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Space's Trash Collector? A Japanese Entrepreneur Wants the Job

Entrepreneur envisions creating the first space trash collection company

By MARTIN FACKLER NOV. 28, 2016

TOKYO — Sitting in a drab industrial neighborhood surrounded by warehouses and factories, Astroscale's Tokyo office seems appropriately located for a company seeking to enter the waste management business.

Only inside do visitors see signs that its founder, Mitsunobu Okada, aspires to be more than an ordinary garbageman. Schoolroom pictures of the planets decorate the door to the meeting room. Satellite mock-ups occupy a corner. Mr. Okada greets guests in a dark blue T-shirt emblazoned with his company's slogan: Space Sweepers.

Mr. Okada is an entrepreneur with a vision of creating the first trash collection company dedicated to cleaning up some of humanity's hardest-to-reach rubbish: the spent rocket stages, inert satellites and other debris that have been collecting above Earth since Sputnik ushered in the space age. He launched Astroscale three years ago in the belief that national space agencies were dragging their feet in facing the problem, which could be tackled more quickly by a small private company motivated by profit.

"Let's face it, waste management isn't sexy enough for a space agency to convince taxpayers to allocate money," said Mr. Okada, 43, who put Astroscale's headquarters in start-up-friendly Singapore but is building its spacecraft in his native Japan, where he found more engineers. "My breakthrough is figuring out how to make this into a business."

Over the last half-century, low Earth orbit has become so littered with debris that space agencies and scientists warn of the increasing danger of collisions for satellites and manned spacecraft. The United States Air Force now keeps track of about 23,000 pieces of space junk that are big enough — about four inches or larger — to be detected from the ground.

Scientists say there could be tens of millions of smaller particles, such as bolts or chunks of frozen engine coolant, that cannot be discerned from Earth. Even the tiniest pieces move through orbit at speeds fast enough to turn them into potentially deadly projectiles. In 1983, the space shuttle Challenger returned to Earth with a pea-size pit in its windshield from a paint-chip strike.

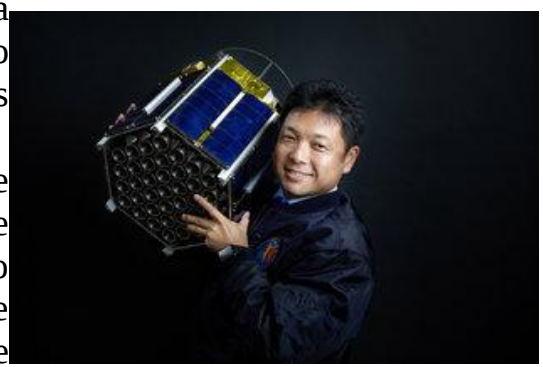
And plans are being made to make low orbit even busier, and more essential for communications on Earth. Companies like SpaceX and OneWeb are aiming to create vast new networks of hundreds or even thousands of satellites to provide global internet connectivity and cellphone coverage. The growth of traffic increases the risk of collisions that could disrupt communications, as in 2009 when a dormant Russian military satellite slammed into a private American communications satellite, causing brief disruptions for satellite-phone users.

Worse, each strike like that creates a cloud of shrapnel, potentially setting off a chain reaction of collisions that could render low orbit unusable.

"If we don't start removing these things, the debris environment will become unstable," said William Ailor, a fellow at the Aerospace Corporation, a federally funded research and development center in California. "We will continue to have a growing debris population that could affect the ability to operate satellites."

Enter Mr. Okada, a former government official and internet entrepreneur, who said a midlife crisis four years ago prompted him to return to his childhood passion of space. As a teenager in 1988, he flew to Alabama to join the United States Space Camp at the U.S. Space and Rocket Center in Huntsville, and later chose to attend business school at Purdue University, the alma mater of his hero, Neil Armstrong.

Later, Mr. Okada realized that he could use his experience in the start-up world — he had founded a software company in 2009 — to get a jump on other space debris projects.



"The projects all smelled like government, not crisp or quick," he said of conferences he attended to learn about other efforts. "I came from the start-up world where we think in days or weeks, not years."

Mitsunobu Okada, the founder of Astroscale, with a model of a satellite designed to intercept and remove debris from low Earth orbit. **Ko Sasaki for The New York Times**

He said he has created a two-step plan for making money from debris removal. First, Astroscale plans to launch a 50-pound satellite called IDEA OSG 1 next year aboard a Russian rocket. The craft will carry panels that can measure the number of strikes from debris of even less than a millimeter. Astroscale will use this data to compile the first detailed maps of debris density at various altitudes and locations, which can then be sold to satellite operators and space agencies, Mr. Okada said.

"We need to get revenue at an early stage, even before doing actual debris removal, to prove that we are commercial, as a business," said Mr. Okada, who added that he had already raised $43 million from investors.

The more ambitious step will come in 2018, when Mr. Okada says Astroscale will launch a craft called the ELSA 1. Larger than its predecessor, the ELSA 1 will be loaded with sensors and maneuvering thrusters that will allow it to track and intercept a piece of debris.

The company settled on a lightweight and simple approach to grabbing space debris: glue. Astroscale has worked with a Japanese chemical company to create an adhesive that would cover a flat surface about the size of a dinner plate on the ELSA 1. The craft would bump into a piece of space junk, which would stick to the craft and be dragged out of orbit. Both the ELSA 1 and the debris would burn up on re-entry.

The concept of deorbiting space junk is not novel. As the debris problem has grown in urgency in recent years, space agencies and companies have released dozens of concepts for cleaning up low Earth orbit. The Air Force has proposed a "laser broom" that would use ground-based lasers to vaporize a spot on an object's surface, creating a puff that would act like an engine to push it down toward the atmosphere. Other proposals call for using robotic arms, nets, tethers and even harpoons to spear debris. The challenge, experts say, is to build an unmanned spacecraft that can be used to track, approach and grab a dark object tumbling through space at 17,000 miles per hour.

"Imagine trying to grab a spinning skater on an ice rink," said Raymond J. Sedwick, a professor of aerospace engineering at the University of Maryland, "except, instead of a person, it's an S.U.V. And instead of you being there in person, you're remotely flying a drone, the lighting is bad, you have limited sensory data, there is no obvious place to grab onto, and you might be operating under a time delay." "That said, we need to do something" about space debris, Dr. Sedwick said.

Even if a technology works, such efforts face another hurdle: the cost. Mr. Okada said the key to bringing down a price tag of tens or even hundreds of millions of dollars is to reduce the weight. He said that the Elsa 1's adhesive would weigh just a few ounces, far less than, say, a 100-pound robotic arm, and that his company's engineers had found ways to bring the spacecraft's weight down to 200 pounds, making it much lighter than other proposed craft.

"In the U.S., aerospace engineers are more interested in working on missions to Mars, not waste management," Mr. Okada said. "Japan doesn't have so many interesting space missions, so engineers were excited by my idea."

He also said that Astroscale would start by contracting with companies that will operate big satellite networks to remove their own malfunctioning satellites. He said that if a company has a thousand satellites, several are bound to fail. Astroscale will remove these, allowing the company to fill the gap in its network by replacing the failed unit with a functioning satellite. “Our first targets won’t be random debris, but our clients’ own satellites,” he said. “We can build up to removing debris as we perfect our technology.”

He said this approach would also get around a hurdle in international law to the removal of space debris — the required permission of the owner. Under a 1967 treaty, man-made objects in space belong to the countries that launched them, and cannot be touched without approval. Mr. Okada said finding ways around these various barriers was more than a business proposition; it would also be the fulfillment of a childhood dream. “I see a business opportunity in solving a problem that nobody knows how to solve,” Mr. Okada said. “But my enthusiasm is because I am going back to my teenage passion: space.”

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Japan is about to build the world’s fastest computer, ever

By 2018 the top spot will belong to Japan

By Mike Wehner on Nov 28, 2016 at 6:53 PM

When it comes to the most powerful computers in the world, the game is dominated by two players: the United States and China. In fact, of the top of five most powerful supercomputing sites on the planet, China owns the top two spots, with the U.S. holding the third, fourth, and fifth places on the list. By 2018, that top spot will belong to Japan, should the company’s plan to build the world’s fastest supercomputer not hit any snags along the way.

Reuters reports that Japan has budgeted $173 million to hold the supercomputing crown, and plans to build a machine capable of 130 petaflops, which will top China’s Sunway TaihuLight — with a max of just over 93 petaflops but theoretical peak of around 125 — to claim the crown of “world’s fastest.”

Japan aims to use the project to revitalize its somewhat stagnant technology industry, which has stumbled in recent years while neighboring China has muscled into the scene.

The supercomputer project, which Japan has named AI Bridging Cloud Infrastructure, or ABCI for short, is currently seeking bids from manufacturers willing to take on the monumental task. ABCI is slated to be ready for action by 2018, when it will be used by Japan to boost its research into artificial intelligence platforms. The country also plans to provide the computer’s power to Japanese companies who currently rely on the likes of Google and Microsoft for their heavy data lifting, for fee, of course.

This won’t be Japan’s first venture into the world of supercomputing, of course, and the country holds the number six and seven spots on the chart behind China and the United States. However, the country’s fastest computer is rated at less than 14 petaflops, so jumping from that to 130 petaflops will definitely be an accomplishment.

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Toxoplasma's balancing act explained

Parasite's method of rewiring our immune response leads to novel tool for drug tests

The parasite Toxoplasma gondii is a silent success. It infects up to 95% of people in many regions of the world, and most of them never know it, due to the parasite's artful manipulation of its host's immune response. Toxoplasma keeps the immune response low enough so that it can thrive, but high enough so that its human hosts generally live healthy lives and can incubate parasites. Scientists at EMBL and the Institute for Advanced Biosciences (IAB, an INSERM - CNRS - Université Grenoble-Alpes research centre) have uncovered one of the ways it maintains this balance, in a paper published today in Structure.

"The parasite rewires the host's inflammatory response," says Matthew Bowler, who led the research at EMBL. "It completely subverts the chain reaction that would normally trigger our body's defenses."

When a cell in your body detects a parasite, it sets off a chain reaction. Inside that cell, a series of molecules activate each other until a protein called p38α is activated and moves into the cell's nucleus. There, it turns on the genes that trigger the inflammatory response. Among other things, the purpose of that response is to eliminate the pathogen. One would expect parasites like Toxoplasma to want to subdue that response, but Mohamed-Ali Hakimi and colleagues at IAB discovered a few years ago that Toxoplasma secretes a protein, GRA24, which does just the opposite: it activates and controls our inflammatory response.

Bowler and Hakimi discovered that GRA24 bypasses the cell's chain reaction, activating p38α directly, and pulling it into the nucleus to turn on inflammatory response genes. Using a combination of techniques, they found that the Toxoplasma protein attaches itself much more strongly to p38α than the cell's own proteins do. So by producing a protein that binds directly, and very tightly, to p38α, Toxoplasma controls the level of the inflammatory response and sustains it by making it inaccessible to the proteins that would usually turn it off. This is why Toxoplasma isn't considered a serious health threat except for pregnant women and people with compromised immune systems.

This research has generated a new way to assess the efficacy of anti-inflammatory drugs, many of which are designed to block p38α. So far it has been difficult to assess how effective they are, because scientists haven't had a good way to produce an active form of p38α in the lab. In producing GRA24 bound to p38α, Bowler, Hakimi and colleagues - with the help of EMBL's Protein Expression and Purification Core Facility - created just that. The tight interaction with the parasite protein keeps p38α in its active state, so researchers can now subject it to the drugs they'd like to test, and evaluate how well they block p38α's active site, which the Toxoplasma protein doesn't interfere with.

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Depression in young people affects the stomach, anxiety the skin

Mental disorders and physical diseases frequently go hand in hand.

For the first time, psychologists at the University of Basel and Ruhr University Bochum have identified temporal patterns in young people: arthritis and diseases of the digestive system are more common after depression, while anxiety disorders tend to be followed by skin diseases.

Physical diseases and mental disorders affect a person's quality of life and present a huge challenge for the healthcare system. If physical and mental disorders systematically co-occur from an early age, there is a risk that the sick child or adolescent will suffer from untoward developments.

Data from 6,500 teenagers

In a project financed by the Swiss National Science Foundation, a research group led by PD Dr. Marion Tegethoff in collaboration with Professor Gunther Meinlschmidt from the University of Basel's Faculty of Psychology has now examined the temporal pattern and relationship between physical diseases and mental disorders in children and young people. In the journal PLOS ONE, they analyzed data from a representative sample of 6,483 teenagers from the US aged between 13 and 18.

