifespan. However, no-one has been able to find differences in DNA sequences that account for differences in lifespans.

Lifespans among vertebrates varies greatly. The pygmy goby (*Eviota sigillata*) is a small fish that lives only eight weeks, whereas individual Greenland sharks (*Somniosus microcephalus*) have been found that lived for more than 400 years.

Knowing the lifespan of wild animals is fundamental for wildlife management and conservation. For endangered species, lifespan can be used to understand what populations are viable. In industries such as fisheries, lifespan is used in population models to determine catch limits.

However, the lifespan of most animals is unknown. Most estimates come from a small number of individuals living in captivity whose ages at death were known. For long-lived species it is difficult to obtain a lifespan as they may outlive a generation of researchers.

Using changes in DNA to measure age

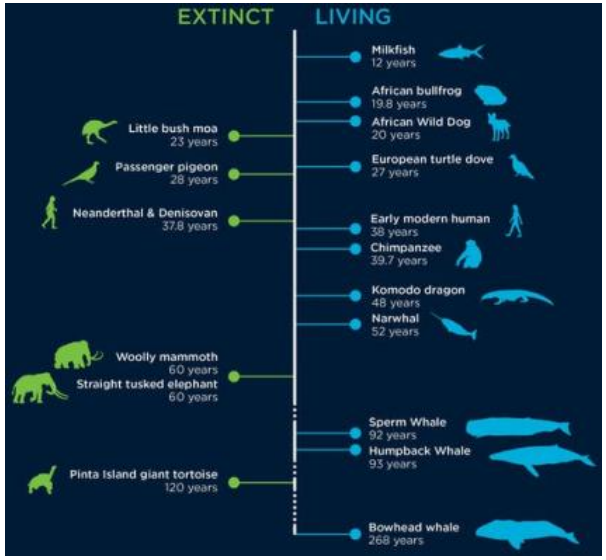
Over the past few years researchers have developed DNA "clocks" that can determine how old an animal is using a special type of change in the DNA called DNA methylation.

DNA methylation does not change the underlying sequence of a gene but controls whether it is active. Other researchers have shown that DNA methylation in specific genes is associated with the maximum lifespan of some mammals such as primates.

Despite DNA methylation being linked to ageing and lifespan, no research until now has used it as a method to estimate the lifespan of animals.

In our research, we have used 252 genomes (full DNA sequences) of vertebrate species that other researchers have assembled and made publicly available in an online database. We then compared these genomes to another database of known animal lifespans.

Using this data, we found that we could estimate the lifespan of vertebrate species by looking at where DNA methylation occurs in 42 particular genes. This method also lets us estimate the lifespans of long-lived and extinct species.



Using DNA analysis, scientists can now estimate the lifespans of long-lived and extinct species. **CSIRO, Author provided**

Extinct species

We found the lifespan of the bowhead whale, thought to be the world's longest lived mammal, is 268 years. This estimate is 57 years higher than the oldest individual that has been found, so they may have a much longer lifespan than previously thought.

We also found the extinct woolly mammoth had a lifespan of 60 years, similar to the 65-year span of the modern-day African elephant.

The extinct Pinta Island giant tortoise had a lifespan of 120 years by our estimate. The last member of this species, Lonesome George, died in 2012 at age 112.

Interestingly, we found Neanderthals and Denisovans, which are extinct species closely related to modern humans, had a maximum lifespan of 37.8 years.

Based on DNA, we also estimated a "natural" lifespan modern humans of 38 years. This matches some anthropological estimates for early modern humans. However, humans today may be an exception to this study as advances in medicine and lifestyle have extended the average lifespan.

As more scientists assemble the genomes of other animals, our method means their lifespans can readily be estimated. This has huge ecological and conservation significance for many species which require better wildlife management.

Disclosure statement

Benjamin Mayne receives funding from CSIRO Environomics Future Science Platform and is supported by the the North West Shelf Flatback Turtle Conservation Program (https://flatbacks.dbca.wa.gov.au/about).

http://bit.ly/2PR7uoW

Artificial intelligence puts final notes on Beethoven's '10th Symphony'

Team of musicologists and programmers is racing to complete a version of the piece using artificial intelligence, before his 250th birthday

AFP-JIJI Dec 13, 2019

BERLIN – A few notes scribbled in a notebook are all that German composer Ludwig van Beethoven left of his 10th Symphony before his death in 1827.

Now, a team of musicologists and programmers is racing to complete a version of the piece using artificial intelligence, ahead of the 250th anniversary of his birth next year.

