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Drug for rare disorder shows promise for treating herpes viruses

A drug currently prescribed to treat a rare enzyme deficiency can help cells clear the herpes simplex 1 and herpes simplex 2 viruses

A drug currently prescribed to treat a rare enzyme deficiency can help cells clear the herpes simplex 1 and herpes simplex 2 viruses, according to a new study published in the journal *Science Advances*. The new data shows that the antiviral activity of the drug -- called phenylbutyrate, or PBA -- was even better when used along with acyclovir, a common HSV-1 treatment. When used in combination, less acyclovir is needed to effectively suppress the virus compared to acyclovir alone -- this is important because acyclovir is also known to have toxic side effects in the kidneys.

"There are very few drugs available to treat herpes simplex viruses, so when new drugs become available, especially drugs that enable fewer side effects, it is a welcome discovery," said Dr. Deepak Shukla, the Marion Schenk Professor of Ophthalmology and UIC professor of microbiology and immunology at the College of Medicine and corresponding author on the paper. "Acyclovir can have very toxic effects on the kidneys, especially when it is given in higher doses for HSV-induced encephalitis, which is rare but can be deadly. By combining acyclovir with PBA, we need less acyclovir to effectively treat HSV-1."

There are two types of herpes simplex virus: herpes simplex 1, which infects the eyes and mouth and is a leading cause of blindness, and herpes simplex 2, a genital infection that may cause painful sores and can seriously impair quality of life.

Treatment for both infections often includes acyclovir -- a systemic medication taken orally. However, long-term use often results in resistance to the drug as well as kidney damage.

Shukla and colleagues investigated the antiviral effects of PBA and found that in cells the drug disrupts the ability of the virus to hijack the cellular machinery used to produce proteins. Normally, viruses infect cells and force them to produce viral proteins so the virus can replicate itself. But the cell also continues to produce proteins for its own use, leading to a lot of stress in the structure -- called the endoplasmic reticulum, or ER for short -- that makes protein.

"We found that PBA reduces stress on the ER, which allows the cell to focus on clearing the virus on its own," said Tejabhiram Yadavalli, a UIC ophthalmology and visual sciences postdoctoral fellow and first author of the paper.

The researchers found that in cells, PBA alone was able to clear HSV-1 from cells of donated human corneas or from donated human skin tissue just as well as acyclovir. In a mouse model of ocular HSV-1 infection, PBA administered intraperitoneally was able to clear the virus from the eyes. In an animal model of HSV-2 vaginal infection, mice that received PBA had no signs of the HSV-2 virus in tissues, similar to mice treated with acyclovir.

When they tested a combination of PBA with acyclovir cells infected with HSV-1, the drug combo was able to completely clear the virus from the cells faster and better than either drug alone. Additionally, in a mouse model of HSV-induced encephalitis, mice treated with PBA or acyclovir alone had significantly reduced death rates, but a combination of PBA and acyclovir was able to prevent death in all mice given this combination.

"PBA is an exciting new therapeutic for treating herpes infections that can help reduce side effects associated with long term or high dose use of acyclovir, a commonly prescribed medication to treat herpes viruses," Shukla said. "The added bonus of this drug already being approved by the FDA to treat a rare enzyme disorder means that we may be able to quickly develop a marketable new combination therapy in the near future."

Rahul Suryawanshi, Raghuram Koganti, James Hopkins, Joshua Ames, Lulia Koujah, Aqsa Iqbal, Krishna Raju and Alex Agelidis of UIC are co-authors on the paper.
This work was funded by grants from National Institutes of Health (R01EY024710 and R01 AI139768), an NIH Fellowship, and funds from Research to Prevent Blindness.

https://bit.ly/37aWHjv

Mount Sinai researchers advance a universal influenza virus vaccine

Induces immune responses to a wide spectrum of influenza virus strains and subtypes

A vaccine that induces immune responses to a wide spectrum of influenza virus strains and subtypes has produced strong and durable results in early-stage clinical trials in humans, Mount Sinai researchers have found. The universal influenza virus vaccine, which produces antibodies that target the part of the surface protein of the influenza virus known to neutralize diverse influenza strains, was described in a study published today in the journal *Nature Medicine*. This chimeric hemagglutinin (HA)-based vaccine has the potential to provide long-lived protection with two or three immunizations, eliminating the need for revaccination.

"An influenza virus vaccine that results in broad immunity would likely protect against any emerging influenza virus subtype or strain and would significantly enhance our pandemic preparedness, avoiding future problems with influenza pandemics as we see them now with COVID-19" says Florian Krammer, PhD, Professor of Microbiology at the Icahn School of Medicine at Mount Sinai, and corresponding author of the study. "Our chimeric hemagglutinin vaccine is a major advance over conventional vaccines which are often mismatched to the circulating strains of virus, impacting their effectiveness. In addition, revaccinating individuals annually is a huge and expensive undertaking."

Seasonal influenza is a major public health concern, triggering as many as 650,000 deaths every year globally, according to the World Health Organization. In addition, influenza pandemics, similar to the current COVID-19 outbreak, occur at irregular intervals and can claim millions of lives.

The most devastating example is the H1N1 pandemic of 1918, which caused approximately 40 million deaths. Influenza virus vaccines -- the best preventive weapon in the public health arsenal against seasonal influenza -- contain three or four strains of the influenza virus that respond to the viruses circulating in the human population. Their inherent weakness, however, is that vaccine strains in the annual formulations are based on global health surveillance and predictions that are often out of sync with the strains that actually circulate.

The situation is compounded in the case of emerging pandemic viruses, since these outbreaks cannot be predicted and emerge suddenly, requiring newly matched vaccines to be generated. This process requires at least six months, leaving large portions of the population vulnerable.

The chimeric HA vaccine seeks to correct this uncertainty by targeting a different part of the hemagglutinin protein, the major surface glycoprotein of the influenza virus that binds to host cell receptors. Conventional vaccines induce neutralizing antibodies that target the distal part of the hemagglutinin, known as the globular head domain.

"Unfortunately, the virus is able to escape neutralization by mutating this part of hemagglutinin through a process known as antigenic drift," explains Peter Palese, PhD, Professor of Microbiology and Chair of the Department of Microbiology at Icahn School of Medicine at Mount Sinai, and co-author of the study.

"This genetic change, or shift, in the virus results in immunity to only specific strains of the influenza virus, requiring frequent re-formulation and re-administration of seasonal vaccines. Our

chimeric HA vaccine, by contrast, is directed at the proximal part of the HA protein -- the stalk domain -- which has been shown to broadly neutralize diverse influenza virus strains in both animal models and humans."

A vaccine construct based on the hemagglutinin stalk domain has been a major focus of the research community.

"The beauty part of this vaccine is that it's not only broad, but multifunctional with stalk-specific antibodies that can neutralize many kinds of influenza viruses," emphasizes Dr. Adolfo García-Sastre, Director of the Global Health and Emerging Pathogens Institute and Professor of Microbiology at the Icahn School of Medicine at Mount Sinai and also co-author of the study. "This universal vaccine could be particularly beneficial to low and middle income countries that don't have the resources or the logistics to vaccinate their populations each year against influenza."

Mount Sinai's Phase 1 clinical trial evaluated the safety and immunogenicity of the vaccine in 65 participants in the U.S., and was found to produce a strong immune response that endured for at least 18 months following vaccination.

"This phase of our clinical work significantly advances our understanding of the immune response in terms of its longevity," says Dr. Krammer, "and leaves us greatly encouraged about future progress for this potentially breakthrough vaccine."

Collaborative efforts between Mount Sinai, PATH, GSK, the University of Chicago Pritzker School of Medicine, Cincinnati Children's Hospital Medical Center and Duke University School of Medicine in North Carolina contributed to the successful testing of this vaccine candidate.

The study was funded in part by the Bill and Melinda Gates Foundation and the NIH. Basic research leading to the design of the vaccine were initially funded by NIAID's Centers of Excellence for Influenza Research and Surveillance (CEIRS) and analysis of the immune response at later stages was also funded through NIAID's Collaborative Influenza Vaccine Innovation Centers (CIVIC).

https://bit.ly/3qMqyGt

Study shows that Japanese bats urgently require conservation action

90% of endemic species threatened with extinction

Here's a fun fact: Japan has more bat species than any other order of mammal in the country, and a third of these are endemic. But the bad news is that 90% of the endemic species are at risk of extinction.

Bats play crucial ecological roles, including in pollination and pest control. But while they have been a focus of research in many fields of science—including epidemiology—they remain underrepresented in conservation, particularly in Japan.

The Okinawan Least Horseshoe Bat, one of the endemic species found in central and southern Ryukyu Islands of Japan. **Credit: Kyoto University/Island Bat Research Group**

Publishing in *Mammal Review*, researchers from Kyoto University's Graduate School of Informatics describe a systematic survey of the state of Japanese bat research and their analysis of the possible roots of the problem.

The study authors found poor alignment between conservation needs and allocation of research resources. Although research effort has increased gradually since the year 2000, threatened endemic bats remain significantly less studied than their non-threatened counterparts. "Conservation status alone is not enough to promote research on these threatened species," explains Jason Preble, doctoral candidate and one of the authors of the study.

"We systematically reviewed the literature of the last fifty years, assessing patterns in research distribution across multiple categories in order to identify gaps and future priorities."

The team found a marked shortage of both ecological and conservation-motivated studies in international journals on nearly half of the extant species in Japan. Moreover, while many threats to Japanese bats have been identified, such as forest loss or alteration, there was a shortage of data measuring the impacts of these threats.

"All of these factors are immensely concerning," says corresponding author Christian E. Vincenot. "We were distressed to see threats such as wind turbines and climate change severely understudied." Based on their results, the team lists recommendations aimed at strengthening Japanese bat conservation. "For example, we need to prioritize research efforts that provide the ecological information needed to design and implement concrete conservation plans," Vincenot explains.

Data disclosure is imperative, he continues. Openness not only helps the research community, but provides valuable resources to government officers, NGOs, and non-professional naturalists who are equally key players in a comprehensive conservation strategy.

The authors also emphasize the importance of communicating research findings to the public, which in turn can facilitate support from funding agencies. "While hopeful signs of improvement exist, ultimately a stronger spirit of research and collaboration—along with informed conservation practices—will determine if these creatures can reach the road to recovery or ultimately decline into extinction," says Vincenot.

"In the Shadow of the Rising Sun: A Systematic Review of Japanese Bat Research and Conservation" Mammal Review, DOI: 10.1111/mam.12226

https://bit.ly/3qJVF5E

A study predicts smooth interaction between humans and robots

According to a new study by Tampere University in Finland, making eye contact with a robot may have the same effect on people as eye contact with another person.