The researchers noted that some physical diseases tend to occur more frequently in children and adolescents if they have previously suffered from certain mental disorders. Likewise, certain mental disorders tend to occur more frequently after the onset of particular physical diseases. Affective disorders such as depression were frequently followed by arthritis and diseases of the digestive system, while the same relationship existed between anxiety disorders and skin diseases. Anxiety disorders were more common if the person had already suffered from heart disease. A close association was also established

for the first time between epileptic disorders and subsequent eating disorders.

Epilepsy and eating disorders

The results offer important insights into the causal relationship between mental disorders and physical diseases. The newly identified temporal associations draw attention to processes that could be relevant both to the origins of physical diseases and mental disorders and to their treatment. In an earlier study, the same authors had already provided evidence for the relationship between mental disorders and physical diseases in young people.

"For the first time, we have established that epilepsy is followed by an increased risk of eating disorders - a phenomenon, that had previously been described only in single case reports. This suggests that approaches to epilepsy treatment could also have potential in the context of eating disorders," explains Marion Tegethoff, the study's lead author. From a health policy perspective, the findings underscore that the treatment of mental disorders and physical diseases should be closely interlinked from an early age on.

Marion Tegethoff, Esther Stalujanis, Angelo Belardi, Gunther Meinlschmidt Chronology of Onset of Mental Disorders and Physical Diseases in Mental-Physical Comorbidity - A National Representative Survey of Adolescents PLOS ONE (2016), doi: 10.1371/journal.pone.0165196

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New drug limits and then repairs brain damage in stroke University of Manchester

Researchers at The University of Manchester have discovered that a potential new drug reduces the number of brain cells destroyed by stroke and then helps to repair the damage.

A reduction in blood flow to the brain caused by stroke is a major cause of death and disability, and there are few effective treatments.

A team of scientists at The University of Manchester has now found that a potential new stroke drug not only works in rodents by limiting the death of existing brain cells but also by promoting the birth of new neurones (so-called neurogenesis).

This finding provides further support for the development of this anti-inflammatory drug, interleukin-1 receptor antagonist (IL-1Ra in short), as a new treatment for stroke. The drug is already licensed for use in humans for some conditions, including rheumatoid arthritis. Several early stage clinical trials in stroke with IL-1Ra have already been completed in Manchester, though it is not yet licensed for this condition.

In the research, published in the biomedical journal Brain, Behavior and Immunity, the researchers show that in rodents with a stroke there is not only reduced brain damage early on after the stroke, but several days later increased numbers of new neurones, when treated with the anti-inflammatory drug IL-1Ra. Previous attempts to find a drug to prevent brain damage after stroke have proved unsuccessful and this new research offers the possibility of a new treatment.

Importantly, the use of IL-1Ra might be better than other failed drugs in stroke as it not only limits the initial damage to brain cells, but also helps the brain repair itself long-term through the generation of new brain cells.

These new cells are thought to help restore function to areas of the brain damaged by the stroke. Earlier work by the same group showed that treatment with IL-1Ra does indeed help rodents regain motor skills that were initially lost after a stroke. Early stage clinical trials in stroke patients also suggest that IL-1Ra could be beneficial.

The current research is led by Professor Stuart Allan, who commented: "The results lend further strong support to the use of IL-1Ra in the treatment of stroke, however further large trials are necessary."

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Researcher suggests kratom may have medical benefit as opioid alternative

The Journal of the American Osteopathic Association author says research into unique pharmacologic properties would likely end if DEA proceeds with Schedule 1 classification

CHICAGO - A delayed U.S. Drug Enforcement Administration ban on kratom would stifle scientific understanding of the herb's active chemical components and documented pharmacologic properties if implemented, according to a special report published today in The Journal of the American Osteopathic Association.

The report cited the pharmacologically active compounds in kratom, including mitragynine, 7-hydroxymitragynine, paynantheine, speciogynine and 20 other substances, as one basis for further study. It also emphasized the extensive amount of anecdotal evidence and current scientific research that indicates kratom may be safer and less addictive than current treatments for pain and opioid withdrawal.

"There's no question kratom compounds have complex and potential useful pharmacologic activities and they produce chemically different actions from opioids," said author Walter Prozialeck, chairman of the Department of Pharmacology at Midwestern University Chicago College of Osteopathic Medicine. "Kratom doesn't produce an intense euphoria and, even at very high doses, it doesn't depress respiration, which could make it safer for users."

Kratom (Mitragyna speciosa) is indigenous to Southeast Asia, where the plant was used for centuries to relieve fatigue, pain, cough and diarrhea and aid in opioid withdrawal. Currently sold in the United States as an herbal supplement, kratom drew DEA scrutiny after poison control centers noted 660 reports of adverse reactions to kratom products between January 2010 and December 2015.

"Many important medications, including the breast cancer treatment tamoxifen, were developed from plant research," said Prozialeck.

"While the DEA and physicians have valid safety concerns, it is not at all clear that kratom is the culprit behind the adverse effects," said Anita Gupta, DO, PharmD and special advisor to the FDA.

Dr. Gupta, an osteopathic anesthesiologist, pain specialist and licensed pharmacist, has treated a number of patients who've used kratom. "Many of my patients are seeking non-pharmaceutical remedies to treat pain that lack the side effects, risk, and addiction potential of opioids," she said.

Kratom is currently banned in states including Alabama, Florida, Indiana, Arkansas, Wisconsin and Tennessee. The DEA is scheduled to decide whether to place kratom on its list of Schedule 1 drugs, a classification for compounds thought to have no known medical benefit. Marijuana, LSD and heroin are Schedule 1 drugs, which prevents the vast majority of U.S.-based researchers from studying those substances.

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Report highlights coffee's potential role in reducing cognitive decline

Symposium at the European Union Geriatric Medicine Society Congress 2016 discusses the role of nutrition in cognitive function as we age

A new report from the Institute for Scientific Information on Coffee (ISIC), a not-for-profit organisation devoted to the study and disclosure of science related to coffee and health, highlights the potential role of coffee consumption in reducing the risk of cognitive decline. The report concludes that a moderate intake of coffee (3-5 cups per day) may provide protection against age-related cognitive decline and other neurodegenerative diseases such as Alzheimer's and Parkinson's.

The report provides a summary of the research presented at ISIC's symposium, titled 'Nutrition, Coffee and Age-Related Cognitive Decline', held during the European Union Geriatric Medicine Society's 2016 Congress in Lisbon, Portugal. The findings are particularly relevant given Europe's ageing population: the number of people aged 60 years or over is projected to rise to 217.2 million by 20301, therefore understanding and communicating diet and lifestyle factors that may limit age-related cognitive decline will help to improve the quality of life for this growing demographic.

The symposium speakers whose insights and research contributed to ISIC's report were:

Professor Lisette de Groot, Professor of Nutrition and Ageing, Division of Human Nutrition at Wageningen University (The Netherlands)

Professor Rodrigo A. Cunha, Professor at the Faculty of Medicine of the University of Coimbra and Principal Investigator at the Centre for Neuroscience and Cell Biology of the University of Coimbra (CNC) (Portugal)

Dr Elisabet Rothenberg, Associate Professor of Nutrition at Kristianstad University (Sweden)

Key highlights about coffee from the report include:

Research published in 2016 suggests that moderate coffee consumption can reduce the risk of developing Alzheimer's by up to 27%2. Research has suggested that it is regular, long-term coffee drinking that is key to helping to reduce the risk of Alzheimer's Disease3.

The association between coffee consumption and cognitive decline is illustrated by a 'U-shaped' pattern in recent meta-analyses, with the greatest protection seen at an intake of approximately 3-5 cups of coffee per day4.

Although the precise mechanisms of action behind the suggested association between coffee and age-related cognitive decline are unknown, caffeine is likely to be involved. There are many other compounds in coffee, such as antioxidants and anti-inflammatory agents, which may also play a role. Caffeic acid, for example, is a polyphenol (antioxidant) found in coffee, and research suggests that these may be associated with improved cognitive function5.

Professor Rodrigo A. Cunha, Professor at the Faculty of Medicine of the University of Coimbra and Principal Investigator at the Centre for Neuroscience and Cell Biology of the University of Coimbra (CNC), Portugal, commented:

"Healthcare professionals have an important part to play in providing patients with accurate research-based information, to help them to follow a healthy diet and lifestyle, and in turn, reduce their risk of age-related cognitive decline. Moderate coffee consumption could play a significant role in reducing cognitive decline which would impact health outcomes and healthcare spending across Europe."

In its Scientific Opinion on the safety of caffeine, the European Food Safety Authority (EFSA) concluded that intakes of up to 400mg of caffeine (the equivalent of up to 5 cups of coffee per day), from all sources, do not raise any concerns for healthy adults6. One cup of coffee provides approximately 75-100mg caffeine.

To read the report, please click here.

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http://bit.ly/2fIDmqd

It's all in the eyes: Women and men really do see things differently

Suggests there is a gender difference in understanding visual cues

Women and men look at faces and absorb visual information in different ways, which suggests there is a gender difference in understanding visual cues, according to a team of scientists that included psychologists from Queen Mary University of London (QMUL).

The researchers used an eye tracking device on almost 500 participants at the Science Museum over a five-week period to monitor and judge how much eye contact they felt comfortable with while looking at a face on a computer screen.

They found that women looked more at the left-hand side of faces and had a strong left eye bias, but that they also explored the face much more than men. The team observed that it was possible to tell the

gender of the participant based on the scanning pattern of how they looked at the face with nearly 80 per cent accuracy. Given the very large sample size the researchers suggest this is not due to chance.

Lead author Dr Antoine Coutrot from QMUL's School of Biological and Chemical Sciences said: "This study is the first demonstration of a clear gender difference in how men and women look at faces.

"We are able to establish the gender of the participant based on how they scan the actors' face, and can eliminate that it isn't based on the culture of the participant as nearly 60 nationalities have been tested. We can also eliminate any other observable characteristics like perceived attractiveness or trustworthiness."

The participants were asked to judge how comfortable the amount of eye contact they made with the actor in a Skype-like scenario. Each participant saw the same actor (there were eight in total) during the testing period, which was around 15 minutes. At the end of the session the researchers collected personality information about the participants through questionnaires.

Co-author Dr Isabelle Mareschal also from QMUL's School of Biological and Chemical Sciences added: "There are numerous claims in popular culture that women and men look at things differently - this is the first demonstration, using eye tracking, to support this claim that they take in visual information in different ways."

The team describe their findings in the Journal of Vision and suggest the gender difference in scanning visual information might impact many research fields, such as autism diagnosis or even everyday behaviours like watching a movie or looking at the road while driving.

The research was funded by the Leverhulme Trust and EPSRC and involved researchers from University College London and University of Nottingham.

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When judging other people, first impressions last

A well-known saying urges people to 'not judge a book by its cover' -- but people tend to do just that -- even after they've skimmed a chapter or 2, according to Cornell University research

ITHACA, N.Y. - A well-known saying urges people to "not judge a book by its cover." But people tend to do just that - even after they've skimmed a chapter or two, according to Cornell University research.

Vivian Zayas, professor of psychology at Cornell University, and her colleagues found that people continue to be influenced by another person's appearance even after interacting with them face-to-face. First impressions formed simply from looking at a photograph predicted how people felt and thought about the person after a live interaction that took place one month to six months later.

"Facial appearance colors how we feel about someone, and even how we think about who they are," said Zayas, an expert in the cognitive and affective processes that regulate close relationships. "These facial cues are very powerful in shaping interactions, even in the presence of other information."

The researchers ran experiments in which 55 participants looked at photographs of four women who were smiling in one instance and had a neutral expression in another. For each photo, participants evaluated whether they would be friends with the woman, indicating likeability, and whether or not her personality was extroverted, agreeable, emotionally stable, conscientious and open to new experiences.

Between one month and six months later, the study participants met one of the photographed women - not realizing they had rated her photograph previously. They played a trivia game for 10 minutes then were instructed to get to know each other as well as possible for another 10 minutes. After each interaction, the study participants again evaluated the person's likeability and personality traits.

The researchers found a strong consistency between how the participants evaluated the person based on the photograph and on the live interaction.

If study participants thought a person in a photograph was likeable and had an agreeable, emotionally stable, open-minded and conscientious personality, that impression carried through after the face-to-face meeting. Conversely, participants who thought the person

in the photograph was unlikeable and had a disagreeable, emotionally unstable, close-minded, and disagreeable personality kept that judgment after they met.

"What is remarkable is that despite differences in impressions, participants were interacting with the same person, but came away with drastically different impressions of her even after a 20-minute face-to-face interaction," Zayas said.