"The progress has been impressive, even if the computer still has a lot to learn," said Christine Siegert, head of archives at Beethoven House in the composer's hometown of Bonn.

Siegert said she was "convinced" that Beethoven would have approved since he too was an innovator at the time, citing his compositions for the panharmonicon — a type of organ that reproduces the sounds of wind and percussion instruments.

And she insisted the work would not affect his legacy because it would never be regarded as part of his oeuvre.

The final result of the project will be performed by a full orchestra on April 28 next year in Bonn, a centerpiece of celebrations for a composer who defined the romantic era of classical music.

Beethoven, Germany's most famous musical figure, is so loved in his homeland that a duty to prepare for the anniversary was written into the governing coalition's agreement in 2013.

The year of celebrations will begin on Monday, Dec. 16 — believed to be his 249th birthday — with the opening of his home in Bonn as a museum after extensive renovation.

Beethoven began working on the Tenth Symphony alongside his Ninth, which includes the world-famous "Ode To Joy." But he quickly gave up on the Tenth, leaving only a few notes and drafts by the time he died at age 57.

In the project, machine-learning software has been fed all of Beethoven's work and is now composing possible continuations of the symphony in the composer's style. Deutsche Telekom, which is sponsoring the project, hopes to use the findings to develop technology such as voice recognition. The team said the first results a few months ago were seen as too mechanical and repetitive but the latest AI compositions have been more promising.

Barry Cooper, a British composer and musicologist who himself wrote a hypothetical first movement for the Tenth Symphony in 1988, was more doubtful. "I listened to a short excerpt that has been created. It did not sound remotely like a convincing reconstruction of what Beethoven intended," said Cooper, a professor at the University of Manchester and the author of several works on Beethoven. "There is, however, scope for improvement with further work."

Cooper warned that "in any performance of Beethoven's music, there is a risk of distorting his intentions" and this is particularly the

case for the Tenth Symphony because the composer had left only fragmentary material.

Similar AI experiments based on works by Bach, Mahler and Schubert have been less than impressive.

A project earlier this year to complete Schubert's Eighth Symphony was seen by some reviewers as being closer to an American film soundtrack than the Austrian composer's work.

http://bit.ly/38Ldd8n

A self-cleaning surface that repels even the deadliest superbugs

New wrap repels everything that comes into contact with it, including viruses and bacteria

A new wrap developed by researchers at McMaster University repels everything that comes into contact with it, including viruses and bacteria. Credit: Georgia Kirkos, McMaster University

A team of researchers at McMaster University has developed a self-cleaning surface that can repel all forms of bacteria, preventing the transfer of antibiotic-resistant superbugs and other dangerous bacteria in settings ranging from hospitals to kitchens.

The new plastic surface—a treated form of conventional transparent wrap—can be shrink-wrapped onto door handles, railings, IV stands and other surfaces that can be magnets for bacteria such as MRSA and *C. difficile*.

The treated material is also ideal for food packaging, where it could stop the accidental transfer of bacteria such as *E. coli*, *Salmonella* and listeria from raw chicken, meat and other foods, as described in a paper published today by the journal *ACS Nano*.

The research was led by engineers Leyla Soleymani and Tohid Didar, who collaborated with colleagues from McMaster's Institute for Infectious Disease Research and the McMaster-based Canadian Centre for Electron Microscopy.

Inspired by the water-repellent lotus leaf, the new surface works through a combination of nano-scale surface engineering and chemistry. The surface is textured with microscopic wrinkles that exclude all external molecules. A drop of water or blood, for example, simply bounces away when it lands on the surface. The same is true for bacteria.

"We're structurally tuning that plastic," says Soleymani, an engineering physicist. "This material gives us something that can be applied to all kinds of things."

The surface is also treated chemically to further enhance its repellent properties, resulting in a barrier that is flexible, durable and inexpensive to reproduce.

"We can see this technology being used in all kinds of institutional and domestic settings," Didar says. "As the world confronts the crisis of anti-microbial resistance, we hope it will become an important part of the anti-bacterial toolbox."

The researchers tested the material using two of the most troubling forms of antibiotic-resistant bacteria: MRSA and Pseudomonas, with the collaboration of Eric Brown of McMaster's Institute for Infectious Disease Research.