The results predict that interaction between humans and humanoid robots will be surprisingly smooth.

With the rapid progress in robotics, it is anticipated that people will increasingly interact with so called social robots in the future. Despite the artificiality of robots, people seem to react to them socially and ascribe humane attributes to them. For instance, people may perceive different qualities - such as knowledgeability, sociability, and likeability - in robots based on how they look and/or behave.

Previous surveys have been able to shed light on people's perceptions of social robots and their characteristics, but the very central question of what kind of automatic reactions social robots evoke in us humans has remained unanswered. Does interacting with a robot cause similar reactions as interacting with another human?

Researchers at Tampere University investigated the matter by studying the physiological reactions that eye contact with a social robot evokes. Eye contact was chosen as the topic of the study for two major reasons. First, previous results have shown that certain emotional and attention-related physiological responses are stronger when people see the gaze of another person directed to them compared to seeing their averted gaze. Second, directing the gaze either towards or away from another person is a type of behaviour related to normal interaction that even current social robots are quite naturally capable of.

In the study, the research participants were face to face with another person or a humanoid robot. The person and the robot looked either directly at the participant and made eye contact or averted their gaze. At the same time, the participants' skin conductance, which reflects the activity of the autonomous nervous systems, the electrical activity of the cheek muscle reflecting positive affective

reactions, and heart rate deceleration, which indicates the orienting of attention, were measured.

The results showed that all the above-mentioned physiological reactions were stronger in the case of eye contact compared to averted gaze when shared with both another person and a humanoid robot. Eye contact with the robot and another human focused the participants' attention, raised their level of arousal and elicited a positive emotional response.

"Our results indicate that the non-linguistic, interaction-regulating cues of social robots can affect humans in the same way as similar cues presented by other people. Interestingly, we respond to signals that have evolved over the course of evolution to regulate human interaction even when these signals are transmitted by robots. Such evidence allows us to anticipate that as robot technology develops, our interaction with the social robots of the future may be surprisingly seamless," says doctoral researcher Helena Kiilavuori.

"The results were quite astonishing for us, too, because our previous results have shown that eye contact only elicits the reactions we perceived in this study when the participants know that another person is actually seeing them. For example, in a video conference, eye contact with the person on the screen does not cause these reactions if the participant knows that his or her own camera is off, and the other person is unable to see him or her. The fact that eye contact with a robot produces such reactions indicates that even though we know the robot is a lifeless machine, we treat it instinctively as if it could see us. As if it had a mind which looked at us," says Professor of Psychology Jari Hietanen, director of the project.

The study was supported by the Pirkanmaa Regional Fund of the Finnish Cultural Foundation and the Academy of Finland.

Kiilavuori, H., Sariola, V., Peltola, M. J., & Hietanen, J. K. (2021). Making eye contact with a robot: Psychophysiological responses to eye contact with a human and with a humanoid robot. Biological Psychology. https://doi.org/10.1016/j.biopsycho.2020.107989

https://wb.md/3naZkay

SUDEP May Explain 3% of All Sudden Deaths in Kids

A prevalence rate that is at least three times greater than previously reported estimates

Pauline Anderson

Sudden unexpected death in epilepsy (SUDEP) may explain 3% of all sudden deaths in children – a prevalence rate that is at least three times greater than previously reported estimates – new research shows

Just a few years ago, the message regarding SUDEP was that "it's very rare in children so you don't need to worry about it," study investigator Vicky Whittemore, PhD, program director at the National Institute of Neurological Disorders and Stroke, told *Medscape Medical News*.

These new study results should refocus the message that "the condition is rare, but not as rare as we thought it was," she said.

The findings were presented at the American Epilepsy Society (AES) 74th Annual Meeting 2020, which was held online this year because of the COVID-19 pandemic.

Population-Based Study

Most of the research examining the pediatric SUDEP rate in the United States is based on convenience samples, with few population-based studies.

The investigators used data from the NIH/CDC Sudden Death in the Young Case Registry. The CDC set up the registry several years ago to record cases of sudden infant death syndrome and sudden deaths in children resulting from violence, trauma, and abuse. Its mandate has since expanded, and the registry now includes data on sudden cardiac death and SUDEP in children.

The current study included children with SUDEP or cardiac/SUDEP who were aged 0 to 17 years from several states or jurisdictions from 2015 to 2017.

Cases were deemed to be SUDEP if the patient had a history of epilepsy, with or without evidence of seizure at the time of death, but excluding status epilepticus.

Criteria for Cardiac/SUDEP cases included having a family history of a heritable cardiac condition or sudden death before age 50 years, a personal history of cardiac disease, or a clinical history suggestive of a cardiac disorder, such as death during exertion.

This second category, said Whittemore, might capture children with Dravet syndrome, a type of epilepsy caused by a genetic mutation that affects both the heart and the brain.

"In these cases, it's sometimes difficult to tell if the child died due to a heart complication or due to epilepsy," she said.

The analysis included 1776 cases. Of these, 3% were categorized as SUDEP, and 1% were categorized as cardiac/SUDEP.

The relatively high prevalence of SUDEP was somewhat unexpected, inasmuch as previous reports estimated the rate to be 0.5% to about 1%, said Whittemore.

She noted that the current study is population based and included all cases of child death, whereas past reports relied on death certificates. "That probably missed a lot of deaths because they weren't recorded accurately on the death certificate or weren't reported in a way that anyone could ascertain that it was a death in someone that had epilepsy," she said.

Racial Differences

Autopsy rates were lower for SUDEP (70%) compared to other categories of death in the registry (81% to 100%).

In most jurisdictions, parents must give consent for an autopsy to be performed for a child, and many parents who have suffered such a sudden loss don't want further investigation, said Whittemore.

"If you know your child had epilepsy, doing an autopsy really isn't going to tell you very much. You already know they had epilepsy; you may not know the cause of the epilepsy, but an autopsy isn't going to reveal as much as it would in children with sudden cardiac death," she said.

SUDEP was equally common in boys and girls. However, the SUDEP mortality rate was higher in Black children (0.32/100,000) than in White children (0.22/100,000).

It's unclear from this study why this is so, but another study that examined SUDEP rates by ZIP code suggested that the higher rate may be due to socioeconomic factors, said Whittemore.

"Black children from a lower-income family who don't have access to care may not be getting as good treatment and so have more uncontrolled seizures, which may lead to higher incidence of SUDEP," she said.

SUDEP occurred at all ages, but mortality rates were highest among patients aged 0 to 1 year (0.53/100,000) and in those aged 14 to 17 years (0.31/100,000).

Whittemore speculated that SUDEP rates were higher among the youngest patients because their seizures have just started, and it may be more difficult to bring them under control. In the past, some of these cases may have been classified as sudden infant death syndrome but are now recognized as SUDEP, she said.

As for the older group, research shows that puberty can result in poorer seizure control, which may put teens at elevated risk for SUDEP, said Whittemore.

She added that as teens continue to age, SUDEP risk may continue to increase. Whittemore suggested that young adults who head off to college may stop taking their antiseizure medications or consume alcohol while taking these drugs.

Failure of Arousal

The study results revealed that most SUDEP cases occurred during sleep without a witness. Whittemore believes that sleeping with one's face in a pillow may prevent the reflex required to turn the head to breathe. "It's sort of a failure of arousal that is potentially

the underlying mechanism," she said. In some cases, there are signs children had a seizure just prior to death, said Whittemore.

The researchers have now collected information for 2018 and 2019 and plan to add these data to the current 3-year results. "We will now expand our analysis to include these new numbers to make sure the trends we saw in those 3 years are continuing," said Whittemore.

The new results should help raise awareness that SUDEP is not as rare as previously believed, she said.

Parents of children with epilepsy can take steps to help reduce the risk for SUDEP, she added. For example, they can use night monitors, and for the children at highest risk (eg, those with Dravet syndrome), they can use an "alarm blanket" that alerts them when the child moves.

Commenting on the study for *Medscape Medical News*, Daniel Goldenholz, MD, PhD, Division of Epilepsy, Department of Neurology, Beth Israel Deaconess Medical Center, New York City, who has participated in SUDEP research, said it "raises important questions about SUDEP in children and about racial disparities in SUDEP."

The understanding of SUDEP so far "leaves much to be desired," said Goldenholz. "We don't yet know why it happens, and we don't yet know how to prevent it."

The current study "brings a couple of new data points to the table which need further validation, confirmation, and explanation," he said.

The Sudden Death in Young Case Registry is supported by the National Heart, Lung and Blood Institute, the National Institute of Neurological Disorders and Stroke, and the Center for Disease Control and Prevention. The investigators and Goldenholz have disclosed no relevant financial relationships.

American Epilepsy Society (AES) 74th Annual Meeting 2020: Abstract 912949 (poster 405). Presented December 6, 2020.

https://bit.ly/3qGrVCe

Study: Bartonella infection associated with psychiatric symptoms and skin lesions

Bartonella bacteria are increasingly recognized as an emerging infectious disease threat.

A new study by North Carolina State University researchers has found additional instances of *Bartonella* infection in humans who exhibited neuropsychiatric symptoms, a subset of whom also had skin lesions. This research adds to the body of evidence that not only can *Bartonella* infection mimic a spectrum of chronic illnesses - including mental illness - but also that dermatological symptoms may accompany infection.

Bartonella henselae is a bacterium historically associated with cat-scratch disease, which until recently was thought to be a short-lived (or self-limiting) infection. There are at least 30 different known *Bartonella* species, of which 13 have been found to infect humans. Improved methods for detecting *Bartonella* infection in animals and humans - it is notorious for "hiding" in the linings of blood vessels and potentially the skin - has led to the diagnosis of bartonelloses in patients with a host of chronic illnesses.

In 2019, Dr. Edward Breitschwerdt, Melanie S. Steele Distinguished Professor of Internal Medicine at NC State, published a case study involving an adolescent boy diagnosed with rapid onset schizophrenia, who had accompanying skin lesions. After Breitschwerdt's research group documented *Bartonella* henselae infection, the patient received antimicrobial therapy and all neuropsychiatric symptoms resolved.

The new study is a follow-up to the 2019 work and is published in the journal *Pathogens*. Thirty-three participants suffering from neuropsychiatric symptoms ranging from sleep disorders and migraines to depression and anxiety enrolled in the study. Twenty-nine of 33 participants were found to have *Bartonella* infections

based upon serology and enrichment blood culture polymerase chain reaction (PCR) testing. Twenty-four of the 29 *Bartonella*-positive participants (83%) reported the appearance of skin lesions during their illness.