Zayas has two explanations for the findings. A concept called behavioral confirmation or self-fulfilling prophecy accounted for, at least in part, consistency in liking judgments. The study participants who had said they liked the person in the photograph tended to interact with them face to face in a friendlier, more engaged way, she said.

"They're smiling a little bit more, they're leaning forward a little bit more. Their nonverbal cues are warmer," she said. "When someone is warmer, when someone is more engaged, people pick up on this. They respond in kind. And it's reinforcing: The participant likes that person more."

Regarding why participants showed consistency in judgments of personality, a halo effect could have come into play, she said. Participants who gave the photographed person a positive evaluation attributed other positive characteristics to them as well. "We see an attractive person as also socially competent, and assume their marriages are stable and their kids are better off. We go way beyond that initial judgment and make a number of other positive attributions," Zayas said.

In a related study, she and her colleagues found that people said they would revise their judgment of people in photographs if they had the chance to meet them in person, because they'd have more information on which to base their assessment.

"And people really think they would revise," she said. "But in our study, people show a lot more consistency in their judgments, and little evidence of revision."

The study, "Impressions Based on a Portrait Predict, 1-Month Later, Impressions Following a Live Interaction," was recently published in Social Psychological and Personality Science.

http://nyti.ms/2qbIl5f

How Good Is a Bad Night's Sleep?

Q. Is a night's sleep physiologically beneficial even if it includes emotionally disturbing nightmares?

By C. CLAIBORNE RAYNOV. 28, 2016

A. Almost certainly yes, said Dr. Neomi Shah, a specialist at the Mount Sinai Integrative Sleep Center in New York. Despite the problems nightmares can cause, sleeping and having them is better than not sleeping, research suggests.

Nightmares can make it difficult to sleep and interfere with daytime functioning, but physiological indicators of sleep patterns and quality do not differ in people who have nightmares, Dr. Shah said.

Frequent long, distressing and vivid dreams often wake people and cause problems like insomnia and poor sleep quality, she said. Research has also consistently demonstrated that nightmares can harm general well-being, affect mood and elevate stress.

Some studies suggest there are measurable sleep problems for people who have nightmares, while others show no difference. The studies that show such a link found that people who woke up stayed awake longer and that certain stages of sleep did not last as long. But people in those studies who had nightmares also had longer periods of rapid eye movement, or REM, sleep, when most dreaming occurs.

A weakness of these studies is that they were not conducted in the subjects' normal sleeping environment. A more recent study in such an environment found no differences in so-called sleep architecture, sleep-cycle and REM durations, or sleep patterns for just the nights with nightmares.

Therefore, Dr. Shah said, despite upsetting nightmares, "sleep architecture appears to be preserved, and subjects with frequent nightmares are likely deriving the physiological benefits of sleep."

http://bit.ly/2fVyFON

Swimming, racquet sports, and aerobics linked to best odds of staving off death

Specific types of sport and exercise seem to be associated with differing risk levels

In terms of exercise, swimming, racquet sports, and aerobics seem to be associated with the best odds of staving off death from any cause and from heart disease and stroke, in particular, suggests research published online in the British Journal of Sports Medicine.

The health benefits of physical activity are legion, but to try and quantify the impact of different types of sports and exercise on the odds of beating death, the researchers analysed data from 11 nationally representative annual health surveys for England and Scotland, carried out between 1994 and 2008.

In all, the analysis included 80,306 adults with an average age of 52. In each of the surveys, participants were quizzed about what type and how much physical activity they had done in the preceding 4 weeks, and whether it had been enough to make them breathless and sweaty.

Physical activity included heavy duty domestic chores, gardening, and DIY/maintenance; walking; and the six most popular forms of sport/exercise practised--cycling; swimming; aerobics/keep fit/gymnastics/dance; running/jogging; football/rugby; and badminton/tennis/squash. Less than half of the respondents (just over 44%) met the recommended weekly physical activity quota when they were surveyed.

The survival of each participant was tracked for an average of 9 years, during which time 8790 of them died from all causes and 1909 from heart disease/stroke. After taking account of potentially influential factors, the analysis of the pooled data indicated varying odds of death according to sport/exercise type.

Overall, compared with the survey respondents who said they had not done a given sport, risk of death from any cause was 47% lower among those who played racquet sports; 28% lower among swimmers; 27% lower among aerobics fans; and 15% lower among cyclists. No such associations were seen for runners/joggers or those who played football/rugby.

When the researchers looked at risk of death from heart disease and stroke, they found that playing racquet sports was associated with a 56% lower risk, with equivalent figures of 41% for swimming and 36% for aerobics, compared with those who did not participate in these sports. Neither cycling, running/jogging, nor football/rugby were associated with a significantly reduced risk of death from cardiovascular disease, the analysis showed.

The researchers did find a 43% reduced risk of death from all causes and a 45% reduced risk from cardiovascular disease among runners and joggers when compared with those who didn't run or jog, but this apparent advantage disappeared when all the potentially influential factors were accounted for.

And few of the survey respondents said they played football or rugby regularly, which might also explain the apparent low impact of these activities on death risk in this study, explain the researchers.

For some sports, the higher the intensity, duration, and volume, the greater was the reduction in risk, while for others a U shaped curve emerged, indicating that lower intensity might be better than higher intensity or no participation at all. But due to the small number of deaths involved, these findings should be regarded as preliminary, say the researchers.

This is an observational study so no firm conclusions can be drawn about cause and effect, added to which the relatively short recall period, the 'seasonality' of certain sports, and the inability to track changes in levels of sports participation throughout the monitoring period, may all have had some bearing on the results, caution the researchers.

Nevertheless, they conclude: "These findings demonstrate that participation in specific sports may have significant benefits for public health," adding that they should help health professionals to bang the

drum for getting involved in regular sports/exercise as good way of staying healthy.

Research: Associations of specific types of sport and exercise with all-cause and cardiovascular disease mortality: a cohort study of 80 306 British adults
http://bjsm.bmj.com/lookup/doi/10.1136/bjsports-2016-096822

http://bit.ly/2qYNqCj

Mayo Clinic finds myocarditis caused by infection on rise globally

Idea of who is affected by myocarditis is becoming a little clearer

JACKSONVILLE, Fla. -- Myocarditis, an assortment of heart disorders often caused by infection and inflammation, is known to be difficult to diagnose and treat. But the picture of who is affected is becoming a little clearer. Men may be as much as twice as likely as women to develop severe and possibly fatal reactions. And the risk of sudden cardiovascular death in the young is relatively high. Myocarditis accounts for about 5 percent of sudden cardiovascular infant deaths and up to 20 percent of sudden cardiovascular death in adolescents. And the chronic disease is responsible for up to 45 percent of heart transplants in the U.S.

This assessment of the global state of myocarditis, published Nov. 29 in the Journal of the American College of Cardiology, points to the need for advanced therapies and prevention strategies, says Leslie Cooper Jr., M.D., cardiologist and chair, Cardiovascular Department, on Mayo Clinic's campus in Florida.

Along with Dr. Cooper, who is an internationally recognized expert on myocarditis, researchers from the Netherlands, Switzerland and Finland contributed to the study. Dr. Cooper also authored the myocarditis section for the 2015 Global Burden of Disease Study, which was published Oct. 7 in the Lancet, and the American Heart Association scientific statement on specific dilated cardiomyopathies, which was published Nov. 3 in Circulation. Cardiomyopathies, which often feature enlarged hearts and heart failure, can result from myocarditis.

Dr. Cooper reported in the Lancet global disease study that cases of myocarditis have increased from about 1.5 million annually to 2.2 million cases from 2013 to 2015. Although the exact incidence of myocarditis in the U.S. has not been reported, it is estimated that several thousand patients - most of them 40 or younger - are diagnosed.

In the Journal of the American College of Cardiology study, he found that the rate of myocarditis and associated death is much higher in men than in women. This is likely due to testosterone-driven inflammation.

Early diagnosis is key to preventing long-term heart damage from myocarditis, Dr. Cooper says. If chronic disease results, scarring in the heart can promote heart failure. Although standard therapies are used to control symptoms of heart failure, new investigational therapies soon may enter clinical trials, and new management of the disorder is being discussed, Dr. Cooper says.

"We are on a quest for advances in treating this disorder," he says.

Myocarditis is a difficult disorder to diagnose and treat, Dr. Cooper says. The most common cause of myocarditis is an infection - usually viral - that can damage heart muscle chronically or acutely in otherwise healthy people, Dr. Cooper says. Infections that affect the heart differ around the globe. In the U.S., a dozen common pathogens can be responsible. An example is coxsackie virus, which up to 70 percent of U.S. residents have been exposed to by the time they are 30. "But only 1 to 2 percent of people with acute coxsackie virus infection develop cardiac symptoms," Dr. Cooper says.

Myocarditis has other causes, including autoimmune diseases, environmental toxins, and adverse reactions to medications. The most clinically important symptoms of the disorder are shortness of breath, which can indicate the start of heart failure, and chest pain - a sign of heart inflammation, he says.

To prevent the disorder from worsening in children, Dr. Cooper suggests that aerobic exercise be limited for several weeks after a

suspected coxsackie virus infection, and "if a child or adolescent develops breathing difficulties or chest pain with evidence of myocarditis, my recommendation is to avoid competitive sports for at least three months," Dr. Cooper says.

A cardiac MRI within two weeks of symptom onset is 80 percent effective in diagnosing cardiomyopathy, but diagnosis is difficult at more chronic stages.

Most people (60-70 percent) with acute cardiomyopathy from myocarditis get better. About 10-15 percent develops irreversible chronic disease due to scars in the heart created by the infection, Dr. Cooper says. These patients are treated with standard heart failure therapies, but 20 percent die during the decade following infection due to heart failure. "I see patients everyday with this disorder," Dr. Cooper says. "We are on the cusp of trying more tailored treatment, and it can't come soon enough."

There was no funding support or relationships with industry for the Journal of the American College of Cardiology study, which Dr. Cooper led.

http://bit.ly/2fJ97WE

Link found between epilepsy drugs and birth defects

A joint study conducted by researchers from the universities of Liverpool and Manchester has found a link between birth defects and certain types of epilepsy medication.

For most women who have epilepsy, continuing their medication during pregnancy is important for their health.Over the last 25 years, research has shown that children exposed to these medications in the womb can be at a higher risk of having a malformation or birth defect.

The study, published in the Cochrane Database of Systematic Reviews, aimed to understand whether pregnant women exposed to antiepileptic drugs (AEDs) during pregnancy were at higher risk of having a child with a malformation.

Minimising fetal risk

The majority of women with epilepsy will be required to continue antiepileptic drug treatment during a pregnancy.

Previous studies have demonstrated a significant increase in risk of having a child with a significant birth defect in the mother was taking certain antiepileptic drugs and therefore treatment decisions should be made carefully and collaboratively and aim to find a balance between maximising maternal health whilst minimising fetal risk.

As part of this systematic review 50 published studies were analysed and it was found that exposure in the womb to the AED sodium valproate was associated with a 10% chance of the child having a significant birth defect and that this rose as the dose of the drug increased.

Skeletal and limb defects

The types of birth defect that were increased were skeletal and limb defects, cardiac defects, craniofacial defects and neural tube defects.

Children exposed to carbamazepine, topiramate or phenytoin were at an increased risk of having a significant birth defect but the exact types of defects were not clear and children exposed to phenobarbital were found to be at an increased risk of cardiac defects.

The review also found that children exposed to lamotrigine or levetiracetam were not found to be at an increased risk of significant birth defects in comparison to control children and had lower risks when directly compared to the children exposed to carbamazepine, phenytoin or topiramate.

Informing complex discussions

Professor of Neurology Tony Marson from the University of Liverpool's Institute of Translational Medicine, said: "This is a really important review that informs complex discussions during consultations about epilepsy treatment choices for women of childbearing potential, who represent around a third of people with epilepsy worldwide.

"Based on current evidence, levetiracetam and lamotrigine appear to be the AEDs associated with the lowest level of risk, but more data are needed, particularly concerning individual types of malformation."

The full study, entitled 'Monotherapy treatment of epilepsy in pregnancy: congenital malformation outcomes in the child (Review)', can be found here http://bit.ly/2gCQWyB

http://bit.ly/2qMjiqN

Using drugs for different diseases than initially intended for

This is how we traditionally think about pharmaceutical drugs, but many of them are actually effective for more than one disease.

Take the drug gabapentin, originally developed for treating epilepsia, but today commonly prescribed as a pain killer. Or sildenafil, originally developed for treating high blood pressure, but today more often used to treat erectile dysfunction.