Engineer Kathryn Grandfield helped the team verify the effectiveness of the surface by capturing electron microscope images showing that virtually no bacteria could transfer to the new surface. The researchers are hoping to work with a commercial partner to develop commercial applications for the wrap.

https://wb.md/35uuoJq

'Remarkable' New Data on Menopausal Hormone Therapy

Two different types of menopausal hormone therapy have opposite effects on breast cancer incidence that persist long after stopping treatment

Megan Brooks

San Antonio, Texas — Two different types of menopausal hormone therapy — estrogen alone and estrogen plus progestin — have opposite effects on breast cancer incidence that persist long after stopping treatment, according to over 19 years of follow-up of the landmark Women's Health Initiative (WHI) released today.

The data indicate that use of conjugated equine estrogens (CEE) alone significantly decreases breast cancer incidence and deaths from breast cancer, while CEE plus medroxyprogesterone acetate (MPA) significantly increases the risk of developing the disease. In both instances, these effects linger for decades after discontinuation.

The data are "remarkable," said lead investigator Rowan T. Chlebowski, MD, PhD, Harbor-UCLA Medical Center, Torrance, California. To date, "no one has been able to reconcile these findings," he acknowledged.

Chlebowski reported the findings at a press briefing here today at the San Antonio Breast Cancer Symposium (SABCS) 2019.

Asked whether these data should influence current guidelines on menopausal hormone therapy, Chlebowski said, "Yes, I would hope so. Women considering estrogen alone should know it's safer and there may be a breast cancer benefit associated with its use," he said. Women considering estrogen plus progestin have "a little more difficult dilemma because they have to be willing to accept a 20-year and maybe lifetime increased breast cancer risk [although] the absolute risk is very small," he said.

50 Years of Controversy, Lingering Questions

After a half-century, hormone therapy's influence on breast cancer "still remains controversial" with discordant findings from observational studies compared with randomized controlled trials, Chlebowski noted.

Most recently, in a meta-analysis of 58 observational studies, estrogen plus progestin and estrogen alone were both associated with a significantly increased risk of breast cancer. And in the Million Women Study, both estrogen plus progestin as well as estrogen alone were associated with a significantly increased risk of dying from breast cancer.

Against this backdrop, Chlebowski provided an update today on breast cancer findings from the WHI randomized controlled trials with more than 19 years of follow-up. The WHI is funded by the National Institutes of Health (NIH).

From 1993 to 1998, more than 27,000 postmenopausal women aged 50 to 79 years with no prior breast cancer enrolled in one of two randomized, placebo-controlled WHI trials implemented at 40 US centers, with follow-up through September 2016.

Women with an intact uterus received CEE (0.625 mg/day) plus MPA (2.5 mg/day) or placebo (n = 8102) for a median of 5.6 years. Women with prior hysterectomy received CEE alone (n = 5310) or placebo (n = 5429) for a median of 7.2 years.

After about 19 years of follow-up, CEE alone resulted in a significant 23% reduction in breast cancer incidence (hazard ratio [HR], 0.77; P = .005), whereas CEE+MPA resulted in a significant 29% increased risk of breast cancer (HR, 1.29; P < .001).

"A woman takes estrogen/progestin for 5 years and she is exposed to a 20-year risk of increasing breast cancer risk...and one could speculate that it will be a lifetime risk for short-term use," said Chlebowski.

In terms of deaths from breast cancer, there was 45% increase (borderline significance) with CEE+MPA (HR, 1.45; P = .06) and a significant 44% reduction with CEE alone (HR, 0.56; P = .02).

Chlebowski said it should be noted that "none of the approved agents for breast cancer risk reduction...have been able to demonstrate a reduction in deaths from breast cancer so this is a very unique finding." Chlebowski has been a consultant for AstraZeneca, Novartis, Amgen, Genentech, Pfizer, Puma, Immunomedics, and has received NIH grant funding.

Commenting on the new data for *Medscape Medical News*, Charles L. Shapiro, MD, professor of medicine, hematology and medical oncology, Icahn School of Medicine at Mount Sinai in New York City, said it's clear that the risk — "both positive and negative" — continues beyond using hormone therapy for at least 10 years.

"Women should be reassured if they had short-term estrogen exposure they are not at increased risk — in fact, the data suggest there is decreased risk," he said.

"Women who had conjugated estrogen and MPA in the past should be aware that their risk may be slightly higher and get their mammograms. Whether that should merit special screening, or more frequent screenings, I don't think we know that," added Shapiro.

San Antonio Breast Cancer Symposium 2019: Abstract GS5-00. Presented December 13, 2019.