Skin lesions ranged from cutaneous eruptions to red, irregular linear lesions randomly located on various parts of the patient's body. Many of these lesions resembled striae distensae (stretch marks); however, typical risk factors for striae distensae, such as body building activities, obesity, pregnancy, prednisone treatment and other known disease associations, were either infrequently or not reported by study participants.

"This research, a follow-up to our initial case report of Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS), was initiated to further investigate a possible association between neuropsychiatric illness, skin lesions and a bacterial infection of emerging biomedical importance," Breitschwerdt says. "We hope that this research will enable physicians to suspect connections between disparate symptoms involving the nervous system and skin that could be associated with an underlying bacterial cause."

Breitschwerdt is the first and corresponding author of the research, which was supported by the Bartonella/Vector-Borne Diseases Research Fund at NC State's College of Veterinary Medicine. NC State research technician Julie Bradley, postdoctoral researcher Erin Lashnits, and research professor Ricardo Maggi, as well as dermatologist Paul Reicherter of the University of Missouri Kansas City Truman Medical Center, contributed to the work.

Note to editors: An abstract follows.

"Bartonella Associated Cutaneous Lesions (BACL) in People with Neuropsychiatric Symptoms" DOI: 10.3390/pathogens9121023

Authors: Ed Breitschwerdt, Julie Bradley, Ricardo Maggi, Erin Lashnits, North Carolina State University; Paul Reicherter, University of Missouri Kansas City

Published: Online Dec. 7, 2020 in Pathogens

Abstract:

Bartonella species are globally important emerging pathogens that were not known to infect animals or humans in North America prior to the human immunodeficiency virus (HIV) epidemic. Ongoing improvements in diagnostic testing modalities have allowed for the discovery of Bartonella species (spp.) DNA in blood; cerebrospinal fluid; and the skin of patients with cutaneous lesions, fatigue, myalgia, and neurological symptoms. We describe Bartonella spp. test results for participants reporting neuropsychiatric symptoms, the majority of whom reported the concurrent development of cutaneous lesions. Study participants completed a medical history, a risk factor questionnaire, and provided cutaneous lesion photographs. Bartonella spp. serology and Bartonella alpha proteobacteria enrichment blood culture/PCR were assessed. Within a 14-month period, 33 participants enrolled; 29/33 had serological and/or PCR evidence supporting Bartonella spp. infection, of whom 24 reported concurrent cutaneous lesions since neuropsychiatric symptom onset. We conclude that cutaneous lesions were common among people reporting neuropsychiatric symptoms and Bartonella spp. infection or exposure. Additional studies, using sensitive microbiological and imaging techniques, are needed to determine if, or to what extent, Bartonella spp. might contribute to cutaneous lesions and neuropsychiatric symptoms in patients.

https://bit.ly/345odNi

More support for induction at 41 weeks' pregnancy, especially for first time mothers

Growing evidence that pregnant women who go beyond term will benefit from induction of labour at 41 weeks

There is growing evidence that pregnant women who go beyond term, especially first time mothers and their infants, will benefit from induction of labour at 41 weeks, instead of expectant management with subsequent induction of labour at 42 weeks if labour will not start spontaneously. This is clearer now that researchers from Sweden and the Netherlands have appraised results from three previous investigations.

The present study, an individual participant data meta-analysis, is published in the journal *PLOS Medicine*. Most of the researchers are connected to the University of Gothenburg and the University of Amsterdam.

In Sweden and the Netherlands, the risk of a baby dying before, during or shortly after birth ("perinatal death") is generally very low. The same is true of the risk of harm or injury to the baby in

conjunction with the birth. However, these risks -- of perinatal death and morbidity (ill-health, trauma or other injury) alike -- are known to rise somewhat, from a low level, the longer a pregnancy goes on after the 40th week.

The purpose of the meta-analysis was to compare outcomes from induction at 41 and expectant management and if not delivered induction at 42 weeks, by combining individual studies addressing the same question. To date, in some respects, it has been unclear what measures best protect the woman and child.

Three randomized studies of the same question have been published, all since the year 2000: SWEPIS (the SWEdish Post-term Induction Study), covering 2,760 women; a Dutch INDEX study (INDuction or Expectant management) of 1,801 women; and a Turkish study of 600 women.

The Swedish and Dutch studies were able to contribute findings at individual level, and the Turkish study was also included in the aggregate appraisal of perinatal death and the proportion of cesarean deliveries. All the women had reached 41 weeks, were healthy and expecting one baby when they participated in the respective studies.

Of the 4561 women included in the analysis of individual data, 2,281 were assigned for induction at 41 full week. In this group, 80 percent underwent induction. For the others, the delivery started spontaneously.

In the Expectant Management group of 2,280 women, spontaneous delivery start was awaited until 42 weeks when induction was otherwise planned. This has been the routine management practice at most birth centers in Sweden and the Netherlands in uncomplicated pregnancies. In the Expectant Management group, 30 percent of the women needed to be induced, while for the others labor began spontaneously.

In terms of the combination of perinatal death and severe morbidity, 10 (0.4%) were affected in the group induced at 41 weeks and 23 (1.0%) in the 42 week group. The difference between the groups is statistically significant. These results hold for women who deliver for the first time. For women who already gave birth once the number of perinatal deaths and morbidity was too low to demonstrate any effect.

There was no difference in the women's state of health after birth between the groups. The proportions of cesarean sections and of instrumental births, using a ventouse (suction cup) or forceps, were also comparable.

Mårten Alkmark, a doctoral student in obstetrics and gynecology at Sahlgrenska Academy, University of Gothenburg, and senior consultant physician at the University Hospital, is one of the two first authors of the study.

"Being able to combine studies at individual level is a good, robust way of investigating questions where what we're studying is very unusual. It means that we've increased the number of women taking part, thereby also boosting the reliability of the results," Alkmark says.

"Our study shows, in agreement with previous research, that the risks of morbidity and perinatal death are lower when induction is carried out at 41 weeks than when it's done at 42 weeks, while it doesn't increase the risks of impaired health in the mothers."

Esteriek de Miranda, assistant professor of Amsterdam UMC of the University of Amsterdam and one of both last authors: "This reduction in risk was only found for women having their first childbirth, not for women who had given birth already one or more times, earlier induction had no benefit for these women and their babies."

Henrik Hagberg, professor of obstetrics and gynecology at Sahlgrenska Academy at the University of Gothenburg and senior

consultant physician at the Sahlgrenska University Hospital, is one of the co-authors.

"If these results are extrapolated to Swedish conditions, where roughly 20,000 women a year are still pregnant at 41 weeks, one might prevent at least 100 cases a year of severe illness or death in the babies when they're induced at 41 weeks' gestation. The other side of the coin is that a lot of inductions then have to be done. To save one child from severe illness or death, statistically, 175 women have to undergo induction at 41 weeks," Hagberg says.

Judit Keulen, doctoral student of Amsterdam UMC and University of Amsterdam and one of both first authors: "Choosing for expectant management means an overall 99% chance of a good perinatal outcome for all women, for multiparous women choosing expectant management, the chance of a good outcome is not different than after induction of labour."

Ulla-Britt Wennerholm, senior clinical physician and associate professor of obstetrics and gynecology at Sahlgrenska Academy at the University of Gothenburg, is one of the two senior authors.

"Pregnant women whose pregnancies last 41 weeks should be informed about the advantages and disadvantages of induction, and those who then want to be induced should be offered this option," Wennerholm says.

Title: Induction of labour at 41 weeks or expectant management until 42 weeks: A systematic review and an individual participant data meta-analysis of randomized trials

https://bit.ly/37WRPNV

Uniquely human gene may drive numerous cancers

Human-specific connection between advanced carcinomas and a gene called Siglec-XII

Humans are more prone to develop carcinomas compared with our closest evolutionary cousins, the great apes. These cancers begin in the epithelial cells of the skin or the tissue that covers the surface of internal organs and glands, and they include prostate, breast, lung, and colorectal cancers. A new study published in *FASEB BioAdvances* reveals a human-specific connection between advanced carcinomas and a gene called *SIGLEC12*.

Additional studies related to this gene, which has several uniquely human features, and the protein it encodes (called Siglec-XII) could potentially lead to broad-based advances in cancer prognostics, diagnostics, and therapeutics.

"Siglecs are typically expressed in immune cells, and it was surprising to find Siglec-XII on epithelial surfaces. While a mutant form of Siglec-XII is expressed only in about 30% of normal humans, it was found to be present in a high proportion of advanced carcinomas. This could help explain why humans are more prone to aggressive carcinomas, which are rare in chimpanzees," said co-author Nissi Varki, MD, Professor of Pathology at the University of California San Diego School of Medicine.

https://bit.ly/345R5F9

Charles Darwin was right about why insects are losing the ability to fly

Most insects can fly. Yet scores of species have lost that extraordinary ability, particularly on islands.

On the small islands that lie halfway between Antarctica and continents like Australia, almost all the insects have done so.

Flies walk, moths crawl.

"Of course, Charles Darwin knew about this wing loss habit of island insects," says Ph.D. candidate Rachel Leihy, from the Monash University School of Biological Sciences.

"He and the famous botanist Joseph Hooker had a substantial argument about why this happens. Darwin's position was deceptively simple. If you fly, you get blown out to sea. Those left on land to produce the next generation are those most reluctant to fly, and eventually evolution does the rest. Voilà."

But since Hooker expressed his doubt, many other scientists have too.

In short, they have simply said Darwin got it wrong.

Yet almost all of these discussions have ignored the place that is the epitome of flight loss—those 'sub-Antarctic' islands. Lying in the 'roaring forties' and 'furious fifties', they're some of the windiest places on Earth.

"If Darwin really got it wrong, then wind would not in any way explain why so many insects have lost their ability to fly on these islands," said Rachel.

Using a large, new dataset on insects from sub-Antarctic and Arctic islands, Monash University researchers examined every idea proposed to account for flight loss in insects, including Darwin's wind idea.

Reporting today in *Proceedings of the Royal Society B*, they show that Darwin was right for this 'most windy of places'. None of the usual ideas (such as those proposed by Hooker) explain the extent of flight loss in sub-Antarctic insects, but Darwin's idea does. Although in a slightly varied form, in keeping with modern ideas on how flight loss actually evolves.

Windy conditions make insect flight more difficult and energetically costly. Thus, insects stop investing in flight and its expensive underlying machinery (wings, wing muscles) and redirect the resources to reproduction.