Value for patients

"With our recent research we predicted yet unknown beneficial effects for many drugs - on different diseases than they were initially developed for. This is of immense value, both for patients and for the pharmaceutical industry - in particular when it comes to avoiding expensive clinical trials on drug safety", says associate professor Jan Baumbach, University of Southern Denmark.

Jan Baumbach is an expert in computational biomedicine and his research focuses on retrieving meaningful information from big data generated nowadays in the health care sector.

Together with his colleagues Peng Sun from the Max-Planck Institute for Informatics in Germany, Jiong Guo from ShanDong University in China, and Rainer Winnenburg from Stanford University in the U.S., Baumbach has used novel big data analytics methods to trawl through massive pharmaceutical data, looking for drugs having a high potential to be what the scientists call "repurposable".

The results are published in the journal Drug Discovery Today.

From inflammatory diseases to Parkinson's

Baumbach's team found ca. thirty thousand "repurposable" drug candidates. Of these ca. eleven thousand have already been mentioned in scientific literature, and about 1,400 are reported in literature as concrete "repurposing" options.

This leaves roughly 19,000 highly confident drug-disease combinations that no one has yet considered to investigate - a huge gold mine for future pharmaceutical research.

One example is prednisone, originally developed to treat inflammatory diseases. This drug turns out to hold promise for treating Parkinson's disease as well. Another example is chlorpromazine, originally developed to treat schizophrenia, but likely to be effective against tuberculosis as well.

Avoiding animal trials

According to Baumbach and his co-authors, the pharmaceutical industry is facing great challenges due to a decreasing speed of new drug discoveries. New approaches are necessary.

"Drug design is extremely expensive, time-consuming and becoming increasingly complicated. Our approach is a way of inferring new purposes of existing drugs computationally - saving a lot of time, money and maybe more important, avoiding potentially dangerous animal and clinical trials", says Baumbach.

In their paper, the researchers write that the development cycle can be reduced through repositioning by as long as five years, compared to traditional drug discovery pipelines, adding:

Reduced safety risk for patients

"Repurposable drugs have significantly reduced safety risks for patients, because already known and registered drugs have been thoroughly studied with respect to their toxicity and possible side-effects."

The total list of the discovered 31,731 candidates is freely available and can be obtained from the researchers or the publication's online supplementary material. The list includes, for instance, a drug used to treat hypertension or one with anti-inflammatory effect given after organ transplantation that might be well suitable for treating certain cancer types.

Side bar: How did they find the candidates?

Computational approaches play an increasingly important part in nowadays pharmaceutical discoveries. In this case, the researchers created a new data model allowing them to mine for shared properties between genes, drugs and diseases, and to combine this novel data structure with an artificial intelligence to mine millions of scientific publications for approving or disproving hints.

http://nyti.ms/2qPGTa3

F.D.A. Agrees to New Trials for Ecstasy as Relief for PTSD Patients

Phase 3 clinical trials of the drug begin — a final step before possible approval of Ecstasy as a prescription drug

By DAVE PHILIPPS NOV. 29, 2016

CHARLESTON, S.C. — After three tours in Iraq and Afghanistan, C. J. Hardin wound up hiding from the world in a backwoods cabin in North Carolina. Divorced, alcoholic and at times suicidal, he had tried almost all the accepted treatments for post-traumatic stress disorder: psychotherapy, group therapy and nearly a dozen different medications.

"Nothing worked for me, so I put aside the idea that I could get better," said Mr. Hardin, 37. "I just pretty much became a hermit in my cabin and never went out."

Then, in 2013, he joined a small drug trial testing whether PTSD could be treated with MDMA, the illegal party drug better known as Ecstasy.

"It changed my life," he said in a recent interview in the bright, airy living room of the suburban ranch house here, where he now lives while going to college and working as an airplane mechanic. "It allowed me to see my trauma without fear or hesitation and finally process things and move forward."

Based on promising results like Mr. Hardin's, the Food and Drug Administration gave permission Tuesday for large-scale, Phase 3 clinical trials of the drug — a final step before the possible approval of Ecstasy as a prescription drug.

If successful, the trials could turn an illicit street substance into a potent treatment for PTSD.

Through a spokeswoman, the F.D.A. declined to comment, citing regulations that prohibit disclosing information about drugs that are being developed.

"I'm cautious but hopeful," said Dr. Charles R. Marmar, the head of psychiatry at New York University's Langone School of Medicine, a leading PTSD researcher who was not involved in the study. "If they can keep getting good results, it will be of great use. PTSD can be very hard to treat. Our best therapies right now don't help 30 to 40 percent of people. So we need more options."

But he expressed concern about the potential for abuse. "It's a feel-good drug, and we know people are prone to abuse it," he said. "Prolonged use can lead to serious damage to the brain."

The Multidisciplinary Association for Psychedelic Studies, a small nonprofit created in 1985 to advocate the legal medical use of MDMA, LSD, marijuana and other banned drugs, sponsored six Phase 2 studies treating a total of 130 PTSD patients with the stimulant. It will also fund the Phase 3 research, which will include at least 230 patients.

Two trials here in Charleston focused on treating combat veterans, sexual assault victims, and police and firefighters with PTSD who had not responded to traditional prescription drugs or psychotherapy. Patients had, on average, struggled with symptoms for 17 years.

After three doses of MDMA administered under a psychiatrist's guidance, the patients reported a 56 percent decrease of severity of symptoms on average, one study found. By the end of the study, two-thirds no longer met the criteria for having PTSD. Follow-up examinations found that improvements lasted more than a year after therapy.

"We can sometimes see this kind of remarkable improvement in traditional psychotherapy, but it can take years, if it happens at all," said Dr. Michael C. Mithoefer, the psychiatrist who conducted the

trials here. “We think it works as a catalyst that speeds the natural healing process.”

The researchers are so optimistic that they have applied for so-called breakthrough therapy status with the Food and Drug Administration, which would speed the approval process. If approved, the drug could be available by 2021.

Under the researchers’ proposal for approval, the drug would be used a limited number of times in the presence of trained psychotherapists as part of a broader course of therapy. But even in those controlled circumstances, some scientists worry that approval as a therapy could encourage more illegal recreational use.

“It sends the message that this drug will help you solve your problems, when often it just creates problems,” said Andrew Parrott, a psychologist at Swansea University in Wales who has studied the brains of chronic Ecstasy users. “This is a messy drug we know can do damage.” Allowing doctors to administer the drug to treat a disorder, he warned, could inadvertently lead to a wave of abuse similar to the current opioid crisis.

During initial studies, patients went through 12 weeks of psychotherapy, including three eight-hour sessions in which they took MDMA. During the sessions, they lay on a futon amid candles and fresh flowers, listening to soothing music.

Dr. Mithoefer and his wife, Ann Mithoefer, and often their portly terrier mix, Flynn, sat with each patient, guiding them through traumatic memories. “The medicine allows them to look at things from a different place and reclassify them,” said Ms. Mithoefer, a psychiatric nurse. “Honestly, we don’t have to do much. Each person has an innate ability to heal. We just create the right conditions.”

Research has shown that the drug causes the brain to release a flood of hormones and neurotransmitters that evoke feelings of trust, love and well-being, while also muting fear and negative emotional memories that can be overpowering in patients with post-traumatic stress disorder. Patients say the drug gave them heightened clarity and ability to address their problems.

For years after his combat deployments, Mr. Hardin said he was sleepless and on edge. His dreams were marked with explosions and death. The Army gave him sleeping pills and antidepressants. When they didn’t work, he turned to alcohol and began withdrawing from the world. “I just felt hopeless and in the dark,” he said. “But the MDMA sessions showed me a light I could move toward. Now I’m out of the darkness and the world is all around me.”

Since the trial, he has gone back to school and remarried.

The chemist Alexander Shulgin first realized the euphoria-inducing traits of MDMA in the 1970s, and introduced it to psychologists he knew. Under the nickname Adam, thousands of psychologists began to use it as an aid for therapy sessions. Some researchers at the time thought the drug could be helpful for anxiety disorders, including PTSD, but before formal clinical trails could start, Adam spread to dance clubs and college campuses under the name Ecstasy, and in 1985, the Drug Enforcement Administration made it a Schedule 1 drug, barring all legal use.

Since then, the number of people seeking treatment for PTSD has exploded and psychiatry has struggled to keep pace. Two drugs approved for treating the disorder worked only mildly better than placebos in trials. Current psychotherapy approaches are often slow and many patients drop out when they don’t see results. Studies have shown combat veterans are particularly hard to treat.

In interviews, study participants said MDMA therapy had not only helped them with painful memories, but also had helped them stop abusing alcohol and other drugs and put their lives back together.

On a recent evening, Edward Thompson, a former firefighter, tucked his twin 4-year-old girls into bed, turned on their night light, then joined his wife at a backyard fire.

“If it weren’t for MDMA … ” he said.

“He’d be dead,” his wife, Laura, finished.

They both nodded.

Years of responding to gory accidents left Mr. Thompson, 30, in a near constant state of panic that he had tried to numb with alcohol and prescription opiates and benzodiazepines.

By 2015, efforts at therapy had failed, and so had several family interventions. His wife had left with their children, and he was considering jumping in front of a bus.

A member of a conservative Anglican church, Mr. Thompson had never used illegal drugs. But he was struggling with addiction from his prescription drugs, so he at first rejected a suggestion by his therapist that he enter the study. “In the end, I was out of choices,” he said.

Three sessions with the drug gave him the clarity, he said, to identify his problems and begin to work through them. He does not wish to take the drug again. “It gave me my life back, but it wasn’t a party drug,” he said. “It was a lot of work.”

http://bit.ly/2fSOlio

A method for storing vaccines at room temperature

Shipping vaccines in an unbroken temperature-controlled supply chain (a "cold chain") all the way to recipients is a major logistical and financial challenge in remote areas and developing countries.

According to Doctors Without Borders, the need to keep vaccines within a temperature range of 2-8°C is one of the main factors behind low immunization-coverage rates.

Researchers at EPFL's Supramolecular Nanomaterials and Interfaces Laboratory (SUNMIL), in collaboration with scientists in Milan, Turin, Leiden, and Oregon, have come up with three simple and inexpensive vaccine additives to get around this obstacle. Using minute quantities of nanoparticles, or FDA-approved polymer (polyethylene glycol), or higher amounts of sucrose, they were able to stabilize vaccines at room temperature for several weeks or, in some cases, months. Their approach, which was successfully tested on a vaccine for rodents, is published in Nature Communications.

Nanoparticles, polymers and sugar

The study addressed viral-vector vaccines, the most common type of vaccine, which normally only last for a few days at room temperature. At that point, the viral components of the vaccines lose their structural integrity. "These components fluctuate by their very nature," Stellacci, head of SUNMIL - Constellium Chair. "They are combined in a stable form, and the low temperature maintains that balance. But the thermally induced fluctuations eventually lead to a loss of integrity of the viral vector." The scientists' approach, which consists of stabilizing the vaccines against such fluctuations through simple biocompatible additives, has delivered excellent results.

In their first approach, osmotic pressure is applied on the inactivated viruses (the main component of the vaccine) using a cloud of negatively charged nanoparticles. The virus is already subject to an outward osmotic pressure due to its genetic material (RNA or DNA), which has a high negative charge and is held inside the virus. The nanoparticles form a cloud of negatively charged objects that cannot enter the virus, thus generating counter-osmotic pressure that keeps the virus intact. "With this method, infectivity for a virus reached a half-life of 20 days," says Stellacci.

The second approach consists in stiffening the virus's capsid, which envelops the inactivated virus, by adding polymers. This additive mainly stabilizes the virus by slowing its oscillations by changing the stiffness of the capsid. As a result, the vaccine remained fully intact for 20 days with an estimated half-life of ~70 days.

Finally, adding sucrose, a common sugar, to the vaccine makes the environment more viscous and slows down fluctuations. "It's a little like adding honey, where all motion is slowed down," says Stellacci. With this third approach, 85% of the vaccine's properties were intact after 70 days.

Tests on the Chikungunya virus

Using these results, the researchers applied their methods to a vaccine that is currently in development. They were able to stabilize a vaccine

against Chikungunya, a tropical virus, for 10 days, and then successfully inoculated mice with it. "The next step will be to run more extensive tests on specific vaccines, possibly combining the three different approaches."