"It's remarkable that after 160 years, Darwin's ideas continue to bring insight to ecology," said Rachel, the lead author of the paper.

Professor Steven Chown, also from the School of Biological Sciences, added that the Antarctic region is an extraordinary laboratory in which to resolve some of the world's most enduring mysteries and test some of its most important ideas.

More information: *Wind plays a major but not exclusive role in the prevalence of insect flight loss on remote islands, Proceedings of the Royal Society B, rspb.royalsocietypublishing.or … .1098/rspb.2020.2121*

https://bit.ly/37ZX53c

Can sting rays and electric rays help us map the ocean floor?

Electric rays and sting rays equipped with pingers will be able to map the seabed through natural exploration

Researchers at the RIKEN Center for Biosystems Dynamics Research (BDR) in Japan have completed a feasibility study indicating that electric rays and sting rays equipped with pingers will be able to map the seabed through natural exploration

The ocean is a big place full of natural resources including fossil fuels, minerals, and of course, fish.

The problem is that many of these resources are on the ocean floor in places we have yet to find. Ocean exploration is therefore necessary, and currently automated vehicles, sonar, and satellites are all used with varying advantages and disadvantages. At RIKEN BDR, scientists led by Yo Tanaka are developing a completely different system that relies on the natural swimming behavior of electric rays and sting rays.

"Electric rays and sting rays are benthic animals, meaning that they spend most of their time swimming around the ocean floor in deep places," explains Tanaka. "By combining simple pinger technology and digital cameras with this natural behavior, we think we can use rays to map the ocean floor, and at the same time collect meaningful data about ocean wildlife, biota, and resources."

Additionally, this method could be much more cost effective as Tanaka and his team have already shown that electric rays can use their own electricity to power the small pingers.

A pinger is a device that emits and ultrasonic sound. When a pinger's sound is picked up by several receivers, the position of the receivers and the time when the sound is detected can be used to calculate the position of the pinger.

By placing cameras on rays and linking the timing of the recorded video to the timing and locations determined by the pingers, the researchers believe they can create accurate maps of the ocean floor. In their proof-of-concept study, the team conducted two experiments that showed that their idea to use rays is feasible.

The first study took place in a large water tank. A setup with cameras in three planes--front, side, and top--verified that both types of ray swam near the bottom of the tank. The images taken by the camera allowed 3-D reconstruction of movements over time. They also verified that a camera could be attached the rays to record video of their exploration. With these positive results, the team was ready to test their system out in the real world--an area off the coast of Okinawa in Japan. As this was a proof-of-concept experiment, they chose an area with a relatively flat seabed.

They attached pingers to both sting rays and electric rays and lowered them into the ocean from a large boat along with four ultrasound receivers. The depth of the ocean was about 20 m (60 ft) and the rays were allowed to swim about 40 m (120 ft) out from the boat.

The researchers recorded the pinger-derived positions as the rays swam near the boat for about two hours. Afterward, they compared the data with a seabed map of the area that already exists and confirmed that the rays' positions were within about 10 cm of those in the public map. Similar results from both types of ray were important because rays are seasonal animals

"In our ocean experiment, in addition to the pinger positioning, we were able to confirm that electric rays actually move around the seabed," says Tanaka. "In the near future we will test the system for long-term monitoring." Long-term monitoring will require pingers that the electric rays can self-charge as well as wearable battery packs for the sting rays. The next test will also monitor an area with a more varied seabed with complex geometry.

https://bit.ly/3oKMSOX

Breakthrough forensic approach to help crack down on the sale of fake drugs

Fake medicines are one of the biggest health problems in the world today.

The International Criminal Police Organization (INTERPOL) saw a rise in fake medical products related to the outbreak of COVID-19, including counterfeit facemasks, substandard hand sanitisers and unauthorized antiviral medication, when it led an international operation in March 2020.

During the operation 121 people were arrested and more than 2,500 websites were taken offline.

Dr. Matteo Gallidabino, an expert in forensic science at Northumbria University, has worked with Professor Francesco Saverio Romolo, a world-leading forensic scientist from the University of Bergamo, in Italy, to develop a new method of testing that quickly and accurately characterizes illegal pharmaceutical products, assessing their risk to human health, while also speeding up the exchange of data between laboratories around the world.

Their method is unique and is based on nuclear analysis techniques—the use of neutrons and protons—to analyze illegal medicines. They are working with the support of the International Atomic Energy Agency (IAEA), the world's central intergovernmental forum for scientific and technical co-operation in the nuclear field, seeking to promote the safe, secure, and peaceful use of nuclear technologies.

"Illegal medicines can contain toxic chemical substances and need comprehensive analytical approaches," said Dr. Gallidabino. "Full analysis of these medicines at an elemental level provides the most comprehensive technique we have to date. It allows both early warning whenever there is a serious threat to public health, as well

as providing effective and easily sharable information about the manufacturing and the supply chain of illegal products."

Professor Romolo, who has more than 25 years of experience in crime scene investigation and chemical analysis related to major criminal cases around the world, says that it is still challenging today to exchange data between different forensic laboratories because the analytical techniques used are not 'as standard' on a global scale.

"International collaborations between countries are difficult and, in a lot of cases, between laboratories in the same country," he said. "In policing this is what is known as 'linkage blindness' – where police departments fail to share information that connects criminal activities, because of a lack of cooperation or information-sharing technology. "To effectively protect public health and to allow criminal investigation, we cannot keep facing global issues with local approaches.

"This new method is invaluable for intelligence, investigation and criminal prosecution as information can be shared quickly and accurately among laboratories around the world."

Selling fake medicines is big criminal business, given the products' high profit margins and the low risks of detection and prosecution, weak penalties, and the ease in which buyers can be deceived into believing that the counterfeit products are genuine.

Dr. Gallidabino and Professor Romolo tested their new technique specifically on Viagra, which is the most counterfeit medicine in Europe and the U.S.. However, it could be applied to a large range of different products, not only medicines, but also supplements and foods, as well as drugs of abuse such as cannabis, cocaine and heroin. "This is an exciting alternative to current testing approaches," said Dr. Gallidabino. "We can protect public health by drilling down exactly what is contained in potential harmful and even life-threatening illegal medicines."

"As this method can be applied to drugs of abuse, it can be used to establish associations between drugs hauls around the world and help policing, especially when dealing with large criminal organizations."

More information: *Francesco Saverio Romolo et al. Ion beam analysis (IBA) and instrumental neutron activation analysis (INAA) for forensic characterisation of authentic Viagra® and of sildenafil-based illegal products, Talanta (2020). DOI: 10.1016/j.talanta.2020.121829*

https://bit.ly/37UrK25

Natural antibiotics produced in wounds increase sleep and survival after injury

They signal across tissues from the site of injury to the brain, sending a message to increase sleep and raise the chances for surviving the injury.

The results have been published in the journal *Current Biology*.

Sleep is the best medicine, as the old saying goes. Indeed, studies showed that longer sleep leads to a better recovery. It is no surprise that our brains respond to an injury by extending our sleep. But how does that happen? How does the brain know about the injury? Is there some kind of long-range message sent to the brain from the wound?

A team of scientist focused on these questions by looking at injury and sleep in worms. "C. elegans worm is the simplest animal which we could look at to study sleep. It is a model that allows for a wide range of molecular biology techniques to explore fundamental biological processes in detail" explains Prof. Bringmann, research group leader at the Biotechnology Center (BIOTEC) of the TU Dresden and guest group leader at Max Planck Institute for Biophysical Chemistry.

A team led by Prof. Bringmann started by looking for genes responsible for prolonging sleep in worms. They conducted a large-scale genetic screen and analyzed over 4,500 different genetic mutations. One of the genes they found caught their particular

attention. Boosting activity of that gene led to an enormous increase in production of antimicrobial peptides (AMPs). The AMPs are natural antibiotics that the body produces inside the wound to fight off the pathogens locally.

To find out the connection between the antimicrobial peptides and sleep signaling, the scientists from Dresden worked with immunologists, Dr. Nathalie Pujol and Dr. Jonathan Ewbank from Centre d'Immunologie de Marseille-Luminy (CIML) in France. Together, the team has manipulated gene expression of worms. They switched off production of the natural antibiotics and looked at what happens to the injured worms. What sounds like flipping a switch was in reality not an easy task at all. It turned out that antimicrobial peptides are highly redundant. The scientists found that a total of 19 different genes responsible for producing AMPs had to be simultaneously switched off to observe a striking difference. "We have seen that the worms which did not produce antimicrobial peptides had much less sleep following an injury" explains Prof. Bringmann. "Normally, worms survive injuries quite well. However, we observed that sleep loss increased the number of worms that did not survive a seemingly non-threatening injury" adds Prof. Bringmann.

The researchers could show that once released from the skin wound, the AMPs act as a messenger and activate receptors in the brain. This activation works as a switch and further prompts sleep neurons to increase sleep. "AMPs have long been known to act locally, but our work suggested that they also act as long-range messenger molecules to signal need for sleep from wounds to the nervous system" says Prof. Bringmann.

These results further strengthen the role of sleep in recovery from injuries. "Since sleep occurs in virtually all animals, our results hint at how sleep could be crucial to recover and survive an injury not only for C. elegans worms but also for other animals and possibly even humans" concludes Prof. Bringmann. His group is funded by the European Research Council (ERC) Starting Grant SLEEPCONTROL.

Publication: *Marina P. Sinner, Florentin Masurat, Jonathan J. Ewbank, Nathalie Pujol, Henrik Bringmann: Innate immunity promotes sleep through epidermal antimicrobial peptides. Current Biology (November 2020) Doi: 10.1016/j.cub.2020.10.076*
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https://wb.md/3oK7WoP

Man With Quadriplegia Controls Prosthetic Arms With His Mind

A man with quadriplegia has been able to simultaneously control a pair of prosthetic arms with only his thoughts by virtue of electrodes implanted in both sides of his brain and a brain-computer interface.

Megan Brooks

Until now, brain-computer interface research for quadriplegia has largely focused on only one arm that was controlled from only one side of the brain, Gabriela Cantarero, PhD, assistant professor of physical medicine and rehabilitation, Johns Hopkins University School of Medicine, Baltimore, Maryland, told *Medscape Medical News.*

Patient "Buz" Chmielewski is able to control his prosthetic arms using only his thoughts.

"We're using two sides of the brain to control two limbs at the same time," Cantarero said.

The patient, Robert "Buz" Chmielewski, age 49, has been paralyzed with only minimal movement in his arms and hands since a surfing accident when he was a teenager.

In January 2019, surgeons implanted electrodes into the primary motor cortex and the primary somatosensory cortex in the right and left hemispheres of the brain in a 10-hour operation.

The goal was to improve sensation in his hands and enable the patient to mentally operate two arm prostheses.

Now, almost 2 years later, and with lots of practice, Chmielewski has reached an important milestone, the Johns Hopkins team reports. He can now use both of his robotic appendages to perform simple tasks such as feeding himself.

"A Clear Step Forward"

"Being able to control two robotic arms performing a basic activity of daily living — in this case, cutting a pastry and bringing it to the mouth using signals detected from both sides of the brain via implanted electrodes — is a clear step forward to achieve more complex task control directly fed from the brain," Pablo Celnik, MD, professor and director of physical medicine and rehabilitation at the Johns Hopkins University School of Medicine, said in a news release.

The team has released a video showing Chmielewski cutting food with his left hand and feeding himself with the right, at times simultaneously controlling both robotic arms.

The technology uses a system of devices that automates a portion of the robotic control with artificial intelligence.

"Our goal is to make activities such as eating easy to accomplish by having the robot do one part of the work and leaving the user in charge of the details: which food to eat, where to cut, how big the cut piece should be, and so on," said David Handelman, PhD, a senior roboticist at Johns Hopkins University's Applied Physics Laboratory, in the release.

"By combining brain-computer interface signals with robotics and artificial intelligence, we allow the user to focus on the parts of the task that matter most," he added.

The research team says next steps include expanding the number and types of activities of daily living that can be performed using this human-machine interface. Another is to provide the user with additional sensory feedback as tasks are conducted.

https://bit.ly/2LmI6ZC

Tomatoes offer affordable source of Parkinson's disease drug

Scientists have produced a tomato enriched in the Parkinson's disease drug L-DOPA in what could become a new, affordable source of one of the world's essential medicines.

The development of the genetically modified (GM) tomato has implications for developing nations where access to pharmaceutical drugs is restricted.

This novel use of tomato plants as a natural source of L-DOPA also offers benefits for people who suffer adverse effects - including nausea and behavioral complications - of chemically synthesised L-DOPA .

Tomato fruit enriched in L-DOPA **Phil Robinson**

Tomato - was chosen as a widely cultivated crop that can be used for scaled up production and potentially offering a standardised and controlled natural source of L-DOPA .

The John Innes Centre led team modified the tomato fruit by introducing a gene responsible for the synthesis of L-DOPA in beetroot where it functions in the production of the pigments betalains.

L-DOPA is produced from tyrosine, an amino acid found in many foods. The research team inserted a gene encoding a tyrosinase, an enzyme that uses tyrosine to build molecules such as L-DOPA . This elevated the level of L-DOPA specifically in the fruit part of

the plant and led to higher yields than those associated with L-DOPA production in the whole plant.

The levels achieved in the tomato fruit - 150mg of L-DOPA per kg of tomatoes - were comparable those observed in other L-DOPA accumulating plants - without some of the known drawbacks that have hampered plant metabolic production of the drug previously.

The aim now is to create a production pipeline where L-DOPA is extracted from the tomatoes and purified into the pharmaceutical product.

Professor Cathie Martin (FRS), corresponding author of the study explains: "The idea is that you can grow tomatoes with relatively little infrastructure. As GMOs (genetically modified organisms) you could grow them in screen houses, controlled environments with very narrow meshes, so you would not have pollen escape through insects.

"Then you could scale up at relatively low cost. A local industry could prepare L-DOPA from tomatoes because it's soluble and you can do extractions. Then you could make a purified product relatively low tech which could be dispensed locally."

Parkinson's disease is a growing problem in developing countries where many people cannot afford the daily $2 price of synthetic L-DOPA . L-DOPA is an amino acid precursor of the neuro-chemical dopamine and is used to compensate for the depleted supply of dopamine in Parkinson's disease patients.

Also known as Levodopa, L-DOPA has been the gold standard therapy for Parkinson's disease since its establishment as a drug in 1967. It is one of the essential medicines declared by the World Health Organisation (WHO) and its market value is in the hundreds of billions of dollars. The most common form of the drug is produced by chemical synthesis, but natural sources are also available. Only a few plants have been reported to contain measurable quantities of the molecule, mainly in seeds.

The most studied is the velvet bean, Mucuna pruriens, which contains up to 10% L-DOPA in its seeds. But this is problematic because the plant is covered in urticating hairs that contain mucunian that can cause irritation and allergic reactions in field workers who harvest the crop. The beans themselves cause elevated levels of tryptamines that can cause hallucinations in Parkinsons disease patients.

"We have demonstrated that the use of the tyrosinase-expressing tomatoes as a source of L-DOPA is possible. It's a further demonstration of tomato as a strong option for synthetic biology. Additionally, there were surprising beneficial effects including improvement in shelf-life and raised levels of amino-acids that we can investigate," says first author Dr Dario Breitel.

The study: Metabolic engineering of tomato fruit enriched in L-DOPA appears in the journal, Metabolic Engineering.

https://bit.ly/2KmZDAq

A surgeon's birthday may be a dicey day for older patients

Study shows higher mortality rates for those needing emergency procedures

Older people who undergo emergency surgeries on their operating surgeon's birthday may be more likely to die within a month than patients who go through similar procedures on other days, a new UCLA-led study suggests.

The study, published today in the peer-reviewed medical journal *BMJ*, shows that 30-day mortality rates are approximately 23% higher for patients 65 and older who are treated on a surgeon's birthday. While the authors suspect that surgeons may be more distracted on their birthdays than other days, they said more research is needed to explain why this may happen.

There have long been questions about how the work environment impacts a surgeon's performance, said the study's senior author, Dr.

Yusuke Tsugawa, an assistant professor of medicine in the division of general internal medicine and health services research at the David Geffen School of Medicine at UCLA. But relevant data has been difficult to collect, so the researchers narrowed their focus to surgeons' birthdays in order to begin exploring this question.

"Our study is the first to show the association between a surgeon's birthday and patient mortality, but further research is needed before we make a conclusion that birthdays indeed have a meaningful impact on surgeons' performance," Tsugawa said. "At this point, given that evidence is still limited, I don't think patients need to avoid a surgical procedure on the surgeon's birthday."

The researchers measured postoperative 30-day mortality for Medicare beneficiaries between the ages of 65 and 99 who underwent one of 17 emergency surgical procedures from 2011 to 2014. They analyzed nearly 981,000 surgeries performed by approximately 48,000 surgeons. Of those, 2,064 procedures, or 0.2 %, were performed on the surgeons' birthdays.

The researchers adjusted for patient characteristics and the surgeon who performed the procedure, effectively comparing their performance on their birthday with other days. They found a 6.9% mortality rate among patients who underwent surgeries on surgeons' birthdays, compared with a 5.6% rate among those who underwent procedures on other days. This gap represents a 23% difference in mortality rates between the two groups.

The researchers note that there are some limitations to their findings. For instance, they were unable to understand the precise mechanisms that led to higher mortality among the patients in question and so could not evaluate the causal link between surgeons' birthdays and patient deaths. In addition, they focused on elderly patients who underwent one of the common emergency procedures, so these findings may not apply to younger people or to elective procedures.

In addition to Tsugawa, who is also an assistant professor of health policy and management at the UCLA Fielding School of Public Health, study co-authors were? Hirotaka Kato of UCLA and Keio University in Japan, and Anupam Jena of Harvard Medical School.

Kato was funded by a grant from the Japan Society for the Promotion of Science, and Jena was funded by the National Institutes of Health.

https://bit.ly/3nhIXsI

Shocking adaptations discovered in electric fish of Brazil's Amazon

Electric fish are able to interact with each other over longer distances than known possible in a way similar to AM radio.

by Jesse Jenkins, New Jersey Institute of Technology

A study of weakly electric fishes from a remote area of the Brazilian Amazon Basin has not only offered a unique window into how an incredibly rare fish has adapted to life in caves over tens of thousands of years, it has also revealed for the first time that electric fish are able to interact with each other over longer distances than known possible in a way similar to AM radio.

In findings published in the journal *Frontiers*, researchers have shown how a cave-adapted glass knifefish species of roughly 300 living members (Eigenmannia vicentespelea) has evolved from surface-dwelling relatives (Eigenmannia trilineata) that still live just outside their cave door—by sacrificing their eyes and pigmentation, but gaining slightly more powerful electric organs that enhance the way they sense prey and communicate in absolute darkness.

The study, which analyzed the fishes' electric-based communication and behavior, has detailed the discovery that weakly electric fishes tap into a special channel for long-distance messaging via changes in the amplitude of electrical signals sent to one another. Researchers have adapted Einstein's famous quote on the theory of quantum entanglement—"spooky interaction at a distance"—to describe how the weakly electric fishes perceive these social

messages, altering each other's behavior at distances up to several meters apart.

Of the nearly 80 species of cavefish known today to have evolved from surface-dwelling fish, all have developed sensory enhancements of some kind for enduring cave life, commonly adapting over millions of years while losing sensory organs they no longer need in the process.

However, biologists have questioned how weakly electric fishes, which use their electrical senses for navigating the dark and murky conditions of the Amazon River, might also adapt—either evolving heightened electric senses to see and communicate in absolute darkness, or by powering down their electric fields to save on energetic cost when most caves have few food resources.

"One of the big questions about fish that successfully adapt to living in caves is how they adapt to life without light," said Eric Fortune, lead author of the study and biologist at New Jersey Institute of Technology (NJIT). "My colleagues were split between two groups ... one group that predicted that the electric fields of the cavefish would be weaker due to limited food supplies, and another that bet that the electric fields would be stronger, allowing the fish to use their electric signals to see and talk more clearly in the complete darkness of the cave.

"It seems that using their electric sense to detect prey and communicate with each other is quite valuable to these animals; they have greater electric field strengths. Interestingly, our analysis of their electric fields and movement shows that they can communicate at distances of meters, which is quite a long way for fish that are around 10cm in length."

"Nearly all research of cavefish species until now has been limited to behavioral experiments in labs, and that is why this study is special," said Daphne Soares, NJIT associate professor of biology and co-author on the study. "This is the first time we've been able to continuously monitor the behavior of any cavefish in their natural setting over days. We've gained great insight into their nervous system and specialized adaptations for cave life, but it's just as exciting to learn how sociable and chatty they are with each other ... it's like middle school."

Spooky Interactions & Shocking Adaptations

For the investigation, NJIT and Johns Hopkins researchers teamed with biologist Maria Elina Bichuette from the Federal University of São Carlos, who began studying the two groups of fish nearly two decades ago in the remote São Vicente II Cave system of Central Brazil's Upper Tocantins river basin.