Cheaper access

This study could really impact the effort to increase immunization coverage. Currently, in areas where electricity and refrigeration are limited, vaccines are moved from one refrigerated space to the next and then delivered to recipients in coolers. This complicated process accounts for nearly 80% of the cost of vaccination programs. And that, up until now, has been a significant impediment.

Source: M. Pelliccia, P. Andreozzi, J. Paulose, M. D'Alicarnasso, V. Cagno, M. Donalisio, A. Civra, R. M. Broeckel, N. Haese, P. Jacob Silva, R P. Carney, V. Marjoma, D. N. Streblow, D. Lembo, F. Stellacci, V. Vitelli & S. Krol. Additives to improve thermal stability of adenoviruses from hours to months: implications for vaccine storage. Nature Communications

http://bit.ly/2qOdTSi

Aspirin regimen for older adults has long-term benefits

A new USC study seeks to clarify confusion over aspirin and finds that older Americans could reduce their risks of heart disease and cancer, with wider use

For older Americans with a high risk of heart disease, taking low-dose aspirin every day could reduce their risk of a heart attack, prevent some cancers and cancer death, extend their lives and save the lives of hundreds of thousands of patients over the course of 20 years, according to a new USC study.

In addition, USC researchers who conducted the study found that a daily aspirin regimen by older patients would result in an estimated net health benefit worth $692 billion for the U.S. population. Their findings were published Wednesday in the journal PLOS ONE.

"Although the health benefits of aspirin are well established, although few people take it," said lead author David B. Agus, the founding director and CEO of the Lawrence J. Ellison Institute for Transformative Medicine at USC, and a USC professor of medicine and engineering. Our study shows multiple health benefits and a reduction in healthcare spending from this simple, low-cost measure that should be considered a standard part of care for the appropriate patient."

The long-term benefits of low-dose, daily aspirin were questioned this year after the U.S. Preventive Services Task Force (USPSTF), a government-backed panel of experts, issued updated aspirin guidelines that declared the clinical benefit of aspirin, but seemed at odds with the U.S. Food and Drug Administration. The FDA is concerned that some patients, particularly those 60 and older, face an increased risk of stroke and bleeding - both gastrointestinal and in the brain - if they take aspirin daily.

"The problem that this creates for Americans and medical professionals is that the information about aspirin is confusing," said study co-author Étienne Gaudette, an assistant professor in the USC School of Pharmacy and policy director of the USC Roybal Center for Health Policy Simulation. "This means some Americans who would benefit from aspirin aren't taking it. Through our study, we sought to make it much easier for everyone to understand what the long-term benefits are. "

Cardiovascular disease is the leading cause of death in both men and women. One in every 4 deaths in the United States each year is attributed to heart disease, according to the Centers for Disease Control and Prevention. Aspirin can help patients at risk of heart disease because it thins the blood and prevents clotting.

Last April, the USPSTF ultimately recommended low-dose aspirin use to prevent heart disease and colorectal cancer for only certain older adults: those 50 to 59 years old who have at least a 10 percent or greater risk of developing heart disease in 10 years, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years. (The risks for heart disease include high blood pressure and high cholesterol.)

Adults 60 to 69 years old who face a greater-than-10-percent risk of developing heart disease and a risk of bleeding may decide individually whether to take aspirin every day. Anyone else in that age bracket who is expected to live another 10 years is more likely to benefit.

Its recommendations were based on a data from the American College of Cardiology/American Heart Association/American Heart Association, which had based its conclusions on a cohort. For their study, the USC researchers utilized representative data from several national surveys.

Simulating elderly lives

To assess the long-term benefits of aspirin, the USC researchers ran two scenarios through the USC Leonard D. Schaeffer Center for Health Economics and Policy's Future Elderly Model, which projects the health of older Americans and their trajectory in aging. It relies on national data sets: the U.S. Health and Retirement Study of Americans 51 and older, the large-scale Medical Expenditure Panel Survey of non-institutionalized Americans, and the Medicare Current Beneficiary Survey. The researchers also relied on data from the National Health and Nutrition Examination Survey.

The model accounts for individual health characteristics such as chronic disease, the ability to conduct daily activities, body mass index and mortality.

The first scenario in the USC aspirin study, the "Guideline Adherence," focused on determining the potential health and savings benefits and drawbacks of following the task force's guidelines from 2009. The second scenario, "Universal Eligibility," was not realistic and aimed to measure the full potential benefits and drawbacks if all Americans 51 and older, regardless of the guidelines, took aspirin every day.

The researchers found that following the guidelines would prevent 11 cases of heart disease and four cases of cancer for every 1,000 Americans aged 51 to 79. Life expectancy would improve by 0.3 years (largely disability-free), so out of 1,000 people, eight more Americans would reach age 80 and three more would reach the age of 100.

Also, by 2036, an estimated 900,000 more Americans would be alive.

The researchers found no significant reduction for stroke incidence. Also, the rate of gastrointestinal bleeding would increase 25 percent from the current rate, and this means that 2 out of 63 Americans could expect to suffering a bleeding incident between age 51 to 79.

The optimistic Universal Eligibility scenario, which assumes that the clinically-proven benefits of aspirin extend to all older Americans, showed slightly larger health benefits than the Guideline Adherence scenario. Although longer lifespans mean an increase in lifetime medical costs, "observing the guidelines would yield positive and significant net value," the researchers wrote.

"The irony of our findings is that aspirin may be too cheap," says study co-author Dana Goldman, director of the Schaeffer Center for Health Policy and Economics and distinguished professor of public policy, pharmacy, and economics. "Only 40 percent of Americans are taking aspirin when they should, and providers have little incentive to push that number up, despite the obvious health benefits and healthcare savings." "Until we figure out how to reward providers - and manufacturers -- for long-term outcomes, no one is going to do anything about this problem," he added.

Andrew Messali of Analysis Group was also an author on the study.

http://bit.ly/2qO5Epo

Benefits of daily aspirin outweigh risk to stomach

Stomach bleeds caused by aspirin are considerably less serious than the spontaneous bleeds that can occur in people not taking the drug, concludes a study led by Cardiff University.

Published in the journal Public Library of Science, the extensive study of literature on aspirin reveals that while regular use of the drug increases the risk of stomach bleeds by about a half, there is no valid evidence that any of these bleeds are fatal.

Professor Peter Elwood from Cardiff University's School of Medicine said: "Although many people use aspirin daily to reduce the risk of health problems such as cancer and heart disease, the wider use of the drug is severely limited because of the side effect of bleeding from the stomach. With our study showing that there is no increased risk of death from stomach bleeding in people who take regular aspirin, we hope there will be better confidence in the drug and wider use of it by older people, leading to important reductions in deaths and disablement from heart disease and cancer across the community."

Heart disease and cancer are the leading causes of death and disability across the world, and research has shown that a small daily dose of aspirin can reduce the occurrence of both diseases by around 20-30%.

Recent research has also shown that low-doses of aspirin given to patients with cancer, alongside chemotherapy and/or radiotherapy, is an effective additional treatment, reducing the deaths of patients with bowel, and possibly other cancers, by a further 15%.

The study 'Systematic review and meta-analysis of randomised trials to ascertain fatal gastrointestinal bleeding events attributable to preventive low-dose aspirin: No evidence of increased risk' can be found in Public Library of Science.

This study was a systematic review and meta-analysis of randomised trials. This type of research provides the strongest evidence for drawing causal conclusions because it draws together all of the best evidence.

http://bit.ly/2fT57hA

How highs and lows in testosterone levels 'shock' prostate cancer cells to death

Munich, Germany: A strategy of alternately flooding and starving the body of testosterone is producing good results in patients who have metastatic prostate cancer that is resistant to treatment by chemical or surgical castration, according to new findings.

In a presentation at the 28th EORTC-NCI-AACR [1] Symposium on Molecular Targets and Cancer Therapeutics in Munich, Germany, today (Thursday), researchers reported that results from 47 men who have completed at least three cycles of bipolar androgen therapy (BAT) showed that the strategy was safe and effective. Prostate specific antigen (PSA) levels [2] fell in the majority of the men, tumours shrank in some men, in several the disease did not progress and this included some whose disease continued to be stable for more than a year. One man appears to have been "cured", in that his PSA levels dropped to zero after three months and have remained so for 22 cycles of treatment, with no trace of the disease remaining. The researchers are planning to treat a group of 60 men in total.

Sam Denmeade MD, professor of oncology at Johns Hopkins University School of Medicine (Baltimore, USA) told the Symposium: "We think the results are unexpected and exciting. We are still in the early stages of figuring out how this works and how to incorporate it into the treatment paradigm for prostate cancer."

Traditionally, treatments for prostate cancer have involved lowering the levels of the male hormone (or androgen) testosterone using drugs called luteinising hormone-releasing hormone (LHRH) agonists, as it was thought that androgens stimulate the cancer cells to grow. However, Prof Denmeade says there is no evidence that testosterone promotes cancer.

"Indeed, earlier research in prostate cancer cell lines has shown that treatment with high doses of testosterone could inhibit growth and kill cancer cells. The exact mechanism is not known and there may be many things happening since the androgen receptor is the key signalling pathway in prostate cancer," he said. "In our lab we have observed that testosterone interferes with part of the cell division process in cancer cells called DNA licensing; it also seems to cause prostate cancer cells to make breaks in their DNA. So too much testosterone can cause cancer cells to die. It can also induce something we call senescence, which means the cancer cells become like old men who sit around and tell stories but don't make much trouble."

In an ongoing study called RESTORE, 47 men with castration resistant prostate cancer that had started to spread to other parts of the body (metastasise), who showed no symptoms but whose disease had become resistant to treatment with either abiraterone (17 patients) or enzalutamide (30 patients) receive a high dose of testosterone (400 mg), injected into the muscle every 28 days. At the same time the men continued on their LHRH agonist therapy to clamp down on testosterone produced naturally by the testicles. The men also stopped taking abiraterone or enzalutamide. These two anti-cancer therapies work by inhibiting androgen receptor signalling.

"Our goal is to shock the cancer cells by exposing them rapidly to very high followed by very low levels of testosterone in the blood," explained Prof Denmeade. These alternating extremes in testosterone levels are why the researchers call the therapy "bipolar".

Men with declining PSA levels or stable disease continued with BAT after three cycles, and if their disease started to progress they were treated again with abiraterone or enzalutamide.

The study has completed enrolment of the required 30 men in the first arm of the study who were treated with testosterone after their disease became resistant to enzalutamide and started to progress. Presenting results from this group, Prof Denmeade said: "Thus far we have observed dramatic PSA response in a subset of men; PSA levels declined in about 40% of men and in about 30% of men levels fell by more than 50%. Some men also have objective responses with a decrease in the size of measurable disease, mostly in lymph nodes. Many of the men have stable disease that has not progressed for more than 12 months. I think we may have cured one man whose PSA dropped to zero after three months and has remained so now for 22 cycles. His disease has all disappeared."

So far, 17 of the 30 men in the second arm of the study whose disease had started to progress again after treatment with abiraterone have received testosterone. Prof Denmeade said: "PSA responses were also observed in this group, but full results will not be presented until all 30 men have been enrolled over the next year."

All men in the study were tested for circulating tumour cells in their blood and six of them were found to have a protein called androgen-receptor splice variant (AR-V7), which may be associated with resistance to treatment with enzalutamide. After BAT treatment, AR-V7 disappeared from the blood of all six men, and two of the men had declines in PSA levels of 50% and over.

So far, BAT has been well-tolerated by patients with no dose-limiting toxicities. One patient had an increase in pain and one had a problem with retention of urine. "The benefits of the treatment are particularly evident in men who have had no sexual function for many years due to impotence caused by hormone deprivation. These men are quite happy with the new treatment. Other positives include increase in muscle strength, increased energy and decreased fatigue. This does not occur in every man and we are not sure exactly why."

More research still needs to be conducted on BAT. Prof Denmeade said: "We caution that this is still experimental. In particular, this therapy should only be given to men who are asymptomatic. Testosterone treatment can definitely worsen pain in men with prostate cancer who have pain from their disease."

A multi-centre randomised trial in the USA called TRANSFORMER is testing BAT versus enzalutamide in men with metastatic castrate-resistant prostate cancer whose disease had progressed after being treated with abiraterone. So far it has recruited 111 men with a target of 180. "If we find testosterone is superior then we would hope to move on to larger trials. Our problem is this is not a drug that is owned by a pharmaceutical company; it is generic testosterone. So moving forward is going to be difficult due to issues with finding funds to run a bigger trial," concluded Prof Denmeade.

Chair of the scientific committee for the Symposium, Professor Jean Charles Soria from the Institut Gustave Roussy (France), commented: "The use of testosterone in men with castration-resistant prostate

cancer is an intriguing concept that was previously advocated some years ago, but this is the first time we have clinical data in patients whose disease has progressed after treatment with abiraterone or enzalutamide."

[1] EORTC [European Organisation for Research and Treatment of Cancer, NCI [National Cancer Institute], AACR [American Association for Cancer Research].

[2] PSA is a protein produced by normal cells in the prostate and also by prostate cancer cells. PSA levels rise as men get older, but abnormally high levels may be an indication of cancer and PSA levels are measured to see whether anti-cancer treatments are working or not.

[3] The initial pilot study (in just 14 men in the era before abiraterone or enzalutamide) was funded by the One-in-Six Foundation, set up by one of Professor Denmeade's patients who was suffering from prostate cancer and wanted to make a difference. Based on the preliminary data, the researchers received funding from the USA's National Institutes of Health (NIH) to perform RESTORE and a Transformative Impact grant from the Department of Defense Prostate Cancer Research Program to perform TRANSFORMER.

http://bit.ly/2qOiCDq

Human ancestor 'Lucy' was a tree climber, new evidence suggests

Evidence preserved in the skeletal structure Lucy suggests the ancient human species frequently climbed trees

AUSTIN, Texas -- Evidence preserved in the internal skeletal structure of the world-famous fossil, Lucy, suggests the ancient human species frequently climbed trees, according to a new analysis by scientists from The Johns Hopkins University and The University of Texas at Austin.

Since Lucy's discovery in Ethiopia 42 years ago this month by Arizona State University anthropologist Donald Johanson and graduate student Tom Gray, paleontologists have debated whether the 3.18 million-year-old specimen of Australopithecus afarensis -- or southern ape of Afar -- spent her life walking on the ground or combined walking with frequent tree climbing.

A new analysis of the partially fossilized skeleton, to be published Nov. 30 in the journal PLOS ONE, shows that Lucy's upper limbs were heavily built, similar to tree-climbing chimpanzees, supporting the idea that she often used her arms to pull herself up, most likely onto tree branches. Researchers also suggest that because her foot was better adapted for bipedal locomotion -- or upright walking -- rather than grasping, Lucy had to rely on upper-body strength when climbing, which resulted in more heavily built upper-limb bones.

"It may seem unique from our perspective that early hominins like Lucy combined walking on the ground on two legs with a significant amount of tree climbing, but Lucy didn't know she was unique," said UT Austin paleoanthropologist John Kappelman, whose most recent study proposed Lucy probably died after falling from a tall tree, where she may have been nesting to avoid predators. A nightly ascent would equate to one-third of her life spent in trees -- or more if she occasionally foraged there, Kappelman said.

"We were able to undertake this study thanks to the relative completeness of Lucy's skeleton," said the study's lead author, Christopher Ruff, a professor of functional anatomy and evolution at the Johns Hopkins University School of Medicine. "Our analysis required well-preserved upper and lower limb bones from the same individual, something very rare in the fossil record."

The research team first examined Lucy, who is among the oldest, most complete skeletons of any adult, erect-walking human ancestor, during her U.S. museum tour in 2008, when the fossil was detoured briefly to the High-Resolution X-ray Computed Tomography Facility (UTCT) in the UT Jackson School of Geosciences. For 10 days, Kappelman and UT Austin geological sciences professor Richard Ketcham carefully scanned all of her bones to create a digital archive of more than 35,000 CT slices.

"We all love Lucy, but we had to face the fact that she is a rock," said Ketcham, adding that conventional CT is not powerful enough to image the internal structure of Lucy's heavily mineralized skeleton. "The time for standard medical CT scanning was 3.18 million years ago. This project required a scanner more suited to her current state."

Since then, researchers have relied on the scans to look for clues about how Lucy lived, died and used her body -- estimated to be about 3 feet

6 inches and 60 pounds -- during her lifetime. The most recent study focused on the internal structure of Lucy's right and left humeri (upper arm bones) and left femur (thigh bone).

A major issue in the debate about Lucy's tree climbing has been how to interpret skeletal features that might be simply "leftover" from a more primitive ancestor that had relatively long arms, for example. The advantage of the new study, Ruff said, is that it focused on characteristics that reflect actual behavior during life. Some evidence even suggests she was right-handed, researchers said.

"Our study is grounded in mechanical engineering theory about how objects can facilitate or resist bending," Ruff said. "Our results are intuitive because they depend on the sorts of things that we experience about objects -- including body parts -- in everyday life. If, for example, a tube or drinking straw has a thin wall, it bends easily, whereas a thick wall prevents bending. Bones are built similarly."

Lucy's scans were compared with CT scans from a large sample of modern humans, who spend the majority of their time walking on two legs on the ground, and with chimpanzees, a species that spends more of its time in the trees and, when on the ground, usually walks on all four limbs.

"It is a well-established fact that the skeleton responds to loads during life, adding bone to resist high forces and subtracting bone when forces are reduced," Kappelman said. "Tennis players are a nice example: Studies have shown that the cortical bone in the shaft of the racquet arm is more heavily built up than that in the non-racquet arm."

Other comparisons in the study suggest that even when Lucy walked upright, she may have done so less efficiently than modern humans do, limiting her ability to walk long distances on the ground, Ruff said. In addition, all of her limb bones were found to be very strong relative to her body size, indicating that she had exceptionally strong muscles, more like those of modern chimpanzees than modern humans. A reduction in muscle power later in human evolution may be linked to better technology that reduced the need for physical exertion and the increased metabolic demands of a larger brain, the researchers said.

Other scholastic materials and the 3-D files are available on eLucy.org. Permissions to scan, study and photograph Lucy were granted by the Authority for Research and Conservation of Cultural Heritage and the National Museum of Ethiopia of the Ministry of Tourism and Culture. The UTCT was supported by three grants from the U.S. National Science Foundation.

http://bit.ly/2h2dKLA

After concussion, rest may not always be the best medicine, experts say

Growing body of evidence suggests that a more active, targeted approach might provide better outcomes for some patients

Prescribed rest--both physical and mental--is the standard treatment for concussion. But a growing body of evidence suggests that a more active, targeted approach might provide better outcomes for some patients, reports a special article in the December issue of Neurosurgery, official journal of the Congress of Neurological Surgeons (CNS). The journal is published by Wolters Kluwer.

"Matching treatments to specific symptoms, impairments, and clinical profiles may...improve recovery after concussion," according to the statement by panel of medical and other experts. While more research is needed, the panel cites emerging evidence that "multiple active rehabilitation strategies" might be more effective than simply recommending rest for every patient with concussion. Michael W. Collins, PhD, of University of Pittsburgh is lead author of the new report.

'Active and Targeted Treatments' May Enhance Recovery after Concussion

Dr. Collins and coauthors present a series of "statements of agreement" by a team of concussion experts from various healthcare disciplines as well as from sport, military, and public health organizations. The "Targeted Evaluation and Active Management" (TEAM) panel met at a conference held in Pittsburgh in 2015, sponsored by the National Football League and University of Pittsburgh Medical Center.

Conference participants indicated their level of agreement with a series of statements regarding current and evolving treatment strategies for concussion. Current approaches emphasize immediately removing the injured person from sports or other activity, followed by a prescribed period of physical and cognitive (mental) rest and gradual return to participation.

But the panel agreed that there is "limited empirical evidence" to support the effectiveness of prescribed rest--and that rest may not be the best approach for all patients. "Concussions are characterized by diverse symptoms and impairments and evolving clinical profiles," Dr. Collins and colleagues write. "[R]ecovery varies on the basis of modifying factors, injury severity, and treatments."

The panel also weighed the emerging evidence on the "TEAM approach" as an alternative to prescribed rest. Preliminary research suggests that active treatment can be started early after concussion, and that matching targeted and active treatments to the patient's clinical profile may improve recovery. For example, some patients might receive individualized management to support them in returning to school or work. Others might receive medications to treat certain concussion-related symptoms and impairments.

Yet so far, there's little high-quality research to support specific treatments or medications for concussion management. The panel highlights severe key areas for further research--especially the need for multisite, prospective studies of specific treatments across various time points after concussion.

"No single treatment strategy will be effective for all patients after concussion because of the individualized natures of the injury and its clinical consequences," Dr. Collins and coauthors write. "Research is needed on concussion clinical profiles, biomarkers, and the effectiveness and timing of treatments."

The TEAM panel hopes their experience will help to increase awareness that all concussions are not the same and that, for some patients, treatment based on individual clinical profiles might be more effective than prescribed rest. They write, "Concussion symptoms and impairments are treatable, and active rehabilitations involving a multidisciplinary treatment team may enhance recovery."

Click here to read "Statements of Agreement From the Targeted Evaluation and Active Management (TEAM) Approaches to Treating Concussion Meeting Held in Pittsburgh, October 15-16, 2015."

Article "Statements of Agreement From the Targeted Evaluation and Active Management (TEAM) Approaches to Treating Concussion Meeting Held in Pittsburgh, October 15-16, 2015" (doi: 10.1227/NEU.0000000000001447)

http://bit.ly/2g4rUdB

Parkinson's disease may start in the gut and travel to the brain

It seems the nerve damage behind Parkinson's starts in the stomach or colon before spreading to brain cells - but we don't know what's causing it

By Clare Wilson

WE HAVE been thinking about Parkinson's disease all wrong. The condition may arise from damage to the gut, not the brain.

If the idea is correct, it opens the door to new ways of treating the disease before symptoms occur. "That would be game-changing," says David Burn at Newcastle University, UK. "There are lots of different mechanisms that could potentially stop the spread."

Parkinson's disease involves the death of neurons deep within the brain, causing tremors, stiffness and difficulty moving. While there are drugs that ease these symptoms, they become less effective as the disease progresses.

One of the hallmarks of the condition is deposits of insoluble fibres of a substance called synuclein. Normally found as small soluble molecules in healthy nerve cells, in people with Parkinson's, something causes the synuclein molecules to warp into a different shape, making them clump together as fibres.

The first clue that this transition may start outside the brain came about a decade ago, when pathologists reported seeing the distinctive synuclein fibres in nerves of the gut during autopsies – both in people

with Parkinson's and in those without symptoms but who had the fibres in their brain. They suggested the trigger was some unknown microbe or toxin. "Knowing the location of the first strike allows for early detection – and treatment"

The finding made sense because people with Parkinson's often report digestive problems – mainly constipation – starting up to 10 years before they notice tremors. Interestingly, another early symptom of Parkinson's is loss of smell. It may be no coincidence, says Burn, that the nose and gut are two organs where nerve cells are exposed to the outside world – and to potentially problematic toxins and microbes.

Now, the synuclein fibres have been shown travelling from the gut to deep within the brain. Collin Challis at the California Institute of Technology and his colleagues injected synuclein fibres into the stomach and intestine of mice. Three weeks later the fibres could be seen at the base of the brain, and by two months they had travelled to parts of the brain that control movement. The mice also became less agile – similar to people with Parkinson's disease. The work was reported at the Society for Neuroscience meeting in San Diego last month.

This study builds on a growing body of work that the gut plays a role in Parkinson's, says Burn. For example, people who have had the main nerve to their stomach cut – an old treatment for stomach ulcers – have a lower risk of the condition.

No single bacterium or virus has been pinpointed as the cause. But early evidence suggests that people with Parkinson's have different gut bacteria to healthy people. Some doctors are already experimenting with treating patients with antibiotics or faecal transplants.

"It could be that having the wrong bacteria in your gut triggers inflammation," says Sébastien Paillusson at King's College London. "We know that inflammation makes synuclein more likely to aggregate."

Other studies have shown that farmers exposed to certain pesticides, and people who get their drinking water from wells – which might be contaminated with pesticides – are more likely to get Parkinson's. Perhaps these chemicals can also damage nerves in the gut.

Whatever the culprit, knowing the location of the first strike allows for early detection – and treatment. For instance, drugs that mop up synuclein fibres or block their formation are in the works. If these are given to people before the fibres reach the brain they should have a better chance of success. It might also be possible one day to screen for fibres in the nerves of the gut during colonoscopies for early-stage cancers, says Burn.

http://bit.ly/2fZ2Kyv

Portions of the brain fall asleep and wake back up all the time, Stanford researchers find

When we are in a deep slumber our brain's activity ebbs and flows in big, obvious waves, like watching a tide of human bodies rise up and sit down around a sports stadium. It's hard to miss.