Over several days, the team applied a customized electric fish-tracking technique involving placing electrode grids throughout the fishes' water habitats to record and measure the electric fields generated by each fish, allowing the team to analyze the fishes' movements and electricity-based social interactions.

The researchers were able to track more than 1,000 electrical-based social interactions over 20-minute-long recordings taken from both surface and cavefish populations, discovering hundreds of specialized long-distance exchanges.

Contrast between two distantly-related species of transparent knifefish neighboring each other in Central Brazil's Upper Tocantins river basin, state of Goiás. The surface-dwelling fish Eigenmannia trilineata (left) inhabits the Rio da Lapa at the mouth of the São Vicente II Cave where the blind cavefish Eigenmannia vicentespelea (right) has adapted to life without light over tens of thousands of years. **Credit: NJIT**

"When I began studying these fishes, we could watch behavior associated with these fishes' unique and specialized morphology, but in this project, it was fascinating to apply these new technical

approaches to reveal just how complex and refined their communication could be," said Bichuette.

"Basically, our evidence shows that the fishes are talking to each other at distance through electricity using a secret hidden channel, amplitude modulations that emerge through the summation of their electric signals. It is not unlike how an AM radio works, which relies on amplitude modulations of a radio signal." said Fortune.

The recordings also showed that strengths of electric discharges in the cavefish were about 1.5 times greater than those of surface fish despite coming at a cost of up to a quarter of their overall energy budget. The team conducted CT scans of both species, showing that the cavefish also possess relatively larger electric organs than their stream-mates, which could explain the source of the cavefishes' extra electrical power.

Another consequence of trading their eyes and surface life for heightened electrosensory perception is that the cavefish were more social and territorial at all hours. Unlike their freely-foraging surface relatives that sleep during the day and forage at night, the cavefish lacked a day-night cycle.

For now, the discovery of the fishes' AM radio-style distant interactions is noted by Fortune as the first of its kind reported among electric cavefish, though he says similar phenomena is now being reported in some other species as well, recently by researchers in Germany who have observed a form of long-distance electrical communication among a group of fish known as Apteronotus. Fortune says the finding could have implications for the field of neurobiology, where weakly electric fish is a unique and powerful model for exploring the nature of the brain-body connection in other animals including humans.

"Electric fish are great systems for understanding the neural basis of behavior, so we have been studying their brains for decades," said Fortune. "These new data are forcing a reexamination of the neural circuits used for the control of behavior of these fishes."

More information: *Eric S. Fortune et al, Spooky Interaction at a Distance in Cave and Surface Dwelling Electric Fishes, Frontiers in Integrative Neuroscience (2020). DOI: 10.3389/fnint.2020.561524*

https://bit.ly/3oJTKwb

Deadly, emergent cancer becoming endemic in Tasmanian devils, reducing extinction threat

An emergent transmissible cancer that once threatened Tasmanian devils with extinction appears to be transitioning to a state of endemism, researchers report.

The findings of the study, which used an epidemiological phylodynamic approach to reveal the pattern of emergence and spread of the disease, bring hope for the continued persistence of the iconic species. First discovered in 1996, Tasmanian devil facial tumor disease (DFTD) - a fatal, transmissible form of facial cancer - is found across 95% of the animal's geographic range and is estimated to be responsible for a species-wide population decline of 80%. Emerging infectious diseases like DFTD are among the primary contributors to species endangerment and have led to species extinction.

Recently, phylodynamics has become an important tool for characterizing the epidemiological parameters of rapidly evolving, emergent pathogens and has become notable in its application to understanding novel human viruses, including SARS-Cov-2.

However, its application to nonviral pathogens has been limited by the challenges associated with their larger genome sizes. DFTD, for example, has a genome thousands of times larger than any virus.

Despite initial predictions that DFTD would lead to the extinction of the species, Tasmanian devil populations persist - and may even be recovering - in long-diseased areas.

To better understand this discrepancy, Austin Patton and colleagues applied phylodynamics to characterize the epidemiological history of DFTD. Patton et al. discovered that DFTD is becoming endemic in Tasmanian devils and is exhibiting a pattern of transmission rate decline.

The findings suggest that, if left to evolve naturally, DFTD may go extinct or even coexist in devil populations; either way, devil extinction is unlikely, they say. What's more, the study demonstrates that phylodynamic studies need not be limited to viruses and can be applied to a wide range of other emergent pathogens across species.

https://bit.ly/2IPUOzm

Distinct Microbiome and Metabolites Linked with Depression

Gastrointestinal tracts of people with major depressive disorder harbor a signature composition of viruses, bacteria, and their metabolic products

Rachael Moeller Gorman

The gastrointestinal tracts of people with major depressive disorder harbor a signature composition of viruses, bacteria, and their metabolic products, according to the most comprehensive genomic and metabolomic analysis in depression to date.

The human gut microbiome is a world in miniature, populated by a chatty community of bacteria, viruses, fungi, and protozoa nestled within various gastrointestinal niches.

Over the past decade, researchers have linked disturbances within this complicated microbial society to a variety of diseases.

Major depressive disorder (MDD) is one such condition, but the studies have been small and the findings imprecise.

A study published December 2 in *Science Advances* changes all that with its vivid description of a distinct microbiome associated with major depressive disorder, as well as the profile of molecules these organisms produce.

The researchers were able to use this microbial "fingerprint" to distinguish between individuals with MDD and healthy controls, solely on the composition of a few microbes and compounds in their fecal matter.

"What this paper does is bring the complexity of the ecology of the microbiome into focus," says neuroscientist John Cryan at APC Microbiome Ireland and University College Cork who was not part of the study team. "It's a welcome addition to the field."

"The strength of the paper is this dual approach to both the metagenomics to identify the key taxa as well as the metabolites, because in the end we need to link whatever the biosignature of the taxa are to the host," McMaster University's Jane Foster, who was not part of the study, tells *The Scientist*.

She adds that it's one of the first studies to conduct metagenomics and metabolomics in the same sample for depression.

Microbiome researchers studying MDD have been using an inexact technique called 16S ribosomal RNA sequencing, which can identify bacteria only down to the genus level within a batch of microorganisms, and it excludes viruses.

But psychiatrist Shaohua Hu at Zhejiang University School of Medicine in China and his group wanted a more precise picture of the organisms present, so they gathered fecal samples from 236 people, half of whom had been diagnosed with MDD and were unmedicated, and half who were healthy.

They sequenced the total genomic DNA of all the bacteria and viruses in the samples, and then used statistical programs to analyze the differences and similarities between people with MDD and healthy controls.

They found that 18 bacterial species were more abundant in people with MDD (mainly belonging to the genus Bacteroides) and 29

were less common (primarily the genera Blautia and Eubacterium) compared to healthy controls.

Hu and his team also found three bacteriophages (viruses that infect bacteria) whose levels were different in MDD versus healthy controls, the first time the virome has been studied in MDD.

Sequencing entire microbial genomes allowed the team to distinguish between organisms that are genetically similar, but functionally very unique, writes University of Melbourne, Australia, researcher Carra Simpson in an email.

"Compared to the commonly employed marker gene sequencing approaches, [the authors] have greater resolution to distinguish these species and within a comparatively large sample size." This helps to "elucidate the functional implications of bacterial alterations on the host."

To determine the effect of these changes, Hu and the group analyzed the so-called "functional readout"—the molecules the microorganisms produce—of the entire gut microbiome using gas chromatography-mass spectrometry (GC-MS).

It turns out that MDD patients harbored significantly more of 16 metabolites and less of 34 compounds than did healthy controls; most of these molecules were involved in amino acid metabolism.

The three most important pathways were related to gamma-aminobutyric acid (GABA) metabolism, phenylalanine metabolism, and tryptophan metabolism. Hu's team then created a biomarker panel consisting of two species of bacteria, two types of bacteriophage viruses, and two different metabolites.

In a separate group of 75 subjects (half with MDD, half healthy controls), the biomarker panel was able to accurately pick out those with depression around 90 percent of the time.

Possible microbial effects on depression—and vice versa

The researchers point out that GABA is a neurotransmitter in the brain, but it's also made by gut microbes; fecal levels of GABA and certain of its metabolites were decreased in the MDD patients, and the team also found that GABA-related microbial genes were altered in MDD patients, suggesting that microbes modulate GABA levels.

Hu and his team hypothesize that this may dysregulate the function of GABA in the brain, and could lead to depressive symptoms.

In addition, the scientists hypothesize that perhaps the increase in Bacteroides bacteria, which induce cytokine production, could increase inflammation, a condition that has been linked to MDD.

Also, decreased Blautia, which has been shown to have anti-inflammatory effects, could contribute to MDD.

Other studies have also found that when researchers transplant the entire microbiota of a person with MDD into a germ-free rat, the rat starts to behave depressed.

These are speculative assertions, and Hu says this one cross-sectional study can't determine causality, and rather, "I think it's a bi-directional axis.

The depressed symptoms can influence our diet behavior, so it can influence our gut characteristics and composition, and also on the other side, our bacteria can produce some special metabolites and have a special pathway that can influence our brain function."

"This sets the scene for a lot more work to validate whether any of these pathways are actually causally related to depression," says Cryan, who receives research funding from Dupont Nutrition, Cremo SA, and Nutricia Danone.

"There's a whole emerging field in nutritional psychiatry right now. Can we target the microbiome through diet, could we alleviate some of the effects of depression?"

J. Yang et al., "Landscapes of bacterial and metabolic signatures and their interaction in major depressive disorders," Science Advances, 6:eaba8555, 2020.

https://bit.ly/34alpys

Diet modifications - including more wine and cheese - may help reduce cognitive decline

The foods we eat may have a direct impact on our cognitive acuity in our later years.

Ames, Iowa - This is the key finding of an Iowa State University research study spotlighted in an article published in the November 2020 issue of the *Journal of Alzheimer's Disease*.

The study was spearheaded by principal investigator, Auriel Willette, an assistant professor in Food Science and Human Nutrition, and Brandon Klinedinst, a Neuroscience PhD candidate working in the Food Science and Human Nutrition department at Iowa State. The study is a first-of-its-kind large scale analysis that connects specific foods to later-in-life cognitive acuity.

Willette, Klinedinst and their team analyzed data collected from 1,787 aging adults (from 46 to 77 years of age, at the completion of the study) in the United Kingdom through the UK Biobank, a large-scale biomedical database and research resource containing in-depth genetic and health information from half-a-million UK participants. The database is globally accessible to approved researchers undertaking vital research into the world's most common and life-threatening diseases.

Participants completed a Fluid Intelligence Test (FIT) as part of touchscreen questionnaire at baseline (compiled between 2006 and 2010) and then in two follow-up assessments (conducted from 2012 through 2013 and again between 2015 and 2016). The FIT analysis provides an in-time snapshot of an individual's ability to "think on the fly."

Participants also answered questions about their food and alcohol consumption at baseline and through two follow-up assessments. The Food Frequency Questionnaire asked participants about their intake of fresh fruit, dried fruit, raw vegetables and salad, cooked vegetables, oily fish, lean fish, processed meat, poultry, beef, lamb, pork, cheese, bread, cereal, tea and coffee, beer and cider, red wine, white wine and champaign and liquor.

Here are four of the most significant findings from the study:

1. ***Cheese, by far, was shown to be the most protective food against age-related cognitive problems, even late into life;***
2. ***The daily consumption of alcohol, particularly red wine, was related to improvements in cognitive function;***
3. ***Weekly consumption of lamb, but not other red meats, was shown to improve long-term cognitive prowess; and***
4. ***Excessive consumption of salt is bad, but only individuals already at risk for Alzheimer's Disease may need to watch their intake to avoid cognitive problems over time.***

"I was pleasantly surprised that our results suggest that responsibly eating cheese and drinking red wine daily are not just good for helping us cope with our current COVID-19 pandemic, but perhaps also dealing with an increasingly complex world that never seems to slow down," Willette said. "While we took into account whether this was just due to what well-off people eat and drink, randomized clinical trials are needed to determine if making easy changes in our diet could help our brains in significant ways."

Klinedinst added, "Depending on the genetic factors you carry, some individuals seem to be more protected from the effects of Alzheimers, while other seem to be at greater risk. That said, I believe the right food choices can prevent the disease and cognitive decline altogether. Perhaps the silver bullet we're looking for is upgrading how we eat. Knowing what that entails contributes to a better understanding of Alzheimer's and putting this disease in a reverse trajectory."

Willette and Klinedinst acknowledge the valuable contributions of the other members of the research team: Scott Le, Colleen Pappas, Nathan Hoth, Amy Pollpeter and Qian Wang in the Iowa State department of Food Science and Human Nutrition; Brittany Larsen, Neuroscience graduate program at Iowa State; Yueying Wang and Li Wang, department of Statistics at Iowa State; Shan Yu, department of Statistics, University of Virginia; Karin

Allenspach, department of Veterinary Clinical Sciences at Iowa State; Jonathan Mochel, department of Biomedical Sciences at Iowa State; and David Bennett, Rush Alzheimer's Disease Center, Rush Medical Center, Rush University.

https://bit.ly/3qXv0Tc

Animal behaviour: Cognitive performance of four-months-old ravens may parallel adult apes

By four months cognitive performance of ravens in experimental tasks may be similar to those of adult great apes

By four months of age the cognitive performance of ravens in experimental tasks testing their understanding of the physical world and how they interact with other ravens may be similar to those of adult great apes, according to a study published in *Scientific Reports*.

Simone Pika and colleagues tested the cognitive skills of eight hand-raised ravens at four, eight, 12 and 16 months of age using a series of tests. The skills the authors investigated included spatial memory, object permanence - understanding that an object still exists when it is out of sight - understanding relative numbers and addition, and the ability to communicate with and learn from a human experimenter.

The authors found that the cognitive performance of ravens was similar from four to 16 months of age, suggesting that the speed at which the ravens' cognitive skills develop is relatively rapid and near-to-complete by four months of age. At this age ravens become more and more independent from their parents and start to discover their ecological and social environments. Although task performance varied between individuals, ravens generally performed best in tasks testing addition and understanding of relative numbers and worst in tasks testing spatial memory.

Comparing the cognitive performance of the ravens with those of 106 chimpanzees and 32 orang-utans who completed similar tasks in a previous study, the authors found that with the exception of spatial memory, the cognitive performance of the ravens was very similar to those of orang-utans and chimpanzees.

The findings provide evidence that ravens, similarly to great apes, may have evolved general, sophisticated cognitive skills. The authors propose that ravens developed these skills in response to living in a constantly changing environment where survival and reproduction are reliant on cooperation and alliances between ravens. However, the authors caution that the performance of the ravens studied may not be representative of the species in general.

Ravens parallel great apes in physical and social cognitive skills
DOI: 10.1038/s41598-020-77060-8

https://bit.ly/3nc03YZ

Melatonin: finally, a supplement that actually boosts memory

Melatonin and its metabolites promote the formation of long-term memories in mice and protect against cognitive decline

Researchers at Tokyo Medical and Dental University (TMDU) in Japan show that melatonin and its metabolites promote the formation of long-term memories in mice and protect against cognitive decline.

Chiba, Japan -- Walk down the supplement aisle in your local drugstore and you'll find fish oil, ginkgo, vitamin E, and ginseng, all touted as memory boosters that can help you avoid cognitive decline. You'll also find melatonin, which is sold primarily in the United States as a sleep supplement. It now looks like melatonin marketers might have to do a rethink. In a new study, researchers led by Atsuhiko Hattori at Tokyo Medical and Dental University (TMDU) in Japan have shown that melatonin and two of its metabolites help memories stick around in the brain and can shield mice, and potentially people, from cognitive decline.

One of the easiest ways to test memory in mice is to rely on their natural tendency to examine unfamiliar objects. Given a choice,

they'll spend more time checking out unfamiliar objects than familiar ones. The trick is that for something to be familiar, it has to be remembered. Like in people, cognitive decline in mice manifests as poor memory, and when tested on this novel object recognition task, they behave as if both objects are new.

The group of researchers at TMDU were curious about melatonin's metabolites, the molecules that melatonin is broken down into after entering the body. "We know that melatonin is converted into N1-acetyl-N2-formyl-5-methoxykynuramine (AFMK) and N1-acetyl-5-methoxykynuramine (AMK) in the brain," explains Hattori, "and we suspected that they might promote cognition." To test their hypothesis, the researchers familiarized mice to objects and gave them doses of melatonin and the two metabolites 1 hour later. Then, they tested their memory the next day. They found that memory improved after treatment, and that AMK was the most effective. All three accumulated in the hippocampal region of the brain, a region important for turning experiences into memories.

For young mice, exposure to an object three times in a day is enough for it to be remembered the next day on the novel object recognition task. In contrast, older mice behave as if both objects are new and unfamiliar, a sign of cognitive decline. However, one dose of AMK 15 min after a single exposure to an object, and older mice were able to remember the objects up to 4 days later.

Lastly, the researchers found that long-term memory formation could not be enhanced after blocking melatonin from being converted into AMK in the brain. "We have shown that melatonin's metabolite AMK can facilitate memory formation in all ages of mice," says Hattori. "Its effect on older mice is particularly encouraging and we are hopeful that future studies will show similar effects in older people. If this happens, AMK therapy could eventually be used to reduce the severity of Mild Cognitive Impairment and its potential conversion to Alzheimer's disease."

The article, "The melatonin metabolite N1-acetyl-5-methoxykynuramine facilitates long-term object memory in young and aging mice," was published in Journal of Pineal Research at DOI: https://doi.org/10.1111/jpi.12703.

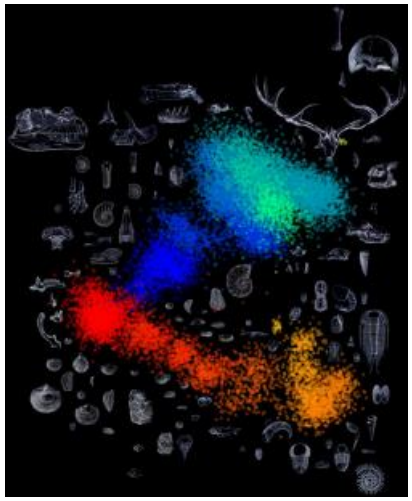
https://bit.ly/3a8SD55

Artificial intelligence finds surprising patterns in Earth's biological mass extinctions

The idea that mass extinctions allow many new types of species to evolve is a central concept in evolution, but a new study using artificial intelligence to examine the fossil record finds this is rarely true, and there must be another explanation

Charles Darwin's landmark opus, *On the Origin of the Species*, ends with a beautiful summary of his theory of evolution, "There is a grandeur in this view of life, with its several powers, having been originally breathed into a few forms or into one; and that, whilst this planet has gone cycling on according to the fixed law of gravity, from so simple a beginning endless forms most beautiful and most wonderful have been, and are being, evolved." In fact, scientists now know that most species that have ever existed are extinct. This extinction of species has on the whole been roughly balanced by the origination of new ones over Earth's history, with a few major temporary imbalances scientists call mass extinction events. Scientists have long believed that mass extinctions create productive periods of species evolution, or "radiations," a model called "creative destruction." A new study led by scientists affiliated with the Earth-Life Science Institute (ELSI) at Tokyo Institute of Technology used machine learning to examine the co-occurrence of fossil species and found that radiations and extinctions are rarely connected, and thus mass extinctions likely rarely cause radiations of a comparable scale.

Creative destruction is central to classic concepts of evolution. It seems clear that there are periods in which suddenly many species suddenly disappear, and many new species suddenly appear. However, radiations of a comparable scale to the mass extinctions, which this study, therefore, calls the mass radiations, have received far less analysis than extinction events. This study compared the impacts of both extinction and radiation across the period for which fossils are available, the so-called Phanerozoic Eon.



A new study applies machine learning to the fossil record to visualise life's history, showing the impacts of major evolutionary events. This shows the long-term evolutionary and ecological impacts of major events of extinction and speciation. Colours represent the geological periods from the Tonian, starting 1 billion years ago, in yellow, to the current Quaternary Period, shown in green. The red to blue colour transition marks the end-Permian mass extinction, one of the most disruptive events in the fossil record. **J. Hoyal Cuthill and N. Guttenberg.**

The Phanerozoic (from the Greek meaning "apparent life"), represents the most recent ~ 550-million-year period of Earth's total ~4.5 billion-year history, and is significant to palaeontologists: before this period most of the organisms that existed were microbes that didn't easily form fossils, so the prior evolutionary record is hard to observe. The new study suggests creative destruction isn't a good description of how species originated or went extinct during the Phanerozoic, and suggests that many of the most remarkable times of evolutionary radiation occurred when life entered new evolutionary and ecological arenas, such as during the Cambrian explosion of animal diversity and the Carboniferous expansion of forest biomes. Whether this is true for the previous ~ 3 billion years dominated by microbes is not known, as the scarcity of recorded information on such ancient diversity did not allow a similar analysis.