Now, Stanford researchers have found, those same cycles exist in wake as in sleep, but with only small sections sitting and standing in unison rather than the entire stadium. It's as if tiny portions of the brain are independently falling asleep and waking back up all the time. What's more, it appears that when the neurons have cycled into the more active, or "on," state they are better at responding to the world. The neurons also spend more time in the on state when paying attention to a task. This finding suggests processes that regulate brain activity in sleep might also play a role in attention.

"Selective attention is similar to making small parts of your brain a little bit more awake," said Tatiana Engel, a postdoctoral fellow and co-lead author on the research, which is scheduled to publish Dec. 1 in Science. Former graduate student Nicholas Steinmetz was the other co-lead author, who carried out the neurophysiology experiments in the lab of Tirin Moore, a professor of neurobiology and one of the senior authors.

Cycling on and off

Understanding these newly discovered cycles requires knowing a bit about how the brain is organized. If you were to poke a pin directly into the brain, all the brain cells you'd hit would respond to the same types of things. In one column they might all be responding to objects in a particular part of the visual field - the upper right, for example.

The team used what amounts to sets of very sensitive pins that can record activity from a column of neurons in the brain. In the past, people had known that individual neurons go through phases of being more or less active, but with this probe they saw for the first time that all the neurons in a given column cycled together between firing very rapidly then firing at a much slower rate, similar to coordinated cycles in sleep.

"During an on state the neurons all start firing rapidly," said Kwabena Boahen, a professor of bioengineering and electrical engineering at Stanford and a senior author on the paper. "Then all of a sudden they just switch to a low firing rate. This on and off switching is happening all the time, as if the neurons are flipping a coin to decide if they are going to be on or off."

Those cycles, which occur on the order of seconds or fractions of seconds, weren't as visible when awake because the wave doesn't propagate much beyond that column, unlike in sleep when the wave spreads across almost the entire brain and is easy to detect.

Pay attention

The team found that the higher and lower activity states relate to the ability to respond to the world. The group had their probe in a region of the brain in monkeys that specifically detects one part of the visual world. The monkeys had been trained to pay attention to a cue indicating that something in a particular part of the visual field - the upper right, say, or the lower left - was about to change slightly. The monkeys then got a treat if they correctly identified that they'd seen that change.

When the team gave a cue to where a change might occur, the neurons within the column that senses that part of the world all began spending more time in the active state. In essence, they all continued flipping between states in unison, but they spent more time in the active state if they were paying attention. If the stimulus change came when the cells were in a more active state, the monkey was also more likely to correctly identify the change.

"The monkey is very good at detecting stimulus changes when neurons in that column are in the on state but not in the off state," Engel said. Even when the monkey knew to pay attention to a particular area, if the neurons cycled to a lower activity state the monkey frequently missed stimulus change.

Engel said this finding is something that might be familiar to many people. Sometimes you think you are paying attention, she pointed out, but you will still miss things.

The scientists said the findings also relate to previous work, which found that more alert animals and humans tend to have pupils that are more dilated. In the current work, when the brain cells were spending more time in an active state the monkey's pupils were also more dilated. The findings demonstrate an interaction between synchronous oscillations in the brain, attention to a task and external signs of alertness.

"It seems that the mechanisms underlying attention and arousal are quite interdependent," Moore said.

Low energy states

A question that comes out of this work is why the neurons cycle into a lower activity state when we're awake. Why not just stay in the more active state all the time in case that's when the saber tooth tiger attacks?

One answer could relate to energy. "There is a metabolic cost associated with neurons firing all the time," Boahen said. The brain uses a lot of energy and maybe giving the cells a chance to do the energetic equivalent of sitting down allows the brain to save energy.

Also, when neurons are very active they generate cellular byproducts that can damage the cells. Engel pointed out that the low-activity states could allow time to clear out this neuronal waste.

"This paper suggests places to look for these answers," Engel said.

Additional co-authors include colleagues from Newcastle University. Kwabena Boahen is also a member of Stanford Bio-X and the Stanford Neurosciences Institute. Tirin Moore is also an HHMI investigator as well as a member of Stanford Bio-X, the Stanford Neurosciences Institute and the Child Health Research Institute.

The work was funded by the NIH, Stanford NeuroVentures, the HHMI, the MRC and the Wellcome Trust.

http://bit.ly/2fYRBhh

Not much evidence behind advice to 'drink plenty of fluids' when unwell

Doctors often advise patients to 'drink plenty of fluids' and 'keep well hydrated' when unwell, but a new report calls for more research behind this advice.

Writing in the journal BMJ Case Reports, doctors explain the case of a 59-year-old woman who developed hyponatraemia -- a condition that occurs when the level of sodium is abnormally low -- from drinking too much water to help with a recurring urinary tract infection.

The patient was admitted to the Royal London Hospital Emergency Department, and was prescribed antibiotics and painkillers for her urinary tract infection. However, she became progressively shaky, muddled, vomited several times, and had significant speech difficulties. Tests revealed hyponatraemia - her sodium level was 123 mmol/L (normal range 135-145) - which the doctors say was the cause of these progressively worsening symptoms, and can result from water intoxication.

The patient revealed that throughout the day, she had consumed several litres of water based on medical advice she recalled from previous similar episodes to 'flush out her system'.

The condition is a medical emergency and requires prompt recognition and action. A mortality rate of almost 30% has been reported for patients with sodium levels of less than 125 mmol/L.

Doctors restricted her fluid intake to 1 litre over the following 24 hours, and by the following morning, she felt improved, her blood tests were normal, and she was discharged that day.

Fatal water intoxication has also been reported in endurance exercise, use of the drug MDMA, and anecdotally during university initiation activities as well as during water-based torture rituals.

This incident mirrors a previous case report, in which a woman developed hyponatraemia, and later died from drinking excessive amounts of water during an episode of gastroenteritis.

The doctors say it's very rare to develop water intoxication with normal renal function. However, some illnesses drive up levels of antidiuretic hormones, which reduce renal excretion of water. For these type of conditions, the doctors ask, should increased water intake be recommended?

They conclude: "There is a paucity of evidence behind the advice to 'drink plenty of fluids' in the management of mild infective illness. This needs to be addressed, especially considering the significant morbidity and mortality of acute hyponatraemia."

BMJ Case Report: When plenty is too much: water intoxication in a patient with a simple urinary tract infection http://casereports.bmj.com/content/2016/bcr-2016-216882

http://bit.ly/2qrYHXT

Frequency of tornado clusters in US is increasing

The frequency and magnitude of tornado outbreaks with many, or clusters, of tornadoes has increased in the United States over the past 50 years, a new study reports.

But whether this trend is driven by human-induced climate change, or other factors, remains unclear, making it difficult to predict whether it will continue.

Tornado outbreaks are sequences of six or more tornadoes that occur in close succession; in the United States, these so-called clusters caused 79% of tornado-related fatalities between 1972 and 2010. In analyzing how tornado outbreaks have changed between 1965 and 2015, Michael K. Tippett and colleagues found that, over five-year

periods, the estimated number of tornadoes in the most extreme outbreaks roughly doubled - from 40 in 1965 to nearly 80 in 2015. Even if the data is adjusted for differences in weather monitoring and recording, a significant increase in both frequency and intensity has occurred over recent decades. Intriguingly, the authors found that this increase did not correspond with factors that are associated with climate change, such as convective available potential energy.

They propose that another factor, such as one that drives low-frequency climate variability, may be at play. One example of such a driver is the Atlantic Multidecadal Oscillation (AMO), an oscillating pattern of sea surface temperatures that's known to affect climate in North America. Indeed, changes in the AMO do correlate with changes in tornado outbreaks; however, more evidence is needed to truly pinpoint the underlying cause of the increase.

A better understanding of the cause of these gustier, more frequent events is important for predicting whether this trend will continue in the future, the authors conclude.

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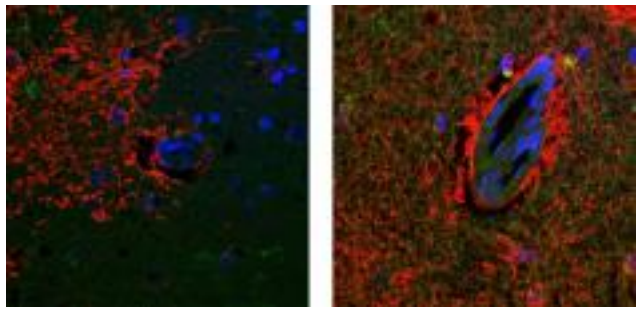
Study suggests possible new target for treating and preventing Alzheimer's

OHSU researchers compare prevalence of aquaporin-4 in the brains of those who had Alzheimer's to those who didn't have the disease

PORTLAND, Ore. - A new scientific discovery may provide a future avenue for treatment and prevention of Alzheimer's disease.

A study published Nov. 28 in the journal JAMA Neurology examined aquaporin-4, a type of membrane protein in the brain. Using brains donated for scientific research, researchers at OHSU discovered a correlation between the prevalence of aquaporin-4 among older people who did not suffer from Alzheimer's as compared to those who had the disease.

"It suggests that aquaporin-4 might be a useful target in preventing and treating Alzheimer's disease," said senior author Jeffrey Iliff, Ph.D., an Assistant Professor in the Department of Anesthesiology and Perioperative Medicine in the OHSU School of Medicine. "However, we aren't under any illusion that if we could just fix this one thing, then we'd be able to cure Alzheimer's Disease."



Two images compare brain scans from an older individual who had Alzheimer's (on the left) with an older cognitively healthy individual (n the right). The red fluorescence is the membrane protein aquaporin-4. The cognitively healthy individual has relatively even aquaporin-4 expression throughout the tissue and a stark enhancement of expression around the blood vessel, whereas the individual with Alzheimer's has uneven, "patchy" expression of aquaporin-4.
OHSU

Alzheimer's is a progressive disease, most often associated with aging, that causes problems with memory, thinking and behavior. It is the leading cause of dementia worldwide and is currently the sixth leading cause of death in the United States. The disease has no known cure but there are treatments available for some of its symptoms.

Aquaporin-4 is a key part of a brain-wide network of channels, collectively known as the glymphatic system, that permits cerebral-spinal fluid from outside the brain to wash away proteins such as amyloid and tau that build up within the brain. These proteins tend to accumulate in the brains of some people suffering from Alzheimer's, which may play a role in destroying nerve cells in the brain over time.

"This system, and the failure of the system, may be one of many things that goes wrong in people with Alzheimer's disease," Iliff said.

The study closely examined 79 brains donated through the Oregon Brain Bank, a part of the OHSU Layton Aging and Alzheimer's Disease Center. They were separated into three groups: People younger than 60 without a history of neurological disease; people older than 60 with a history of Alzheimer's; and people older than 60 without Alzheimer's.

Researchers found that in the brains of younger people and older people without Alzheimer's, the aquaporin-4 protein was well organized, lining the blood vessels of the brain. However within the brains of people with Alzheimer's, the aquaporin-4 protein appeared disorganized, which may reflect an inability of these brains to efficiently clear away wastes like amyloid beta. The study concluded that future research focusing on aquaporin-4 - either through its form or function - may ultimately lead to medication to treat or prevent Alzheimer's disease.

In 2015, a multidisciplinary team of scientists from OHSU led by Iliff was awarded a $1.4 million grant from the Paul G. Allen Family Foundation to use to develop new imaging techniques based on MRI to see these processes at work in the aging human brain for the first time.

In addition to Iliff, co-authors included Douglas M. Zeppenfeld; Matthew Simon, J. Douglas Haswell, and Daryl D'Abreo of the OHSU Department of Anesthesiology and Perioperative Medicine; Charles Murchison, Joseph F. Quinn, M.D., and Jeffrey Kaye, M.D., of the OHSU Department of Neurology; and Marjorie R. Grafe, M.D., Ph.D., and Randall L. Woltjer, M.D., Ph.D., of the Department of Pathology.

This work was supported by funding from the American Heart Association, grant 12SDG11820014, the Oregon Partnership for Alzheimer's Research, grants from the Research and Development Office of the Department of Veterans Affairs and the National Institutes of Health (NS089709), including Alzheimer's Disease Center grant AG08017 from the National Institute on Aging that supported the longitudinal follow-up and subsequent brain autopsies providing the human brain samples used in this study.

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Research shows patients ineligible for studies may benefit from trial participation

Some leukemia patients with existing medical conditions may be safely treated

Patients who potentially could benefit most from participation in clinical trials due to poor prognoses often are not included based on eligibility criteria, such as existing medical illnesses. A novel study at The University of Texas MD Anderson Cancer Center revealed some patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS), who traditionally could not be considered for clinical trials, responded well and were safely treated in this setting.