Palaeontologists have identified a handful of the most severe, mass extinction events in the Phanerozoic fossil record. These principally include the big five mass extinctions, such as the end-Permian mass extinction in which more than 70% of species are estimated to have gone extinct. Biologists have now suggested that we may now be entering a "Sixth Mass Extinction," which they think is mainly caused by human activity including hunting and land-use changes caused by the expansion of agriculture. A commonly noted example of the previous "Big Five" mass extinctions is the Cretaceous-Tertiary one (usually abbreviated as "K-T," using the German spelling of Cretaceous) which appears to have been caused when a meteor hit Earth ~65 million years ago, wiping out the non-avian dinosaurs. Observing the fossil record, scientists came to believe that mass extinction events create especially productive radiations. For example, in the K-T dinosaur-exterminating event, it has conventionally been supposed that a wasteland was created, which allowed organisms like mammals to recolonise and "radiate," allowing for the evolution of all manner of new mammal species, ultimately laying the foundation for the emergence of humans. In other words, if the K-T event of "creative destruction" had not occurred, perhaps we would not be here to discuss this question.

The new study started with a casual discussion in ELSI's "Agora," a large common room where ELSI scientists and visitors often eat lunch and strike up new conversations. Two of the paper's authors, evolutionary biologist Jennifer Hoyal Cuthill (now a research fellow at Essex University in the UK) and physicist/machine learning expert Nicholas Guttenberg (now a research scientist at Cross Labs working in collaboration with GoodAI in the Czech Republic), who were both post-doctoral scholars at ELSI when the

work began, were kicking around the question of whether machine learning could be used to visualise and understand the fossil record. During a visit to ELSI, just before the COVID-19 pandemic began to restrict international travel, they worked feverishly to extend their analysis to examine the correlation between extinction and radiation events. These discussions allowed them to relate their new data to the breadth of existing ideas on mass extinctions and radiations. They quickly found that the evolutionary patterns identified with the help of machine learning differed in key ways from traditional interpretations.

The team used a novel application of machine learning to examine the temporal co-occurrence of species in the Phanerozoic fossil record, examining over a million entries in a massive curated, public database including almost two hundred thousand species.

Lead author Dr Hoyal Cuthill said, "Some of the most challenging aspects of understanding the history of life are the enormous timescales and numbers of species involved. New applications of machine learning can help by allowing us to visualise this information in a human-readable form. This means we can, so to speak, hold half a billion years of evolution in the palms of our hands, and gain new insights from what we see."

Using their objective methods, they found that the "big five" mass extinction events previously identified by palaeontologists were picked up by the machine learning methods as being among the top 5% of significant disruptions in which extinction outpaced radiation or *vice versa*, as were seven additional mass extinctions, two combined mass extinction-radiation events and fifteen mass radiations. Surprisingly, in contrast to previous narratives emphasising the importance of post-extinction radiations, this work found that the most comparable mass radiations and extinctions were only rarely coupled in time, refuting the idea of a causal relationship between them.

Co-author Dr Nicholas Guttenberg said, "the ecosystem is dynamic, you don't necessarily have to chip an existing piece off to allow something new to appear."

The team further found that radiations may in fact cause major changes to existing ecosystems, an idea the authors call "destructive creation." They found that, during the Phanerozoic Eon, on average, the species that made up an ecosystem at any one time are almost all gone by 19 million years later. But when mass extinctions or radiations occur, this rate of turnover is much higher.

This gives a new perspective on how the modern "Sixth Extinction" is occurring. The Quaternary period, which began 2.5 million years ago, had witnessed repeated climate upheavals, including dramatic alternations of glaciation, times when high latitude locations on Earth, were ice-covered. This means that the present "Sixth Extinction" is eroding biodiversity that was already disrupted, and the authors suggest it will take at least 8 million years for it to revert to the long term average of 19 million years. Dr Hoyal Cuthill comments that "each extinction that happens on our watch erases a species, which may have existed for millions of years up to now, making it harder for the normal process of 'new species origination' to replace what is being lost."

Reference

J. F. Hoyal Cuthill[1,2,3], N. Guttenberg[2,4,5] and G. E. Budd[6], Impacts of speciation and extinction measured by an evolutionary decay clock, Nature, DOI: 10.1038/s41586-020-3003-4*

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https://bit.ly/3oIEP5q

'The robot made me do it': Robots encourage risk-taking behaviour in people

New research has shown robots can encourage people to take greater risks in a simulated gambling scenario than they would if there was nothing to influence their behaviours.

Increasing our understanding of whether robots can affect risk-taking could have clear ethical, practiCal and policy implications, which this study set out to explore.

Dr Yaniv Hanoch, Associate Professor in Risk Management at the University of Southampton who led the study explained, "We know that peer pressure can lead to higher risk-taking behaviour. With the ever-increasing scale of interaction between humans and technology, both online and physically, it is crucial that we understand more about whether machines can have a similar impact."

A SoftBank Robotics Pepper robot was used in the two robot conditions. Pepper, 1.21-meter-tall with 25 degrees of freedom, is a medium-sized humanoid robot designed primarily for Human-Robot Interaction (HRI).
University of Southampton

This new research, published in the journal *Cyberpsychology, Behavior, and Social Networking*, involved 180 undergraduate students taking the Balloon Analogue Risk Task (BART), a computer assessment that asks participants to press the spacebar on a keyboard to inflate a balloon displayed on the screen. With each press of the spacebar, the balloon inflates slightly, and 1 penny is added to the player's "temporary money bank". The balloons can explode randomly, meaning the player loses any money they have won for that balloon and they have the option to "cash-in" before this happens and move on to the next balloon.

One-third of the participants took the test in a room on their own (the control group), one third took the test alongside a robot that only provided them with the instructions but was silent the rest of the time and the final, the experimental group, took the test with the robot providing instruction as well as speaking encouraging statements such as "why did you stop pumping?"

The results showed that the group who were encouraged by the robot took more risks, blowing up their balloons significantly more frequently than those in the other groups did. They also earned more money overall. There was no significant difference in the behaviours of the students accompanied by the silent robot and those with no robot.

Dr Hanoch said: "We saw participants in the control condition scale back their risk-taking behaviour following a balloon explosion, whereas those in the experimental condition continued to take as much risk as before. So, receiving direct encouragement from a risk-promoting robot seemed to override participants' direct experiences and instincts."

The researcher now believe that further studies are needed to see whether similar results would emerge from human interaction with other artificial intelligence (AI) systems, such as digital assistants or on-screen avatars.

Dr Hanoch concluded, "With the wide spread of AI technology and its interactions with humans, this is an area that needs urgent attention from the research community."

"On the one hand, our results might raise alarms about the prospect of robots causing harm by increasing risky behavior. On the other hand, our data points to the possibility of using robots and AI in preventive programs, such as anti-smoking campaigns in schools, and with hard to reach populations, such as addicts."

https://bit.ly/2K4PXeb

Scientists build whole functioning thymus from human cells

Researchers have rebuilt a human thymus using human stem cells and a bioengineered scaffold

Researchers at the Francis Crick Institute and University College London have rebuilt a human thymus, an essential organ in the immune system, using human stem cells and a bioengineered scaffold. Their work is an important step towards being able to build artificial thymi which could be used as transplants.

The thymus is an organ in the chest where T lymphocytes, which play a vital role in the immune system, mature. If the thymus does not work properly or does not form during foetal development in the womb, this can lead to diseases such as severe immunodeficiency, where the body cannot fight infectious diseases or cancerous cells, or autoimmunity, where the immune system mistakenly attacks the patient's own healthy tissue.

In their proof-of-concept study, published in *Nature Communications* today [Friday 11th December], the scientists rebuilt thymi using stem cells taken from patients who had to have the organ removed during surgery. When transplanted into mice, the bioengineered thymi were able to support the development of mature and functional human T lymphocytes.

While researchers have previously rebuilt other organs or sections of organs, this is the first-time scientists have successfully rebuilt a whole working human thymus. The study, which was mainly funded by the European Research Council (ERC),* is an important step not only for further research into and treatment of severe immune deficiencies but also more broadly for developing new techniques to grow artificial organs.

Sara Campinoti, author and researcher in the Epithelial Stem Cell Biology and Regenerative Medicine Laboratory at the Crick says: "Showing it is possible to build a working thymus from human cells is a crucial step towards being able to grow thymi which could one day be used as transplants".

To rebuild this organ, the researchers collected thymi from patients and in the laboratory, grew thymic epithelial cells and thymic interstitial cells from the donated tissue into many colonies of billions of cells.

The next step for the researchers was to obtain a structural scaffold of thymi, which they could repopulate with the thymic cells they had cultured. For this, researcher Asllan Gjinovci developed a new approach to remove all the cells from rat thymi, so only the structural scaffolds remained. They had to use a new microvascular surgical approach for this, as conventional methods are not effective for the thymus.

Asllan says: "This new approach is important because it enables us to obtain scaffolds from larger organs like the human thymus, something essential to bringing this beautiful work to the clinic."

The researchers then injected the organ scaffolds with up to six million human thymic epithelial cells as well as interstitial cells from the colonies they had grown in the lab. The cells grew onto the scaffolds and after only five days, the organs had developed to a similar stage as those seen in nine-week old foetuses.

Finally, the team implanted these thymi into mice. They found that in over 75% of cases, the thymi were able to support the development of human lymphocytes.

Roberta Ragazzini, another author of the paper, adds: "The fact that we can extensively expand thymic stem cells taken from human donors into large colonies is really exciting. It makes it possible to scale up the process with a view to build 'human size' thymi."

Paola Bonfanti, senior author and group leader at the Crick and professor in the Division of Infection and Immunity at UCL says: "As well as providing a new source of transplants for people

without a working thymus, our work has other potential future applications.

"For example, as the thymus helps the immune system to recognise self from non-self, it poses a problem for organ transplants as it can cause the immune system to attack the transplant.

"It is possible that we could overcome this by also transplanting a thymus regrown from cells taken from the thymus of the organ donor. We are confident that this may prevent the body attacking the transplant. The research behind this is still in early days, but it is an exciting concept which could remove the need for patients to take immune suppressors for the rest of their life.

The researchers are continuing their work rebuilding thymi to refine and scale up the process.

For further information, contact: press@crick.ac.uk or +44 (0)20 3796 5252

Notes to Editors

Reference: Campinoti, S et al. (2020). Reconstitution of a functional human thymus by postnatal stromal progenitor cells and natural whole-organ scaffolds. Nature Communications. DOI number: 10.1038/s41467-020-20082-7.

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