The study, led by Guillermo Garcia-Manero, M.D., professor of Leukemia, followed 109 patients with AML and MDS undergoing treatment with azacitidine (AZA) and vorinostat. Research results were presented Dec. 3 at the 58th Annual Meeting of the American Society for Hematology in San Diego.

"Most cancer clinical studies exclude patients with co-morbidities, active or recent malignancies, organ dysfunction or poor performance status," said Garcia-Manero. "How these criteria protect patients is unclear. Although some are based on clinical reasoning, it seems these criteria are in place more to protect the drug or intervention being studied rather than the patient."

The study initially enrolled 30 patients age 17 and older who had not previously been treated for AML or MDS. Patients eligible for the study had either poor performance, poor renal or hepatic function or any other active systemic disorder such as other cancer.

Sixty-day survival was 83 percent with low-grade gastrointestinal side effects reported. The study was expanded to include an additional 79 patients. Sixty-day survival for the second group was 79 percent with a median overall survival of 7.6 months. The average event-free survival was 4.5 months. Again, only low-grade gastrointestinal side effects were observed.

The study was designed with "stopping rules" that included monitoring of side effects and complete response rates. Patients were immediately placed on another therapy if their assigned therapy did not indicate there would be a complete response within a 60-day period. To define the minimum expected survival and response rates that would trigger the stopping rules, researchers relied on prior data of 181 patients previously treated at MD Anderson.

"Participation in clinical trials is fundamental for the development of new therapeutic interventions," said Guillermo Montalban-Bravo, M.D., fellow in Leukemia, a research team member. "Despite this

need, only three to five percent of patients with cancer treated in the U.S. currently are enrolled in clinical trials."

The study points to further evaluation of standard exclusion criteria, potentially increasing the pool of patient likely to benefit from therapy, with the aim of future larger clinical trials specifically treating patients with AML and MDS.

MD Anderson research team participants included: Elias Jabbour, M.D.; Gautam Borthakur, M.D.; Courtney DiNardo, M.D.; Naveen Pemmaraju, M.D.; Jorge Cortes, M.D.; Srdan Verstovsek, M.D.; Tapan Kadia, M.D.; Naval Daver, M.D.; William Wierda, M.D., Ph.D.; Yesid Alvarado, M.D.; Marina Konopleva, M.D., Ph.D.; Farhad Ravandi, M.D.; Zeev Estrov, M.D.; Nitin Jain, M.D.; Ana Alfonso Pierola, M.D., Ph.D.; Mark Brandt; Troy Sneed; Hui Yang, M.D., Ph.D.; Sherry Pierce; Elihu Estey, M.D.; Zachary Bohannan, and Hagop Kantarjian, M.D., all of Leukemia; Carlos Bueso-Ramos, M.D., Ph.D., Hematopathology; and Xuelin Huang, Ph.D. and Hsiang-Chun Chen, Biostatistics.

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http://bit.ly/2h4Xeqn

Marijuana Extract May Help Treat Severe Epilepsy, New Studies Show

A drug made from marijuana that does not produce a "high" may help reduce seizures in people with certain types of epilepsy that are difficult to treat, new research suggests.

By Rachael Rettner, Senior Writer

In two new studies, researchers tested the drug, which is a purified solution of cannabidiol (CBD), a compound found in marijuana. Although CBD affects the brain, it does not produce euphoria or intoxication, according to the National Institute on Drug Abuse.

One study involved 120 children with a rare and severe form of epilepsy called Dravet syndrome that had caused them to experience at least four seizures in the past month. The children were randomly assigned to take either the CBD medicine or a placebo, twice a day. After 14 weeks, the patients in the CBD group experienced a 39 percent reduction in the frequency of their seizures on average, compared with a 13 percent average reduction in the placebo group.

The other study involved 171 children and adults with a type of epilepsy called Lennox-Gastaut syndrome. The participants in that study also took either CBD or a placebo for 14 weeks. To be included in that study, participants had to experience at least two "drop" seizures a week. Drop seizures mean they went limp and fell to the ground.

The researchers found that the patients in the CBD group experienced an average reduction of 44 percent in the frequency of their drop seizures, compared with an average reduction of 22 percent in the placebo group. The finding suggests that CBD may be able to help treat patients with epilepsy who haven't benefited from standard epilepsy medications, the researchers said.

The CBD medicine "is not a silver bullet, but there are children who benefit from this more than they have from other treatments," Dr. Elizabeth Thiele, who worked on both studies and is the director of the Pediatric Epilepsy Program at Massachusetts General Hospital, said in a statement.

The patients in the new studies had tried four to six other anti-epilepsy drugs, which hadn't helped their seizures. During the studies, they continued taking any other drugs they were already on - an average of three anti-epilepsy drugs - along with the CBD or placebo treatment.

The new medicine, called Epidiolex (manufactured by GW Pharmaceuticals), is not yet approved by the Food and Drug Administration, and is also not yet available for sale, even in states where medical marijuana is legal. The studies were funded by GW Pharmaceuticals.

The findings add to previous research suggesting that Epidiolex can reduce seizures in patients with epilepsy. The new studies were more rigorous than earlier ones, because the new studies included a placebo group, while the earlier studies had not.

However, some patients in the new studies experienced mild to moderate side effects while taking CBD, including drowsiness, diarrhea, decreased appetite, fatigue, fever and vomiting. About 8 to 10 percent of patients experienced serious side effects that were thought to be related to the drug, including abnormal levels of liver enzymes.

Epilepsy patients who take CBD should be monitored closely, and have routine blood and liver tests, the researchers said. Patients may need to adjust other medications they are taking during their CBD treatment, they said.

A third, separate study tested the CBD medicine in 81 patients who had any type of epilepsy and had already tried at least four anti-epilepsy medications that hadn't helped their seizures. More than half (58 percent) of these participants experienced a 50 percent reduction in their seizure frequency, and a small number (9 percent) were seizure-free after the six-month study, the researchers said.

Still, not all patients benefited from the CBD treatment, and a few got worse, said study researcher Dr. Jerzy Szaflarski, director of the University of Alabama at Birmingham Epilepsy Center. Szaflarski said that more research is needed to determine why CBD helps some patients with epilepsy, but not others.

The studies were presented this week at the American Epilepsy Society Annual Meeting in Houston, and are not yet published in a peer-reviewed journal. GW Pharmaceuticals plans to submit Epidiolex for FDA approval in 2017, according to the American Epilepsy Society.

http://bit.ly/2qaC7Fd

Sydney schoolboys take down Martin Shkreli, the 'most hated man in the world'

a handful of year 11 students in Sydney have shown Shkreli up, cooking the same drug in their school lab for about $2 a dose

Marcus Strom

Martin Shkreli was the "big pharma bro" who outraged the world by hiking the price of an essential drug from $US13.50 ($18) to $US750 a tablet.

Now a handful of year 11 students in Sydney have shown him up, cooking the same drug in their school lab for about $2 a dose.

Daraprim is an anti-parasitic medicine used to treat infections such as toxoplasmosis and malaria. It is on the World Health Organisation's list of essential medicines.

The drug is used to treat people with low immune systems, such as people living with HIV, chemotherapy patients and pregnant women.

In September last year hedge-fund manager Shkreli gained control of Turing Pharmaceuticals and attracted worldwide opprobrium by increasing the price of the drug more than 5000 per cent. He went on to spend $US2 million on the only available copy of a Wu-Tang Clan album.

He was called "a morally bankrupt sociopath", a "scumbag" and "everything that is wrong with capitalism". Hillary Clinton accused him of price gouging and The Atlantic described him as "the face of unapologetic profiteering from the suffering of humans".

University of Sydney chemist Dr Alice Williamson thought it an ideal drug to synthesise in a school lab for chemistry students at Sydney Grammar School.

"The background to this made it seem more important," said James Wood, 17, one of the boys involved in the project. "Working on a real-world problem definitely made us more enthusiastic," said another of the Sydney Grammar boys, Austin Zhang, 17.

This is the second year that the University of Sydney's Open Source Malaria Consortium has done outreach work with Sydney Grammar. The consortium's guiding principle is to use publicly available drugs and medical approaches to cure malaria.

The work of Dr Williamson and consortium founder Associate Professor Matthew Todd has been praised by Bill Gates, whose foundation is looking for a cure to malaria.

"This has been a great pilot program. The next challenge is to work with kids from all sorts of schools," Dr Williamson said. She said this can happen one of two ways: "We can take students to labs or labs to students. "Not all schools have the lab facilities that Sydney Grammar has," she said. The consortium is looking to raise money to fit-out an RV [recreational vehicle] as a lab to take out to schools.

Given the public scandal from September last year, the boys definitely "shared the outrage of the general public", Dr Williamson said. And this gave more of a focus to the work.

The students started with 17 grams of the raw material 2,4-chlorophenyl acetonitrile, also called (4-chlorophenyl)acetonitrile. You can buy it online at $36.50 for 100 grams.

To make the Daraprim, the boys worked through a number of steps with their chemistry teacher, Dr Malcolm Binns. "We couldn't use the patented route as it involved dangerous reagents," he said.

Dr Williamson, Dr Binns and the boys had to find an innovative pathway from the starting compound to the end result.

They synthesised the end-product last week. Dr Williamson tested its purity in a spectrograph at university. "It's one of the most beautiful spectrographs I've ever seen, actually," she said.

From the 17 grams starting material, the boys produced 3.7 grams of pyrimethamine, the chemical name of Daraprim. "That's about $US110,000 worth of the drug," Dr Williams said, based on the price mark-up of Turing Pharmaceuticals.

But could they sell it on the open market in the US?

"While the drug is out of patent, Turing Pharmaceuticals controls its distribution and sale through a loophole called the 'closed distribution model'," said Associate Professor Todd. "To take the drug to market as a generic, you need to compare it to Turing's product. If Turing won't allow the comparisons to take place, you'd need to fund a whole new trial," he said.

The drug, however, is available in Australia for a reasonable price. Fifty tablets of a 25 milligram dose will cost $12.99.

On Wednesday the boys presented their results at the Royal Australian Chemical Institute NSW Organic Chemistry symposium. They did so alongside honours and postgraduate students, and postdoctorals.

http://bit.ly/2h9w71l

A handful of nuts a day cuts the risk of a wide range of diseases

A large analysis of current research shows that people who eat at least 20g of nuts a day have a lower risk of heart disease, cancer and other diseases.

The analysis of all current studies on nut consumption and disease risk has revealed that 20g a day - equivalent to a handful - can cut people's risk of coronary heart disease by nearly 30 percent, their risk of cancer by 15 percent, and their risk of premature death by 22 percent.

An average of at least 20g of nut consumption was also associated with a reduced risk of dying from respiratory disease by about a half, and diabetes by nearly 40 percent, although the researchers note that there is less data about these diseases in relation to nut consumption.

The study, led by researchers from Imperial College London and the Norwegian University of Science and Technology, is published in the journal BMC Medicine.

The research team analysed 29 published studies from around the world that involved up to 819,000 participants, including more than 12,000 cases of coronary heart disease, 9,000 cases of stroke, 18,000 cases of cardiovascular disease and cancer, and more than 85,000 deaths.

While there was some variation between the populations that were studied, such as between men and women, people living in different regions, or people with different risk factors, the researchers found that nut consumption was associated with a reduction in disease risk across most of them.

Study co-author Dagfinn Aune from the School of Public Health at Imperial said: "In nutritional studies, so far much of the research has

been on the big killers such as heart diseases, stroke and cancer, but now we're starting to see data for other diseases.

"We found a consistent reduction in risk across many different diseases, which is a strong indication that there is a real underlying relationship between nut consumption and different health outcomes. It's quite a substantial effect for such a small amount of food."

The study included all kinds of tree nuts, such as hazel nuts and walnuts, and also peanuts - which are actually legumes. The results were in general similar whether total nut intake, tree nuts or peanuts were analysed.

What makes nuts so potentially beneficial, said Aune, is their nutritional value: "Nuts and peanuts are high in fibre, magnesium, and polyunsaturated fats - nutrients that are beneficial for cutting cardiovascular disease risk and which can reduce cholesterol levels.

"Some nuts, particularly walnuts and pecan nuts are also high in antioxidants, which can fight oxidative stress and possibly reduce cancer risk. Even though nuts are quite high in fat, they are also high in fibre and protein, and there is some evidence that suggests nuts might actually reduce your risk of obesity over time."

The study also found that if people consumed on average more than 20g of nuts per day, there was little evidence of further improvement in health outcomes.

The team are now analysing large published datasets for the effects of other recommended food groups, including fruits and vegetables, on a wider range of diseases.